Anesthesia
for Cardiac Surgery

THIRD EDITION

James A. DiNardo
and David A. Zvara

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Anesthesia for Cardiac Surgery

Dedication

To my wife Denée for her love, support and wisdom.
To my daughter Isabel and her limitless potential.
To my mother Josephine Ann who taught me the value of honesty and perseverance.

James A. DiNardo

To my wife, Bharathi, and daughters, Alexandra, Jessica, Gracie and Olivia: each of you have inspired me in ways that you will never know. I love you and dedicate this book to you and your life's dreams.

Go confidently in the direction of your dreams. Live the life you have imagined. (Henry David Thoreau)

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Preface

Anesthesia for Cardiac Surgery originally published in 1989, and revised in 1998, was written with the intention of filling the perceived void in cardiac anesthesia reference material between definitive, heavily referenced texts and outline-based handbooks. The updated 3rd Edition strives to do the same. This book is intended to provide practical recommendations based on sound principles of physiology. The text provides a comprehensive overview of the contemporary practice of cardiac anesthesia. There is a place for this work as a component of a core curriculum in cardiac anesthesiology training as well as in the library of the busy, practicing clinician. We hope this work helps you in caring for your patients.

JAD
DAZ

Acknowledgements

CHAPTER 1

Introduction

A complete evaluation of the patient's medical history, physical examination, and review of pertinent laboratory and supportive tests is necessary prior to any elective cardiac surgical procedure. The intention of the preoperative evaluation is severalfold: define the status of the patient's medical condition, identify areas of uncertainty that require further evaluation, consultation or testing, devise a strategy to improve or stabilize ongoing medical conditions prior to surgery, determine a prognostic risk classification, and provide information to formulate an intraoperative and postoperative plan. The anesthesiologist must clearly understand the intended surgical procedure. This chapter will present a systems review of the common and significant features found preoperatively in the cardiac surgical patient. There will be a special emphasis on the methodology, limitations, and accuracy of the tests used most commonly in evaluation of cardiac surgical patients.

Cardiovascular evaluation

A directed history and physical examination are essential before any cardiac surgical procedure. The information obtained, in the context of the anticipated surgical procedure, will determine the requirement for subsequent evaluation, consultation or testing.

History and physical examination

There are no controlled trials evaluating the effectiveness of the history and physical; however, conditions discovered in the process help define the anesthetic plan and are often associated with strong prognostic value. For example, a history of myocardial infarction, unstable angina, congestive heart failure, dyspnea, obstructive sleep apnea, and any number of other conditions may directly affect the course of the preoperative evaluation, operative outcome, and patient satisfaction. There are many algorithms for quantifying patient risk, including the American Society of Anesthesiologists Physical Status Classification. The Revised Cardiac Risk Index is a clinically useful example of a preoperative scoring system to define perioperative cardiac risk (Table 1.1).

In most cardiac surgical procedures, the preanesthetic evaluation should take place prior to the day of surgery. This will allow time for additional testing, collection, and review of pertinent past medical records, and appropriate patient counseling. The examination can be obtained on the day of surgery for procedures with relatively low surgical invasiveness. The history provides insight into the severity of the pathologic condition. For example, a history consistent with heart failure is most alarming and requires careful deliberation before proceeding (Table 1.2). In evaluating a patient with angina, it is essential to determine if the symptoms represent unstable angina (Table 1.3). The Canadian Cardiovascular Society Classification of Angina defines anginal symptoms (Table 1.4).

At a minimum, the physical examination must include the vital signs and an evaluation of

Table 1.1 The Revised Cardiac Risk Index.

Ischemic heart disease: Includes a history of myocardial infarction, Q waves on the ECG, a positive stress test, angina, or nitroglycerine use

Congestive heart failure (CHF): Includes a history of CHF, pulmonary edema, paroxysmal nocturnal dyspnea, rales, S3 gallop, elevated β-naturetic peptide, or imaging study consistent with CHF

Cerebrovascular disease: Includes a history of transient ischemic attack or stroke

Diabetes mellitus treated with insulin:

Renal dysfunction (serum creatinine >2)

High-risk surgery: Includes any intraperitoneal, intrathoracic or suprainguinal vascular procedures

CABG, coronary artery bypass surgery; ECG, electrocardiogram.
0–2 risk factors = low risk.
3 or more risk factors = high risk.

the airway, lungs and heart. Auscultation of the chest may reveal wheezing, rales, or diminished breath sounds. Auscultation of the heart is critical in uncovering new murmurs, S4 gallops, and rhythm abnormalities. In patients older than 40 years, new heart murmurs are found in upwards of 4% of patients. Further screening with echocardiography reveals significant valvular pathology in 75% of these patients. Arterial hypertension is common in the cardiac surgical patient; however, there is little evidence for an association between admission arterial pressures less than 180 mmHg systolic or 110 mmHg diastolic and perioperative complications. In patients with blood pressures above this level, there is increased perioperative ischemia, arrhythmias, and cardiovascular lability.

Once the history and physical examination are complete, attention turns to what additional evaluation, consultation or studies are indicated prior to the operative procedure. The decision regarding which test to order should be based upon an analysis of value of the information obtained, resource utilization and timeliness in regards to the scheduled procedure. Several common tests are reviewed below.

Electrocardiogram

A preoperative electrocardiogram (ECG) should be obtained in all cardiac surgical patients. There is no consensus on the minimum patient age for obtaining an ECG, although ECG abnormalities are more frequent in older patients and those with multiple cardiac risk factors. The ECG should be examined for rate and rhythm, axis, evidence of left and right ventricular (RV) hypertrophy, atrial enlargement, conduction defects (both AV nodal and bundle branch block (BBB)), ischemia or infarction, and metabolic and drug effects.

Rate and rhythm abnormalities

There are a large number of rate and rhythm abnormalities which may be present in the cardiac surgical patient. Tachycardia may be a sign of anxiety, drug effect (i.e. sympathomimetics, β-adrenergic agonists, and cocaine intoxication), metabolic disorder (hypothyroidism), fever, sepsis or other conditions. Bradycardia is typically due to medications (β-adrenergic blocking agents), although a slow heart rate may by indicative of other pathology (hypothyroidism, drug effect, hypothermia, conduction defects). Arrhythmias are potentially more serious and require immediate evaluation. Electrolyte abnormalities are common in cardiac surgical patients and may lead to premature ventricular contractions (PVCs). The actively ischemic patient may present with ventricular irritability, frequent or multifocal PVCs, or ventricular tachycardia (VT). Atrial fibrillation is frequently observed in the elderly cardiac surgical patient. The diagnosis of new atrial fibrillation requires evaluation prior to surgery if time and the clinical condition permit.

Axis

Axis refers to the direction of depolarization in the heart. The mean QRS vector (direction of depolarization) is normally downward and to the patient's left (0–90°). This axis will be displaced with physical relocation of the heart (i.e. extrinsic cardiac compression from a mass effect), hypertrophy (axis moves toward hypertrophy), or infarction (axis moves away from infarction). In the normal condition, the QRS is positive in lead I and aV$_F$.

Table 1.2 American College of Cardiology/American Heart Association Classification of chronic heart failure.

Stage	Description
A. High risk for developing heart failure	Hypertension, diabetes mellitus, coronary artery disease, family history of cardiomyopathy
B. Asymptomatic heart failure	Previous myocardial infarction left ventricular dysfunction, valvular heart disease
C. Symptomatic heart failure	Structural heart disease, dyspnea and fatigue, impaired exercise tolerance
D. Refractory end-stage heart failure	Marked symptoms at rest despite maximal medical therapy

Stage A includes patients at risk of developing heart failure but have no structural heart disease at present. A high degree of awareness is important in this group

Stage B includes patients with known structural heart disease but no symptoms. Therapeutic intervention with angiotensin converting enzyme inhibitors or adrenergic beta-blocking agents may be indicated for long-term chronic treatment in this group

Stage C includes patients with structural heart disease and symptomatic heart failure. Operative risk is increased in this group. Medical therapy may include diuretics, digoxin, and aldosterone antagonists in addition to ACE inhibitors and beta-blockers depending upon the severity of symptoms. Cardiac resynchronization therapy also may be considered in selected patients

Stage D includes patients with severe refractory heart failure. These patients frequently present for heart transplantation or bridging therapy with ventricular assist devices. Acute decompensation is managed with inotropes and vasodilator therapy

ACE, angiotensin-converting enzyme.

Table 1.3 The principal presentations of unstable angina.

Rest angina	Angina occurring at rest and usually prolonged greater than 20 minutes
New onset angina	Angina of at least CCSC III severity with onset within 2 months of initial presentation
Increasing angina	Previously diagnosed angina that is distinctly more frequent, longer in duration or lower in threshold (i.e. increased by at least one CCSC class within 2 months of initial presentation to at least CCSC III severity)

CCSC, Canadian Cardiovascular Society Classification.

Left atrial enlargement

In adults, left atrial enlargement (LAE) may be found in association with mitral stenosis, aortic stenosis, systemic hypertension, and mitral regurgitation. In mitral stenosis, LAE occurs secondary to the increased impedance to atrial emptying across the stenotic mitral valve. In aortic stenosis and systemic hypertension, an elevated left ventricular (LV) end-diastolic pressure results in left atrial hypertrophy. In mitral regurgitation, LAE occurs because of the large volumes of blood regurgitated in the left atrium during systole.

Table 1.4   The Canadian Cardiovascular Society Classification System of angina pectoris.

Class I: Ordinary physical activity, such as walking and climbing stairs does not cause angina. Angina occurs with strenuous, rapid, or prolonged exertion

Class II: Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in the cold or wind, under emotional stress or only during the few hours after awakening. Angina occurs on walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and under normal conditions

Class III: Marked limitations of ordinary physical activity. Angina occurs on walking one or two blocks on the level ground and climbing one flight of stairs in normal conditions and at a normal pace

Class IV: Inability to carry on any physical activity without anginal discomfort. Symptoms may be present at rest

Right atrial enlargement

Right atrial enlargement (AAE) may be seen with RV hypertrophy secondary to pulmonary outflow obstruction or pulmonary hypertension. RAE also may be observed in patients with tricuspid stenosis, tricuspid atresia, or Epstein's abnormality.

Left ventricular hypertrophy

In adults, left ventricular hypertrophy (LVH) commonly occurs in LV pressure overload lesions such as aortic stenosis and severe systemic hypertension. In children, LVH may be present with coarctation of the aorta and congenital aortic stenosis.

Right ventricular hypertrophy

Right ventricular hypertrophy (RVH) is a common finding in patients with congenital heart disease and may be seen in pulmonic stenosis, tetralogy of Fallot and transposition of the great arteries. In adults, RVH frequently results from pulmonary hypertension.

Conduction defects

Similar to rate and rhythm abnormalities, there are a wide variety of conduction defects which may be observed in the cardiac surgical patient. Atrioventricular (AV) block may be innocuous (1st and 2nd degree type 1) or clinically significant requiring immediate evaluation of pacemaker placement (2nd degree type 2 and 3rd degree). BBB delay depolarization in the effected ventricle and may lead to ineffective ventricular contraction.

Ischemia and infarction

New findings of active ischemia require immediate attention. In the patient with known coronary artery disease (CAD) and unstable angina, ST segment abnormalities may be observed. In patients with diabetes, there may be episodes of silent ischemia during which the heart is ischemic, but due to autonomic dysfunction and a diminished ability to perceive nociceptive signals, the patient does not experience pain. The presence of Q waves indicates an old transmural myocardial infarction. Determining the timing of the Q wave finding may be clinically relevant. For example, a Q wave not seen on an ECG 6 months prior to the evaluation suggests a myocardial infarction sometime during this recent interval. Perioperative cardiac morbidities are related to timing of surgery after a myocardial infarction, and therefore this information requires attention and clinical resolution.

Metabolic and drug effects

Elevated serum potassium will flatten the P wave, widen the QRS complex, and elevate the T wave. Low serum potassium will flatten of invert the T wave. A U wave may appear. With elevated serum calcium the QT interval shortens; whereas with hypocalcemia, the QT interval is prolonged. Digitalis toxicity will cause a gradual down sloping of the ST segment. There may also be atrial and junctional premature beats, atrial tachycardia, sinus, and AV nodal blocks.

It must be emphasized that a normal ECG does not preclude the presence of significant cardiac disease in the adult, child, or infant. The ECG is normal in 25–50% of adults with chronic stable angina. Likewise, the ECG may be normal in children with LV pressure overload (aortic stenosis) and volume overload (patent ductus arteriosus or ventricular septal defect) lesions.

Chest radiograph

Obtaining a Chest radiograph (CXR) should be based upon the necessity for the planned clinical procedure (i.e. a lateral chest film is essential in a repeat sternotomy), or in assessing the patient's clinical condition. Clinical characteristics suggesting a benefit to obtaining a CXR include a history of smoking, recent respiratory infection, chronic obstructive pulmonary disease (COPD), or cardiac disease. The posterior–anterior and lateral CXR provide a wealth of information including an assessment of pulmonary condition and maybe cardiovascular status. For example, radiographic evidence of pulmonary vascular congestion suggests poor systolic function. For patients with valvular heart disease, a normal CXR is more useful than an abnormal radiograph in assessing ventricular function. The presence of a cardio-to-thoracic ratio less than 50% is a sensitive indicator of an ejection fraction greater than 50% and of a cardiac index greater than 2.5 L/min/m^2. On the other hand, a cardio-to-thoracic ratio greater than 50% is not a specific indicator of ventricular function. For patients with CAD, an abnormal CXR is more useful than a normal radiograph in assessing ventricular function. Cardiomegaly is a sensitive indicator of a reduced ejection fraction, whereas a normal-sized heart may be associated with both normal and reduced ejection fractions.

As with the ECG, efforts should be made to correlate radiographic findings with the clinical history. LAE is expected in mitral stenosis and regurgitation. Enlargement of the pulmonary artery and right ventricle occurs with disease progression. Eccentric LV hypertrophy results from mitral and aortic regurgitation. Aortic stenosis results in concentric LV hypertrophy. In infants and children with increased pulmonary blood flow (as with a large ventricular septal or atrial septal defect), the pulmonary artery and pulmonary vasculature is prominent. In contrast, patients with reduced pulmonary blood flow (as with tetralogy of Fallot or pulmonary atresia) may manifest a small pulmonary artery and diminished vascularity. Some congenital lesions are associated with classic radiographic cardiac silhouettes: the boot-shaped heart of tetralogy of Fallot, the "figure 8" heart of total anomalous pulmonary venous return, and the "egg-on-its-side"-shaped heart seen in D-transposition of the great arteries.

Stress testing

Patients presenting for cardiac surgery frequently undergo stress testing to establish the diagnosis of CAD, assess the severity of known CAD, establish the viability of regions of myocardium, or evaluate anti-anginal therapy. Stress testing may use exercise or pharmacological agents. Pharmacological agents are useful for patients with physical disabilities that preclude effective exercise. It also is useful for patients who cannot reach an optimal exercise heart rate secondary to their medication regimen (i.e. patients on beta-blockers).

Pharmacological stress testing

Pharmacologic stress testing uses dipyridamole, adenosine, or dobutamine. Pharmacologic stress testing can be performed in conjunction with myocardial perfusion scintigraphy or echocardiography.

Adenosine and dipyridamole are potent coronary vasodilators that increase myocardial blood flow three to fivefold independent of myocardial work. Adenosine is a direct vascular smooth muscle relaxant via A_2-receptors; whereas, dipyridamole increases adenosine levels by inhibiting adenosine deaminase. Dobutamine increases myocardial work through increases in heart rate and contractility via β_1-receptors. The increased work produces proportional increases in myocardial blood flow. In this sense, dobutamine stress testing is similar to exercise stress testing.

The hyperemic response to adenosine and dipyridamole produce increased myocardial blood flow in regions supplied by normal coronary arteries. In regions of myocardium supplied by steal prone

anatomy or diseased coronary arteries, myocardial blood flow increases will be attenuated or decreased below resting levels.

Dipyridamole is infused at 0.56–0.84 mg/kg for 4 minutes, followed by injection of the radiopharmaceutical for myocardial perfusion scintigraphy 3 minutes later. If infusion produces headache, flushing, gastrointestinal (GI) distress, ectopy, angina, or ECG evidence of ischemia, the effect can be terminated with aminophylline 75–150 mg intravenously (IV). Adenosine is infused at 140 µg/kg/min for 6 minutes with injection of the radiopharmaceutical for myocardial perfusion scintigraphy 3 minutes later. Side effects are similar to dipyridamole and are terminated by stopping the infusion (the half-life of adenosine is 40 seconds). Dobutamine is infused at 5 µg/kg/min for 3 minutes and then is increased to 10 µg/kg/min for 3 minutes. The dose is increased by 5 µg/kg/min every 3 minutes until a maximum of 40 µg/kg/min is reached or until significant increases in heart rate and blood pressure occur. Injection of the radiopharmaceutical for myocardial perfusion scintigraphy takes place 1 minute after the desired dose is reached, and the infusion is continued for 1–2 minutes after injection. Side effects of dobutamine (headache, flushing, GI distress, ectopy, angina, or ECG evidence of ischemia) can be terminated by discontinuing the infusion (the half-life of dobutamine is 2 minutes).

Exercise stress testing

Exercise stress testing increases in myocardial oxygen consumption to detect limitations in coronary blood flow. Exercise increases cardiac output through increases in heart rate and inotropy. Despite vasodilatation in skeletal muscle, exercise typically increases arterial blood pressure as well. As a result, exercise is accompanied by increases in the three major determinants of myocardial oxygen consumption: heart rate, wall tension, and contractility. To meet the demands of exercise, the coronary vascular bed dilates. The ability of the coronary circulation to increase blood flow to match exercise-induced increases in demand is compromised in the distribution of stenosed coronary arteries because vasodilatory reserve is exhausted in these beds.

All exercise tests increase metabolic rate and oxygen consumption (V_{O_2}). Isometric exercise may be used to increase the workload, but more commonly, dynamic exercise using either a treadmill or a bicycle is used. V_{O_2max} is the maximal amount of oxygen a person can use while performing dynamic exercise. V_{O_2max} is influenced by age, gender, exercise habits, and cardiovascular status. Exercise protocols are compared by using metabolic equivalents (METs). One MET is equal to a V_{O_2} of 3.5 mL oxygen(O_2)/kg/min and represents resting oxygen uptake. Different exercise protocols are compared by comparing the number of METs consumed at various stages.

The Bruce treadmill protocol is the most commonly used protocol for exercise stress testing. This protocol uses seven 3-minute stages. Each progressive stage involves an increase in both the grade and the speed of the treadmill. During stage 1 the treadmill speed is 1.7 miles/h on a 10% grade (5 METs); during stage 5 the treadmill speed is 5 miles/h on an 18% grade (16 METs). The patient progressively moves through the stages until either exhausted, a target heart rate achieved without ischemia, or the detection of ischemic changes on the ECG. Exercise stress testing can be performed in conjunction with traditional ECG analysis, myocardial perfusion scintigraphy, or echocardiography. The details of stress myocardial perfusion scintigraphy, stress radionucleotide angiography, and stress echocardiography are discussed below.

The following factors must be considered in interpretation of an ECG exercise stress test:
- *Angina*. Ischemia may present as the patient's typical angina pattern; however, angina is not a universal manifestation of ischemia in all patients. Ischemic pain induced by exercise is strongly predictive of CAD.
- *V_{O_2max}*. If patients with CAD reach 13 METs, their prognosis is good regardless of other factors; patients with an exercise capacity of less than 5 METs have a poor prognosis.
- *Dysrhythmias*. For patients with CAD, ventricular dysrhythmias may be precipitated or aggravated by exercise testing. The appearance of reproducible sustained (>30 seconds) or symptomatic ventricular

tachycardia (VT) is predictive of multivessel disease and poor prognosis.

- *ST segment changes*. ST segment depression is the most common manifestation of exercise-induced myocardial ischemia. The standard criterion for an abnormal response is horizontal or down sloping (>1 mm) depression 80 ms after the J point. Down sloping segments carry a worse prognosis than horizontal segments. The degree of ST segment depression (>2 mm), the time of appearance (starting with <6 METs), the duration of depression (persisting >5 minutes into recovery), and the number of ECG leads involved (>5 leads) are all predictive of multivessel CAD and adverse prognosis.

- *Blood pressure changes*. Failure to increase systolic arterial blood pressure to greater than 120 mmHg, or a sustained decrease in systolic blood pressure with progressive exercise, is indicative of cardiac failure in the face of increasing demand. This finding suggests severe multivessel or left main CAD.

Comparison of stress test methods

The sensitivity of detection of CAD with exercise myocardial perfusion scintigraphy or exercise echocardiography is superior to that of exercise ECG testing. The superiority of these two modalities over ECG testing in detecting CAD is greatest for patients with single vessel CAD. When comparing myocardial perfusion scintigraphy to stress echocardiography, the data suggest a trend toward greater sensitivity with myocardial perfusion scintigraphy, particularly for patients with single-vessel disease. Moderate to large perfusion defects by either stress echocardiography or thallium imaging predicts postoperative myocardial infarction or death in patients scheduled for elective noncardiac surgery. Negative tests assure the clinician of a small likelihood of subsequent adverse outcome (negative predictive value = 99%). Unfortunately, however, the positive predictive value (i.e. the chance that a patient with a positive test will have an adverse cardiovascular event) is poor ranging from 4% to 20%. In a meta-analysis comparing the two techniques, stress echocardiography is slightly superior to thallium imaging in predicting postoperative cardiac events. The choice of which technique should be made based upon institutional

expertise and patient-specific attribute. In either case, angiography should be considered in patients with moderately large defects.

Limitations of exercise ECG testing are the inability to accurately localize and assess the extent of ischemia. Furthermore, no direct information regarding left ventricle function is available. Stress myocardial perfusion scintigraphy, radionuclide angiography, and echocardiography provide this information. On the other hand, these methods are more expensive and technically more demanding than exercise ECG testing.

Myocardial perfusion scintigraphy

Myocardial perfusion scintigraphy assesses myocardial blood flow, myocardial viability, the number and extent of myocardial perfusion defects, transient stress-induced LV dilatation, and allows for risk stratification. Myocardial perfusion scintigraphy is performed most commonly in conjunction with stress testing. Stress testing can be accomplished with exercise or pharmacologically with dipyridamole, adenosine, or dobutamine. With this technology, it is possible to determine which regions of myocardium are perfused normally, which are ischemic, which are stunned or hibernating, and which are infarcted. The technique is based on the use of radiopharmaceuticals that accumulate in the myocardium proportional to regional blood flow. Single-positron emission computed tomography (SPECT) or planar imaging is used to image regional myocardial perfusion in multiple views and at various measurement intervals. Patients with small fixed perfusion defects have reduced perioperative risk profiles, whereas patients with multiple larger defects are at higher risk.

The radiopharmaceuticals currently in use are thallium-201 and technetium-99m methoxyisobutyl isonitrile (Sestamibi). Thallium has biologic properties similar to potassium and thus is transported across the myocardial cell membrane by the sodium–potassium adenosine triphosphatase (ATPase) pump proportional to regional myocardial blood flow. Sestamibi is not dependent on ATP to enter myocardial cells because it is highly lipophilic but its distribution in myocardial tissue is proportional to blood flow.

Thallium

Thallium-201 is injected at the peak level of a multistage exercise or pharmacological stress test. Scintillation imaging begins 6–8 minutes after injection (early views) and is repeated again 2–4 hours after injection (delayed or redistribution views). Identical views must be used so the early and delayed images can be compared. During stress, myocardial blood flow and thallium-201 uptake will increase in areas of the myocardium supplied by normal coronary arteries. Subsequently, thallium redistributes to other tissues, thus clearing from the myocardium slowly. Areas of myocardium supplied by diseased arteries are prone to ischemia during stress and have a reduced ability to increase myocardial blood flow and thallium-201 uptake. These areas will demonstrate a perfusion defect when compared with normal regions in the early views. In the delayed views, late accumulation or flat washout of thallium-201 from the ischemic areas compared with the nonischemic areas results in equalization of thallium-201 activity in the two areas. These *reversible perfusion* defects are typical of areas of myocardium that suffer transient, stress-induced ischemia. *Nonreversible perfusion defects* are present in both the early stress and delayed redistribution images. These defects are believed to represent areas of nonviable myocardium resulting from old infarctions. *Reverse redistribution* is the phenomenon in which early images are normal or show a defect and the delayed images show a defect or a more severe defect. This is seen frequently in patients who have recently undergone thrombolytic therapy or angioplasty and may result from higher-than-normal blood flow to the residual viable myocardium in the partially infarcted zone.

Modified thallium scintigraphy protocols are useful in detecting areas hibernating myocardium. Hibernating myocardium exhibits persistent ischemic dysfunction secondary to a chronic reduction in coronary blood flow, but the tissue remains viable. Hibernating myocardium has been shown to exhibit functional improvement after surgical revascularization or angioplasty and restoration of coronary blood flow. Stunned myocardium, in contrast, has undergone a period of transient hypoperfusion with subsequent reperfusion. As a result, these regions exhibit transient postischemic dysfunction in the setting of normal coronary blood flow. Stunned myocardium is detected by identifying regions of dysfunctional myocardium in which no perfusion defect exists.

Some regions of myocardium that do not exhibit redistribution at 2.5–4.0 hours exhibit redistribution in late images at 18–24 hours. This late redistribution represents areas of hibernating myocardium. Another approach to detecting hibernating myocardium is reinjection of thallium at rest after acquisition of the 2.5–4.0-hour stress images. Persistent defects that show enhanced uptake after reinjection represent areas of viable myocardium. Finally, serial rest thallium imaging has proved useful in detecting hibernating myocardium. Images are obtained at rest after injection of thallium and then are repeated 3 hours later. Regions of myocardium that exhibit rest redistribution represent areas of viable myocardium.

Increased lung uptake of thallium is related to exercise-induced LV dysfunction and suggests multivessel CAD. Because increased lung uptake of thallium is due to an elevated left atrial pressure (LAP), other factors besides extensive CAD and exercise-induced LV dysfunction (such as mitral stenosis, mitral regurgitation, and nonischemic cardiomyopathy) must be considered when few or no myocardial perfusion defects are detected. Transient LV dilation after exercise or pharmacologic stress also suggests severe myocardial ischemia.

Sestamibi

Sestamibi, unlike thallium, does not redistribute. As a result, the distribution of myocardial blood flow at the time of injection remains fixed over the course of several hours. This necessitates two separate injections: one at rest and one at peak stress. The two studies must be performed so that the myocardial activity from the first study decays enough not to interfere with the activity from the second study. A small dose is administered at rest with imaging approximately 45–60 minutes later. Several hours later, a larger dose is administered at peak stress, with imaging 15–30 minutes later. Reversible and fixed defects are detected by comparing the rest and stress images. As with thallium,

late imaging after Sestamibi stress imaging may be helpful in detecting hibernating myocardium.

Sestamibi allows high-count-density images to be recorded, providing better resolution than thallium. In addition, use of Sestamibi allows performance of first pass radionuclide angiography (see below) to be performed in conjunction with myocardial perfusion scintigraphy. Use of simultaneous radionuclide angiography and perfusion scintigraphy has proved useful in enhanced detection of viable myocardium. Viable myocardium will exhibit preserved regional perfusion in conjunction with preserved regional wall motion.

Radionuclide angiography

Radionuclide angiography allows assessment of RV and LV performance. Two types of cardiac radionuclide imaging exist: first-pass radionuclide angiography (FPRNA) and equilibrium radionuclide angiography (ERNA), also known as radionuclide ventriculography or gated blood pool imaging. ERNA is also known as multiple-gated acquisition (MUGA) or multiple-gated equilibrium scintigraphy (MGES).

FPRNA involves injection of a radionuclide bolus (normally technetium-99m) into the central circulation via the external jugular or antecubital vein. Subsequent imaging with a scintillation camera in a fixed position provides a temporal pictorial presentation of the cardiac chambers as the radiolabeled bolus makes its way through the heart. First-pass studies may be gated or ungated. Gated studies involve synchronization of the presented images with the patient's ECG such that systole and diastole are identified. Ungated studies simply present a series of images over time.

ERNA involves use of technetium-99m-labeled red cells, which are allowed to distribute uniformly in the blood volume. Radiolabeling of red cells is accomplished by initially injecting the patient with stannous pyrophosphate, which creates a stannous-hemoglobin complex over the course of 30 minutes. Subsequent injection of a technetium-99m bolus results in binding of technetium-99m to the stannous-hemoglobin complex, thus labeling the red cells.

After equilibrium of the labeled red cells in the cardiac blood pool, gated imaging with a scintillation camera is performed. A computer divides the cardiac cycle into a predetermined number of frames (16–64). Each frame represents a specific time interval relative to the ECG R wave. Data collected from each time interval over the course of several hundred cardiac cycles are then added together with the other images from the same time interval. The result is a sequence of 16–64 images, each representing a specific phase of the cardiac cycle. The images can be displayed in an endless loop format or individually. The procedure can then be repeated with the camera in a different position.

Below is a summary of the relative advantages and disadvantages of first-pass and equilibration studies. Both types of studies currently are used for adults, infants, and children.

- With both FPRNA and ERNA studies, the number of radioactive counts during end systole and end diastole can be used to determine stroke volume, ejection fraction, and cardiac output.
- Both types of studies allow reliable quantification of LV volume using count-proportional methods that do not require assumptions to be made about LV geometry.
- Although both studies allow determination of RV and LV ejection fractions, determination of RV ejection fraction is more accurate with a first-pass study because the right atrium overlaps the right ventricle in equilibrium studies.
- First-pass studies allow detection and quantification of both right-to-left and left-to-right intracardiac shunts, whereas shunt detection is not possible with equilibration studies.
- First-pass studies allow sequential analysis of right atrial (RA), RV, left atrial (LA), and LV size, whereas equilibration studies do not. Abnormalities in the progression of the radioactive tracer through the heart and great vessels assist in the diagnosis of congenital abnormalities.
- Equilibration studies provide better analysis of regional wall motion abnormalities than first-pass studies due to higher resolution.
- Both types of studies can be used with exercise. First-pass studies can be performed rapidly

but do not allow assessment of ventricular wall motion at different exercise levels, nor do they allow assessment of wall motion from different angles.

- Mitral or aortic regurgitation is detectable with both first-pass and equilibration studies by analysis of the stroke volume ratio. This method tends to overestimate regurgitant fraction and is not reliable for detection of minor degrees of regurgitation.

Echocardiography

Transthoracic and transesophageal echocardiography has revolutionized the noninvasive structural and functional assessment of acquired and congenital heart disease. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) often play a major role in the evaluation of cardiac surgical patients. Routine use of two-dimensional imaging, color flow Doppler, continuous wave Doppler, pulsed wave Doppler, and M-mode imaging allows the following:

- *Assessment of cardiac anatomy.* Delineation of the most complex congenital heart lesions is feasible. In many instances, information acquired from a comprehensive echocardiographic examination is all that is necessary to undertake a surgical repair.
- *Assessment of ventricular function.* A comprehensive assessment of RV and LV diastolic and systolic function is feasible.
- *Assessment of valvular abnormalities.* Assessment of the functional status of all four cardiac valves is possible. In addition, quantification of valvular stenosis and insufficiency is accurate and reliable. Assessment of prosthetic valves also is feasible.
- *Characterization of cardiomyopathies.* Hypertrophic, dilated, and restrictive cardiomyopathies can be identified.
- *Assessment of the pericardium.* Pericardial effusions, cardiac tamponade, and constrictive pericarditis are reliably identified.
- *Assessment of cardiac and extracardiac masses.* Vegetations, foreign bodies, thrombi, and metastatic and primary cardiac tumors can be identified.
- *Contrast echocardiography.* Contrast solutions containing microbubbles enhance the image allowing assessment of myocardial perfusion, intracardiac shunts, enhancement of Doppler signals, and improved assessment of regional and global LV function.
- *Stress echocardiography.* Stress echocardiography is based on the concept that exercise or pharmacologically induced wall motion abnormalities develop early in the course of ischemia. Stress-induced wall motion abnormalities occur soon after perfusion defects are detected by radionuclide imaging because, in the ischemic cascade, hypoperfusion precedes wall motion abnormalities. Comparison of resting and stress images allows resting abnormalities to be distinguished from stress-induced abnormalities. Resting abnormalities indicate prior infarction, hibernating or stunned myocardium; whereas, stress-induced abnormalities are specific for ischemia. Furthermore, dobutamine stress echocardiography may be useful in determining myocardial viability. Regions that are hypokinetic, akinetic, or dyskinetic at rest and improve with dobutamine administration probably contain areas of stunned or hibernating myocardium. Such areas demonstrate functional improvement after myocardial revascularization.

Computerized tomography and magnetic resonance imaging

Advances in imaging techniques have played a major role in defining anatomy in cardiac surgical patients. Computerized tomography (CT) and magnetic resonance imaging (MRI) now allow the clinician detailed anatomy, three-dimensional rendering, and functional assessment of myocardial performance and blood flow (Fig. 1.1). It is likely that new advances in imaging techniques will continue to improve the quality and the anatomic detail afforded by these techniques. Molecular imaging, i.e. imaging of cellular function, is a developing area in cardiac imaging. The applications of these new technologies remain to be seen.

Cardiac catheterization

Cardiac catheterization remains the gold standard for evaluation of acquired and congenital heart disease. Cardiac catheterization is covered in detail in Chapter 2.
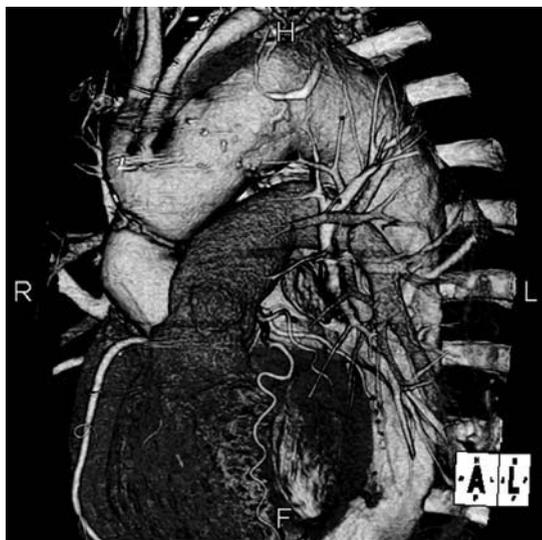
Fig. 1.1 Three dimension reconstruction of the heart and aorta

Respiratory evaluation

A preoperative assessment of pulmonary function (other than CXR) is required in all cardiac surgical patients. The evaluation must include a history of known pulmonary disease, current respiratory symptoms, and a physical examination. Evaluation may include consultation with specialists and specific pulmonary testing (pulmonary function testing, spirometry, pulse oximetry, arterial blood gas analysis). The history should determine the extent and length of tobacco use, the presence of COPD, asthma, recurrent or acute pulmonary infections, and the presence of dyspnea. Physical examination should focus on the detection of wheezes, flattened diaphragms, air trapping, consolidations, and clubbing of the nails. A CXR is indicated in nearly all cardiac surgical patients. Pulmonary function tests (PFTs) play a limited role in preoperative assessment. If there is confusion about whether intrinsic pulmonary disease exists, its cause, and its appropriate treatment, then pulmonary function testing may help guide the clinician. Spirometry measures lung volumes, capacities, and flow. Spirometry of expiratory flow rates allows measurement of the forced expiratory volume in 1 second

(FEV_1), the forced vital capacity (*FVC*), and the forced mid-expiratory flow (*FEF* 25–75%). Arterial blood gases should be obtained for patients in whom carbon dioxide (CO_2) retention is suspected and for those with severe pulmonary dysfunction as determined by history, physical examination, PFTs, or cardiac catheterization.

Pulmonary assessment and congenital heart disease

Lesions that produce excessive pulmonary blood flow (large ventricular septal defect, truncus arteriosus, dextrotransposition of the great arteries, and patent ductus arteriosus) are associated with pulmonary dysfunction. Occasionally, large airway compression occurs in response to enlargement of the pulmonary arteries. More commonly, however, these lesions produce pulmonary vascular changes that affect pulmonary function. The pulmonary vascular smooth muscle hypertrophy that accompanies increased pulmonary blood flow produces peripheral airway obstruction and reduced expiratory flow rates characteristic of obstructive lung disease. In addition, smooth muscle hypertrophy in respiratory bronchioles and alveolar ducts in patients with increased pulmonary blood flow contributes to this obstructive pathology. These changes predispose the patient to atelectasis and pneumonia. Children with Down syndrome have a more extensive degree of pulmonary vascular and parenchymal lung disease than other children with similar heart lesions. This predisposes patients with Down syndrome to greater postoperative respiratory morbidity and mortality.

Patients with lesions that reduce pulmonary blood flow (pulmonary atresia or stenosis, tetralogy of Fallot) also have characteristic pulmonary function changes. These patients have normal lung compliance as compared with the decreased compliance seen in patients with increased pulmonary blood flow. However, the large dead space to tidal volume ratio in these patients greatly reduces ventilation efficiency, and large tidal volumes are required to maintain normal alveolar ventilation. Finally, 3–6% of patients with tetralogy of Fallot will have an absent pulmonary valve and aneurysmal dilatation of the pulmonary arteries. This aneurysmal

dilatation produces bronchial compression and respiratory distress at birth.

Pulmonary assessment and acquired heart disease

Pulmonary dysfunction ranks among the highest predictors of postoperative pulmonary complications. Pulmonary dysfunction is defined as a productive cough, wheeze, or dyspnea. Pulmonary function testing consistent with pulmonary dysfunction shows a $FEV_1 < 70\%$ of predicted or $FEV_1/FVC < 65\%$ of predicted, plus either vital capacity $(VC) < 3.0\,L$ or maximum voluntary ventilation $(MVV) < 80\,L/min$. For patients undergoing valvular surgery, the presence of pulmonary dysfunction is associated with up to a 2.5-fold increase in perioperative mortality and a 2.5-fold increase in postoperative respiratory complications. For patients undergoing only coronary revascularization, pulmonary dysfunction is less predictive of postoperative morbidity and mortality.

Pulmonary assessment and tobacco use

Chronic tobacco use has several physiologic effects that may complicate anesthetic management. Smoking accelerates the development of atherosclerosis. Further, smoking reduces coronary blood flow by increasing blood viscosity, platelet aggregation, and coronary vascular resistance. Nicotine, through activation of the sympathetic nervous system and elevated catecholamine levels, increases myocardial oxygen consumption by increasing heart rate, blood pressure and myocardial contractility. Furthermore, the increased carboxyhemoglobin level, which may exceed 10% in smokers, reduces systemic and myocardial oxygen delivery. This is particularly detrimental to the patient with CAD due to the high extraction of oxygen that normally occurs in the myocardium. The threshold for exercise-induced angina is reduced by carboxyhemoglobin levels as low as 4.5%. Short-term abstinence (12–48 hours) is sufficient to reduce carboxyhemoglobin and nicotine levels and improve the work capacity of the myocardium.

There is an increased incidence of postoperative respiratory morbidity in patients who smoke. These complications include respiratory failure, unanticipated intensive unit admission, pneumonia, airway events during induction of anesthesia (cough, laryngospasm), and increased need for postoperative respiratory therapy. Smoking increases mucus secretion, impairs tracheobronchial clearance, and causes small airway narrowing. For patients undergoing coronary revascularization, abstinence from smoking for 2 months may reduce the incidence of postoperative respiratory complications. Abstinence for less than 2 months is ineffective in reducing the incidence of postoperative respiratory complications. Similar studies of patients undergoing other surgical procedures have confirmed the necessity of a 4–6-week abstinence period. Typically, tobacco-using patients presenting for cardiac surgery will not have had the recommended abstinence period required to reduce complications. Acute cessation of smoking during the perioperative period is not associated with elevated risk. There is no added cardiovascular risk for patients using nicotine replacement therapy (NRT).

Pulmonary assessment and asthma

Asthma is characterized by paroxysmal or persistent symptoms of wheezing, chest tightness, dyspnea, sputum production, and cough with airflow limitation. There is hyper-responsiveness to endogenous or exogenous stimuli. Preoperative evaluation of asthma confirms the diagnosis and evaluates the adequacy of treatment. Adequate control is demonstrated when the patient reports normal physical activity, mild and infrequent exacerbations, no missed school or work days, and less than four doses of β_2-agonist therapy per week. Long-term treatment is largely preventive in nature. First-line pharmacologic treatment often incorporates inhaled corticosteroids (ICSs). Beclomethasone significantly improves FEV_1, peak expiratory flow, and reduces β-agonist use and exacerbations. Leukotriene receptor antagonists (LTRAs) are sometimes used as first-line therapy; however, their role is less clearly established when compared to the ICS agents. Long-acting β_2-agonists are safe and effective medications for improving asthma control in older children and adults when ICSs therapy does not adequately control the disease. Theophylline is

less effective than ICSs and LTRAs in improving asthma control.

For patients in whom bronchospasm is well controlled preoperatively, it is essential to continue therapy during the perioperative period. Beta-2-agonist metered-dose inhaler or nebulizer therapy can be continued until arrival in the operating room and can be restarted soon after emergence from anesthesia. Metered-dose inhalation therapy can be delivered via the endotracheal tube. For patients not on bronchodilator therapy who present for surgery with bronchospasm, a trial of bronchodilators with measurement of PFTs before and after therapy is often helpful. An increase in the FEV_1 of 15% or more after inhalation of a nebulized bronchodilator suggests a reversible component of bronchospasm. Surgery should be delayed until the asthma is controlled. If this is not possible, acute therapy with steroids and β_2-agonists is indicated. Therapy for the cardiac surgical patient should be initiated with a β_2-selective metered-dose inhaler or nebulized solution.

Renal function

Patients presenting for cardiac surgery may possess varying degrees of renal dysfunction ranging from mild elevations in creatinine to dialysis dependence. Assessing renal function preoperatively is vitally important in the cardiac surgical patient. Renal dysfunction after cardiac surgery is associated with increased mortality, morbidity, resource utilization and intensive care unit stay. Depending on the definition of acute renal failure (ARF), anywhere from 5% to 30% of patients demonstrate renal dysfunction after cardiac procedures. Renal dysfunction requiring dialysis is associated with a 50–80% increased risk of death. ARF is among the strongest predictors for death with an odds ratio of 7.9 (95% confidence interval 6–10) in cardiac surgical patients. Identification of high-risk candidates remains important for appropriate patient consent, risk-benefit analysis, and hospital resource utilization planning (Table 1.5).

The dialysis-dependent patient will require dialysis preoperatively. If dialysis is unobtainable preoperatively, it can be managed intraoperatively.

Table 1.5 Risk factors for acute renal failure after cardiac surgery.

Female gender
Congestive heart failure
LV ejection fraction <35%
Preoperative use of an intraaortic balloon pump
Chronic obstructive pulmonary disease
Previous cardiac surgery
Emergency surgery
Valve or valve + CABG surgery
Elevated preoperative creatinine

CABG, coronary artery bypass graft.

Dialysis will correct or improve the abnormalities in potassium, phosphate, sodium, chloride, and magnesium. In addition, the platelet dysfunction that accompanies uremia will be improved. L-deamino-8-D-arginine vasopressin (DDAVP) administration may improve uremia-induced platelet dysfunction and should be considered if clinically significant post-dialysis platelet dysfunction exists. Dialysis will not favorably affect the anemia, renovascular hypertension, or immune-system compromise associated with chronic renal failure.

For nondialysis-dependent patients, preoperative hydration is necessary to prevent prerenal azotemia from complicating the underlying renal dysfunction. This is particularly important after procedures such as cardiac catheterization with arteriography. Creatinine clearance falls after contrast arteriography; in patients with preexisting azotemia, this reduction is much more likely to result in ARF. Hydration ameliorates contrast-induced renal dysfunction. Treatment with acetylcysteine and sodium bicarbonate reduce post-contrast ARF.

Patients with renal transplants occasionally present for cardiac surgical procedures. The extrarenal component of renal blood flow autoregulation is absent in the denervated kidney. Therefore, preoperative hydration and maintenance of systemic perfusion pressure are particularly important to maintain renal perfusion. Sterile technique is mandatory in these immunocompromised patients.

Renal dysfunction often results in electrolyte imbalance. Potassium regulation is often difficult in the cardiac surgical patient. Hyperkalemia

(>5.5 mEq/L) is uncommon in patients with normal renal function; however, it may occur with injudicious potassium administration. The major causes of hyperkalemia result from diminished renal excretion of potassium secondary to reduced glomerular filtration rate (acute oliguric renal failure, chronic renal failure). Reduced tubular secretion may lead to hyperkalemia as seen in Addison's disease, potassium-sparing diuretics and angiotensin converting enzyme inhibitors. Other causes include transcellular shifts of potassium as seen in acidosis, trauma, burns, beta-blockade, rhabdomyolysis, hemolysis, diabetic hyperglycemia, and depolarizing muscle paralysis with succinylcholine. The clinical manifestations relate to alterations in cardiac excitability. Peaked T waves will appear with a potassium level of 6.5 mEq/L. At levels of 7–8 mEq/L the PR interval will prolong and the QRS complex will widen. At 8–10 mEq/L sine waves appear and cardiac standstill is imminent. Treatment is multimodal and includes glucose, insulin, bicarbonate and β-agonists (shifting potassium to the intracellular compartment), diuretics, exchange resins and dialysis (enhancing potassium elimination), and calcium (no change in serum potassium concentration, but calcium counteracts the cardiac conduction effects of hyperkalemia).

Hypokalemia (<3.5 mEq/L) is not uncommon in the cardiac surgical patient. The most common etiology is chronic diuretic therapy, but other causes such as GI loss (nasogastric suction, diarrhea, vomiting), mineralocorticoid excess, acute leukemia, alkalosis, barium ingestion, insulin therapy, vitamin B_{12} therapy, thyrotoxicosis and inadequate intake must be considered. The clinical manifestations of hypokalemia are observed in skeletal muscle, heart, kidneys, and the GI tract. Neuromuscular weakness is observed with levels of 2.0–2.5 mEq/L. Hypokalemia leads to a sagging of the ST segment, depression of the T wave, and the appearance of a U wave on the ECG. In patients treated with digitalis, hypokalemia may precipitate serious arrhythmias. Treatment of hypokalemia involves either oral or parenteral replacement. A deficit in serum potassium reflects a substantial total body deficit. A decrease in plasma potassium concentration of 1 mEq/L with a normal acid-base balance represents

approximately 300 mEq of total body potassium deficiency. In preparing the cardiac surgical patient for surgery, it is reasonable to maintain serum potassium higher than 3.5 mEq/L for patients on digitalis, those at high risk for myocardial ischemia and those who have suffered acute reductions in serum potassium. Potassium replacement is not without risk (iatrogenic hyperkalemia). In general, potassium replacement should not exceed 10–20 mEq/h or 200 mEq/day. Serum potassium must be closely monitored during the replacement therapy.

Endocrine evaluation

A careful evaluation for endocrine abnormalities should be sought in the history and physical examination. Diabetes mellitus (DM) and hypothyroidism deserve special consideration.

Diabetes mellitus

Diabetes mellitus is a risk factor for development of CAD; therefore, perioperative management of DM is a common problem facing those who anesthetize patients for cardiac surgery. Patients with insulin-dependent diabetes have reduced or absent insulin production due to destruction of pancreatic beta cells. Patients with noninsulin-dependent diabetes have normal or excessive production of insulin but suffer from insulin resistance. This resistance may be due to a reduction in insulin receptors, a defect in the second messenger once insulin binds to receptors, or both. Patients with noninsulin-dependent diabetes may be managed with diet, oral hypoglycemic agents (agents that increase pancreatic insulin production), or exogenous insulin. Patients with insulin-dependent diabetes must receive exogenous insulin.

Cardiopulmonary bypass (CPB) is associated with changes in glucose and insulin homeostasis in both diabetic and nondiabetic patients. During normothermic CPB, elevations in glucagon, cortisol, growth hormone, and catecholamine levels produce hyperglycemia through increased hepatic glucose production, reduced peripheral use of glucose, and reduced

insulin production. During hypothermic CPB, hepatic glucose production is reduced and insulin production remains low such that blood glucose levels remain relatively constant. Rewarming on CPB is associated with increases in glucagon, cortisol, growth hormone, and catecholamine levels and is accompanied by enhanced hepatic production of glucose, enhanced insulin production, and insulin resistance. The transfusion of blood preserved with acid-citrate-dextrose, the use of glucose solutions in the CPB prime, and the use of β-adrenergic agents for inotropic support, further increase exogenous insulin requirements. For nondiabetic patients, these hormonally mediated changes usually result in mild hyperglycemia. For diabetic patients, these changes may produce significant hyperglycemia and ketoacidosis.

Management of perioperative glucose is directly related to perioperative outcome. Uncontrolled, or poorly controlled, perioperative glucose is associated with increased mortality, wound infection, and intensive care unit length of stay. This relationship is true in cardiac and noncardiac surgical patients admitted to an intensive care unit setting. The ideal level of glucose is unknown; however, if a target of 130 mg/dL can be achieved, this is associated with improved clinical outcome. Administration of exogenous insulin should be administered early in the perioperative period to achieve this goal. The clinician must remember that achieving this goal may be impossible in some patients. Insulin resistance and the physiologic conditions encouraging hyperglycemia may be too great in some patients. Similarly, the clinician must exercise caution when administering insulin. Serum glucose levels should be checked as frequently as every 15–30 minutes perioperatively while insulin therapy is utilized. Unrecognized hypoglycemia can adversely affect patient outcome.

Because of the varying insulin requirements during cardiac surgery and the unreliable absorption of subcutaneously administered insulin in patients undergoing large changes in body temperature and peripheral perfusion, insulin is best delivered IV for patients undergoing cardiac surgery. The goal of therapy should be maintenance of normoglycemia during the pre-CPB, CPB, and post-CPB

Table 1.6 Recommendations for insulin administration.

Blood glucose (mg/dL)	Insulin infusion rate (U/kg/h)	Rate in 100 kg patient (U/h)*
150–200	0.02	2
200–250	0.03	3
250–300	0.04	4
300–350	0.05	5
350–400	0.06	6

* The actual rate of administration will vary from patient to patient and should be titrated against measured serum glucose levels and patient response.

periods. On the morning of surgery, the usual insulin dose is withheld. On arrival in the operating room, the patient's blood glucose is measured. For tight control, a continuous regular insulin infusion can be started and adjusted to maintain blood glucose between 100 and 150 mg/dL during the operative procedure. Determinations of blood glucose are made every 15–30 minutes. Table 1.6 provides guidelines for insulin administration. It must be emphasized that the alterations in glucose homeostasis and the insulin resistance that accompany hypothermic CPB may necessitate alteration in infusion rates, and therefore insulin must be titrated against demonstrated patient response by measuring serial serum glucose levels.

Patients taking oral hypoglycemic agents should discontinue them at least 12 hours before surgery. For patients managed with these agents and patients managed with diet, blood glucose determinations should be made every 30–60 minutes during the operative procedure. These patients frequently require insulin infusions to maintain glucose homeostasis during surgery.

Hypothyroidism

Hypothyroidism is characterized by a reduction in the basal metabolic rate. In patients with hypothyroidism cardiac output may be reduced by up to 40% due to reductions in both heart rate and stroke volume. In addition, both hypoxic and hypercapnic ventilatory drives are blunted by hypothyroidism.

Furthermore, hypothyroidism may be associated with blunting of baroreceptor reflexes, reduced drug metabolism, renal excretion, reduced bowel motility, hypothermia, hyponatremia from syndrome of inappropriate antidiuretic hormone (SIADH), and adrenal insufficiency. The hypothyroid patient may not tolerate usual doses of antianginal drugs such as nitrates and β-adrenergic blocking agents. Hypothyroid patients on beta-blockers typically require very low anesthetic drug requirements.

Despite these problems, thyroid replacement for cardiac surgical patients, particularly those with ischemic heart disease, is not always desirable. For hypothyroid patients requiring coronary revascularization, thyroid hormone replacement may precipitate myocardial ischemia, myocardial infarction, or adrenal insufficiency. Coronary revascularization may be managed successfully in hypothyroid patients with thyroid replacement withheld until the postoperative period. Mild to moderate hypothyroid patients undergoing cardiac surgery have perioperative morbidity and mortality similar to euthyroid patients. Hypothyroid patients may experience delayed emergence from anesthesia, persistent hypotension, tissue friability, bleeding and adrenal insufficiency requiring exogenous steroids. Hypothyroidism is preferentially treated with levothyroxine (T4). In healthy adults without CAD, a starting dose of 75–100 μg/day is appropriate. In elderly patients, and those with CAD, the initial dose is 12.5–25.0 μg/day and is increased by 25–50 μg every 4–6 weeks allowing for a slow increase in metabolic rate thereby avoiding a mismatch in coronary blood supply and metabolic demand.

Hematologic evaluation

By the nature of the surgery, and the associated cardiovascular medications (heparin, clopidogrel), cardiac surgical patients are at higher perioperative risk of bleeding. A hemoglobin and hematocrit is indicated based on the invasiveness of the procedure (i.e. relative risk of blood loss and transfusion), the history of liver disease, anemia, bleeding, other hematologic disorders or an extreme

in age. Serum chemistry (i.e. potassium, sodium, glucose, renal and liver function studies) are indicated in patients anticipating invasive surgery with possible metabolic alterations, diabetic patients and other patients at specific risk of renal or liver dysfunction. Plasma N-terminal pro-brain naturetic peptide (NTproBNP) is secreted by the left ventricle in response to wall stress. It is elevated in patients with LV dysfunction and heart failure. Preoperative NTproBNP levels greater than 450 ng/L are predictive of cardiac complications with a sensitivity of 100% and a specificity of 89%. Hence, an NTproBNP level may assist in preoperative risk assessment and resource management in selected patients. A urinalysis is usually not indicated unless there are specific urinary findings. A pregnancy test should be considered in all female patients of childbearing age. Coagulation studies are indicated depending on the invasiveness of the procedure, a history of renal or liver dysfunction, and in patients on anticoagulant medications.

Medical management of acute coronary syndromes, myocardial infarction, peripheral vascular disease, atrial fibrillation, and stroke often includes antithrombotic medications such as aspirin, clopidogrel bisulfate, heparin, coumadin, and others. These medications are common in patients presenting for cardiac surgery and may have a major impact on the management and preoperative evaluation of the patient. Patients may present with a long history of aspirin or clopidogrel use. In the acute setting, heparin or shorter acting IIb/IIIa inhibiting agents such as integrelin may be in use. These agents are beneficial in reducing the incidence of stent occlusion, myocardial infarction, or other thrombotic sequaela of peripheral vascular disease or hyper-coagulation. A thoughtful plan regarding the continued administration of these medications is required prior to the operative procedure. In the case of clopidogrel, stable patients presenting for elective surgery may be advised to stop the medication for 5 days to reduce the risk of excessive bleeding during the operation. All of the agents, including aspirin, are associated with increased blood loss during surgery. The relative risk of stopping the agent versus the increased risk of excessive bleeding must

be weighed in each patient. Consultation with surgeon and cardiologist are recommended before discontinuing antithrombotic therapy.

In addition to the medication history, all patients scheduled for cardiac surgical procedures require a careful bleeding history with emphasis on abnormal bleeding occurring after surgical procedures, dental extractions and trauma. Signs of easy bruising should be sought on physical examination. All patients should undergo laboratory screening for the presence of abnormalities in hemostasis. A platelet count, partial thromboplastin time (PTT), and prothrombin time (PT) should be obtained. Time permitting, all abnormalities should be evaluated prior to surgery so that post-CPB hemostasis is not complicated by unknown or unsuspected medical conditions.

PT and PTT elevations

Elevations in PT and PTT should be investigated for factor deficiencies, factor inhibitors, and the presence of anticoagulants such as warfarin and heparin. It is important that documentation of a normal PTT and PT existing before warfarin or heparin administration is initiated so that other causes of an elevated PTT and PT are not overlooked. Deficiencies of factors VIII, IX, and XI are most commonly encountered. These deficiencies and their management are summarized in the following sections.

Factor VIII deficiency (hemophilia A)

The half-life of factor VIII in plasma is 8–12 hours; normal persons have approximately 1 unit of factor VIII activity per 1 mL of plasma (100% activity). Patients with severe hemophilia A will have as little as 1% factor VIII activity, whereas mildly affected patients will have up to 50% activity. Patients present with an elevated PTT and varying degrees of clinical bleeding. The diagnosis is made by a factor assay. Safe conduct of cardiac surgery requires 80–100% factor VIII activity during the operative procedure, with maintenance of activity levels in the 30–50% range for 7 days postoperatively. An infusion of 1.0 unit of factor VIII per kilogram of body weight will increase the patient's factor VIII activity level by 2%. The 12-hour half-life of factor VIII requires that factor VIII be re-infused every 12 hours during the perioperative period. Factor VIII may be provided with cryoprecipitate, which contains 100 units of factor VIII per bag (10–20 mL). Factor VIII concentrates that contain 1000 units of factor VIII in 30–100 mL also may provide factor VIII.

Factor IX deficiency (hemophilia B)

The half-life of factor IX in plasma is 24 hours; normal persons have approximately 1 unit of factor IX activity per 1 mL of plasma (100% activity). Factor IX deficiency is clinically indistinguishable from factor VIII deficiency. Diagnosis is made by factor assay. Safe conduct of cardiac surgery requires 60% factor IX activity during the operative procedure, with maintenance of activity levels in the 30–50% range for 7 days postoperatively. An infusion of 1.0 unit of factor IX per kilogram of body weight will increase the patient's factor IX activity level by 1%. The 24-hour half-life of factor IX requires that factor IX be re-infused only every 24 hours during the perioperative period. Fresh frozen plasma (FFP) contains 0.8 units of all of the procoagulants per milliliter and generally is used to replace factor IX. A 250-mL bag of FFP will provide 200 units of factor IX. For patients in who factor IX replacement with FFP will require infusion of prohibitively large volumes, factor IX concentrates are used.

Factor XI deficiency (Rosenthal syndrome)

The half-life of factor XI in plasma is 60–80 hours; normal persons have approximately 1 unit of factor XI activity per 1 mL of plasma (100% activity). Factor XI deficiency is most common among patients of Jewish descent and is associated with a prolonged PTT. Many of these patients have no symptoms or have a history of bleeding only with surgery or major trauma. The diagnosis is made by factor assay. FFP administration replenishes factor XI. It is recommended that 10–20 mL of FFP/kg/day be used during the preoperative and postoperative periods to manage this deficiency.

Platelet dysfunction

Thrombocytopenia should be evaluated and treated as necessary to avoid excessive operative bleeding. A platelet count and platelet function monitoring are important laboratory evaluations. The bleeding time is not a reliable predictor of perioperative or postoperative bleeding. Other measurements of platelet dysfunction include thromboelastography and assays of activated platelet aggregation (aggregometry). These evaluations provide information on the functional integrity of platelet action. In the case of thromboelastography, clot formation and fibrinolysis are observed. The information gained provides insight into both factor content and platelet function. The activated platelet aggregation assays provide both a total platelet count and a percentage of active platelets. Platelet dysfunction can result from a variety of causes.

Thrombocytopenia

Thrombocytopenia may due to dilution (i.e. with massive fluid replacement), increased peripheral destruction (sepsis, disseminated intravascular coagulation, thrombotic thrombocytopenic prupura, prosthetic valve hemolysis or platelet antibodies) or sequestration (splenomegaly, lymphoma). In the cardiac surgical patient, dilutional thrombocytopenia is common. Thrombocytopenia is also frequently the result of platelet destruction from the CPB circuit and from activation of heparin induced platelet antibodies.

Heparin-induced thrombocytopenia and thrombosis (HITT) occurs due to the presence of an anti-heparin-platelet factor 4 antibodies. The condition can be terminated by withdrawal of heparin therapy. Ideally, heparin therapy should not be restarted until *in-vitro* platelet aggregation in response to heparin no longer occurs. Heparin induced thrombocytopenia may re-occur up to 12 months after the initial episode. Patients with HITT requiring CPB before the antibody can be cleared present a management problem. These patients may be treated by a variety of alternate anticoagulation agents. Direct thrombin inhibitors such as danaparoid, lepirudin, bivalirudin, and argatroban have all been used with success. Other agents such as tirofiban and epoprostenol have been used in combination with unfractionated heparin with good result. In the preoperative setting, identification of patients who have experienced HITT is paramount. If HITT is diagnosed, then the surgery should either be delayed long enough to clear the heparin antibodies (usually 90–100 days), or an alternate anticoagulation strategy devised. If heparin re-exposure is considered, testing for the presence of HITT antibodies, generally by enzyme-linked immunosobent assay (ELISA), is required.

Qualitative platelet defects

Abnormalities in platelet function are observed with some medications, renal failure, hepatic failure, paraproteinemias (i.e. multiple myeloma), myeloproliferative disorders, and hereditary disorders of platelet function. In the cardiac surgical patient, medication related dysfunction, uremic dysfunction are most common.

There is an ever growing list of medications that inhibit platelet function. Some medications altering function and commonly observed in the cardiac surgical patient include aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), thienopyridine adenosine diphosphate (ADP) receptor antagonists (clopidogrel, ticlopidine) and GP IIb/IIIa antagonists (abciximab, integrelin, and tirofiban), dextran, dipyridamole, heparin, plasminogen activators, and beta-lactam antibiotics. NSAIDs inhibit platelet function by blocking platelet synthesis of prostaglandins and platelet function is normalized when these drugs are cleared from the blood. Aspirin irreversibly acetylates prostaglandin synthase (cyclooxygenase) impairing platelet function for the life of the platelet (7–10 days). Like aspirin, the effects of clopidogrel are present for the life of the platelet. It is recommended that for elective surgery, clopidogrel should be held for 5 days allowing adequate time to reestablish a normal platelet response to bleeding. Integrelin inhibits fibrinogen from binding to the platelet surface GP IIb/IIIa receptor. Integrelin should be discontinued 12 hours before surgery to ensure adequate return of platelet function.

Renal dysfunction with uremia inhibits platelet function. The cause of this effect is unknown. In addition to the qualitative defect there is often

thrombocytopenia in these patients. The bleeding time is usually prolonged and there is associated anemia. Bleeding may be treated with platelet transfusion or administration of DDAVP, or cryoprecipitate. DDAVP and cryoprecipitate raise the levels of factor VIII (antihemophilic factor/von Willebrand factor). When DDAVP is used, 0.3 µg/kg is infused IV over 15 minutes and the half-life of its activity is 8 hours.

Coagulopathy and congenital heart disease

Coagulopathies in children with congenital heart disease are common. The etiology of these coagulopathies is multifactorial. Cyanosis has been implicated in the genesis of coagulation and fibrinolytic defects particularly in patients where secondary erythrocytosis produces a hematocrit greater than 60%. Thrombocytopenia and qualitative platelet defects are common. Defects in bleeding time, clot retraction, and platelet aggregation to a variety of mediators have all been described. Platelet count and platelet aggregation response to ADP are inversely correlated with hematocrit and positively correlated with arterial oxygen saturation. In cyanotic patients, generation of platelet microparticles, hypofibrinogenemia, low-grade disseminated intravascular coagulation (DIC), deficiencies in factors V and VIII, and deficiencies in the vitamin-K-dependent factors (II, VII, IX, X) have all been implicated in the genesis of coagulapathy. In patients who are cyanotic and erythrocytotic, the plasma volume and quantity of coagulation factors are reduced, and this may contribute to the development of a coagulopathy. In some instances, erythrophoresis with whole blood removed and replaced with fresh frozen plasma or isotonic saline may be justified.

In addition to the defects induced by cyanosis, defects inherent to normal infants and to children with congenital heart disease are present. Neonatal platelets are hypo-reactive to thrombin (the most potent platelet agonist), epinephrine/ADP, collagen, and thromboxane A_2. In addition, neonatal fibrinogen is dysfunction as compared to older children and adults. An acquired deficiency of the large von Willebrand multimers has been demonstrated in patients with congenital heart disease. Finally, factors synthesized in the liver may be reduced in both cyanotic and acyanotic patients in whom severe right heart failure results in passive hepatic congestion and secondary parenchymal disease.

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Myocardial Physiology and the Interpretation of Cardiac Catheterization Data

The ability to interpret cardiac catheterization data is essential to the cardiac anesthesiologist. Catheterization data provide information about the extent and distribution of coronary stenosis, the type and extent of valvular lesions, the location and quantification of intracardiac shunts, congenital lesions, and an assessment of systolic and diastolic function. This information contributes to a complete preoperative evaluation and serves as a predictor of postoperative functional status.

Right heart catheterization

A fluid-filled catheter capable of making high-fidelity pressure measurements in the right atrium, right ventricle, pulmonary artery, and pulmonary artery occlusion position is passed antegrade via a basilic, cephalic, or femoral vein under fluoroscopic guidance. In addition, the catheter may have the capability of making thermodilution cardiac output and mixed venous oxygen saturation measurements. Angiography is performed by recording several cardiac cycles on cine film while radiographic contrast material is injected into the right heart chambers.

For infants and children, the femoral vein is the usual access site; however, right heart catheterization via the umbilical vein may be possible in the first few days after birth. Catheterization of the right ventricle and pulmonary arteries may be difficult via the umbilical route because umbilical vein catheters tend to pass directly into the left atrium via the foramen ovale. Right atrial, right ventricular, and pulmonary angiography may be performed on infants and children to delineate congenital lesions.

Left heart catheterization

A fluid-filled catheter capable of making high-fidelity systolic, diastolic, and mean pressure measurements and capable of allowing angiographic dye injection is used. The catheter may be passed retrograde via the brachial or femoral artery to the aortic root under fluoroscopic guidance where pressures are recorded. In infants and children the femoral artery is the preferred route. The umbilical artery is small and its course is tortuous; therefore, is not useful except for pressure monitoring and angiography of the descending aorta. Left heart catheterization can be performed antegrade via the right atrium in patients in whom the atrial septum can be crossed via a patent foramen ovale or an atrial septal defect. This is a common approach in infants and children. In patients in whom the retrograde approach to the left ventricle is undesirable, and where an atrial or ventricular level communication does not exist, the atrial septum can be intentionally punctured to gain access to the left atrium using a Brockenbrough needle.

Pressures in the aorta, left ventricle, and left atrium are recorded. Aortography may be performed by recording on cine film the injection of radiographic contrast material into the aortic root.
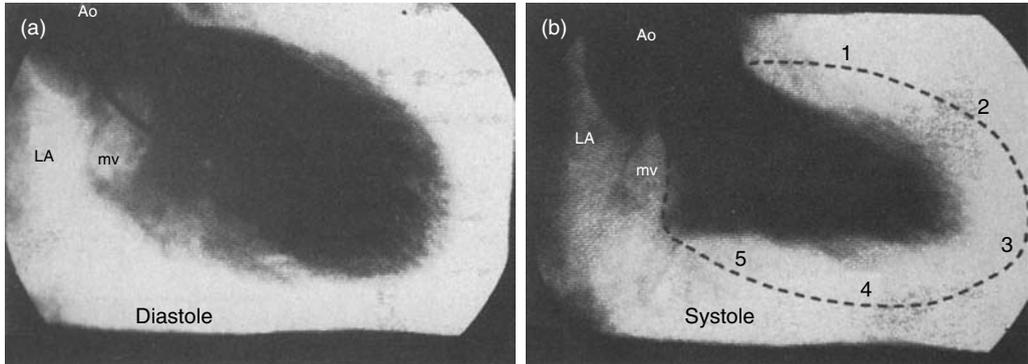
Fig. 2.1 Left ventriculogram in right anterior oblique (RAO) projection. End-diastolic image is shown in (a) while end-systolic image is shown in (b). For purposes of comparison, end diastole is represented by dotted outline on end-systolic image. Numbers 1–5 refer to five segments analyzed for wall motion in RAO projection (see Fig. 2.12). Ao, aorta; LA, left atrium; mv, mitral valve.

This will allow detection of aortic regurgitation, congenital aortic arch abnormalities such as coarctation or aortic arch interruption, and acquired aortic lesions such as aortic dissection. Left atrial and ventricular angiography allows detection of congenital anomalies. Left ventriculography is performed by recording several cardiac cycles on cine film as radiographic contrast material is injected into the mid left ventricle. The left ventriculogram allows detection of mitral regurgitation as well as comparison of both regional and global wall motion in systole and diastole (Fig. 2.1a,b). The left ventriculogram also allows calculation of left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV). The innermost margin of the left ventricular (LV) silhouette in systole and diastole is determined. Computer assisted planimetry calculates LV volumes from these two-dimensional pictures based on the assumption that ventricular shape is approximated by an ellipsoid. Angiographic stroke volume (SV) is then defined as LVEDV – LVESV. Ejection fraction (EF) is defined as (LVEDV – LVESV)/LVEDV, which is SV/LVEDV.

Coronary angiography

Cine recordings of radiographic contrast material selectively injected into the coronary ostia are made. Special catheters are used for the selective
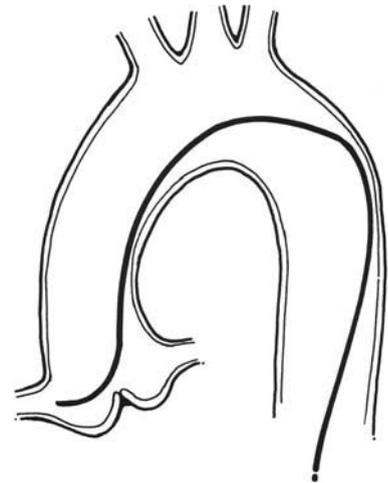
Fig. 2.2 Left anterior oblique (LAO) projection of aorta illustrating use of Judkin's technique to catheterize the right coronary ostia retrograde via femoral artery.

cannulization of the ostia and are advanced under fluoroscopic guidance via the same artery used for left heart catheterization (Figs 2.2 & 2.3).

Cardiac output determination

Two complimentary methods are used to determine cardiac output: the thermodilution technique and the Fick determination. Both methods measure forward cardiac outputs. Forward cardiac output
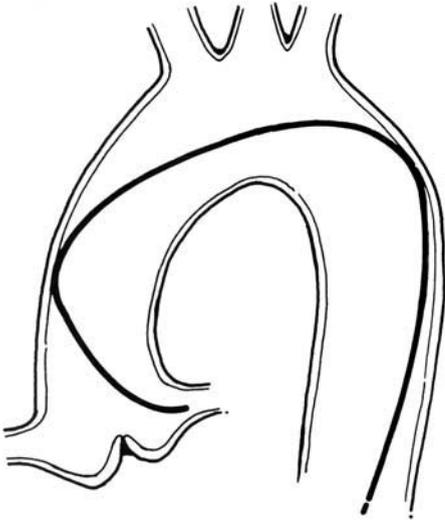
Fig. 2.3 Left anterior oblique (LAO) projection of aorta illustrating use of Judkin's technique to catheterize the left coronary ostia retrograde via femoral artery.

and total cardiac output are equal only if there are no regurgitant lesions or shunt fractions.

Thermodilution cardiac output is a modification of the indicator dilution method, in which flow is determined from the following relationship:

$$\frac{\text{Known amount of indicator injected}}{\text{Measured concentration of indicator}} \times \text{time}$$

In the thermodilution method, cold water is the indicator. A predetermined volume of indicator of known temperature is injected into the right atrium, where the temperature of the blood also is known. The subsequent change in temperature over time is measured by a thermistor in the pulmonary artery. This method measures pulmonary blood flow, which is equal to forward right heart output. It is not accurate at low cardiac outputs, in the presence of tricuspid regurgitation, or where an intracardiac left-to-right shunt exists. Thermodilution cardiac outputs are discussed in detail in Chapter 3.

The Fick determination is based on the relationship:

O_2 consumption/arterial − venous O_2 content difference

Oxygen uptake or consumption (V_{O_2}) can be determined from calculations made on a 3-minute expired air sample collected in a Douglas bag. The bag contents are analyzed for carbon dioxide and, using the respiratory quotient, V_{O_2} is calculated. More commonly, an estimate of V_{O_2} is obtained from tables that relate V_{O_2} to body surface area or to heart rate and age. Arterial–venous oxygen content difference (A–V_{O_2} difference) is calculated from the difference between the arterial and mixed venous oxygen contents where:

Content = (O_2 saturation of arterial or mixed

venous blood × Hb concentration × (1.38))

+ (0.003 × P_{O_2} of arterial or mixed venous blood)

This method measures systemic blood flow; which equals forward left heart output. It also can be used to measure pulmonary blood flow or forward right heart output, when oxygen consumption is divided by pulmonary arterial content subtracted from pulmonary venous content. The method is more accurate at low cardiac outputs, where the arterial to venous oxygen difference is great. It also is accurate in the presence of intracardiac shunts when the mixed venous oxygen content and pulmonary venous oxygen content are properly determined. This will be discussed further in the section on intracardiac shunts.

Resistances

Systemic and pulmonary vascular resistances are made using hemodynamic and cardiac output data as follows:
- Systemic vascular resistance (SVR)
- Pulmonary vascular resistance (PVR)
- Transpulmonary gradient (TPG)
- Mean arterial blood pressure (MAP)
- Mean pulmonary artery pressure (mPAP)
- Pulmonary artery occlusion pressure (PAOP)
- Central venous pressure (CVP)
- Cardiac output (CO)

$$\text{SVR} = \frac{(\text{MAP} - \text{CVP})80}{\text{CO}}$$

$$\text{nl} = 700\text{–}1600 \, \text{dynes/s/cm}^5$$

$$SVR = \frac{(MAP - CVP)}{CO}$$

$$nl = 9\text{--}20 \text{ Wood units}$$

$$PVR = \frac{(mPAP - PAOP)80}{CO}$$

$$nl = 20\text{--}130 \text{ dynes/s/cm}^5$$

$$PVR = \frac{(mPAP - PAOP)}{CO}$$

$$nl = 0.25\text{--}1.6 \text{ Wood units}$$

$$TPG = mPAP - PAOP \quad nl = 5\text{--}10 \text{ mmHg}$$

The use of these parameters in evaluation of patients is discussed in detail in Chapters 4–9.

Saturation data

The oxygen saturation (%) of blood in the low superior vena cava (SVC), the main pulmonary artery, and the aorta are obtained to screen for intracardiac shunts. If an intracardiac shunt is suspected, multiple samples from locations in the great vessels and cardiac chambers are necessary to localize the shunt and determine its magnitude and direction.

Assessment of valve lesions

Analysis of the pressure data from right and left heart catheterization, in combination with analysis of ventriculography and aortography data, will delineate the extent and nature of valvular lesions.

Assessment of pulmonary vascular anatomy

For infants and children with congenital heart disease, special procedures may be necessary to assess the pulmonary vasculature and the extent of pulmonary vascular disease.

Pressure–volume loops

To fully understand catheterization data, it is necessary to be familiar with ventricular pressure–volume loops. A normal LV pressure–volume loop
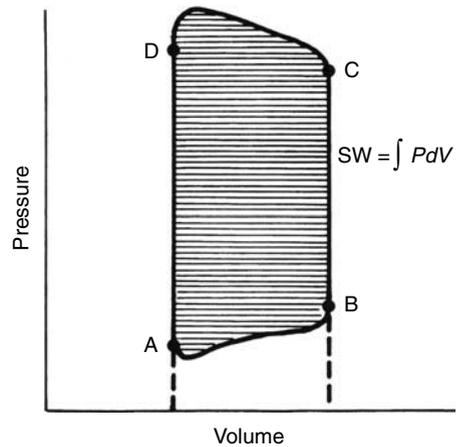
Fig. 2.4 Schematic representation of ventricular pressure–volume loop. Crosshatched area represents stroke work (SW) or total external mechanical work. Curve AB, diastolic filling; BC, isovolumic contraction; CD, systolic ejection; DA, isovolumic relaxation.

is illustrated in Fig. 2.4. Curve AB represents the diastolic pressure–volume relationship. Ventricular filling begins when left atrial pressure (LAP) exceeds left ventricular pressure at point A and the mitral valve opens. Point B represents LVEDP and LVEDV. LVEDV is also known as Ved. Point B also represents the onset of isovolumic contraction at which LV pressure exceeds LAP and the mitral valve closes. Changes in diastolic function can be represented by changes in the position and shape of the curve AB and will be discussed later.

Curve BC represents isovolumic contraction. LV pressure increases while LV volume remains constant. At point C, LV pressure exceeds aortic diastolic pressure and the aortic valve opens.

Curve CD represents the ejection phase of ventricular contraction. At point D, aortic pressure exceeds LV pressure and the aortic valve closes. Point D represents the left ventricular end-systolic pressure (LVESP) and the left ventricular end-systolic volume (LVESV). LVESP is also known as Pes.

Curve DA represents isovolumic relaxation. At this time there is constant LV volume and rapidly decreasing LV pressure.

The area encompassed by ABCD represents the stroke work (SW) that is external mechanical work. Preload is defined as the end-diastolic fiber length or volume and is represented by point B on the curve AB. Augmented preload produces an increase in end-diastolic muscle fiber length represented by a point B further to the right on the curve AB. This increased fiber length enhances the velocity of muscle shortening for a given level of afterload (Frank–Starling mechanism).

A family of pressure–volume loops exists for any ventricle. Experimentally these loops are generated by altering preload over a physiologic range using partial inferior vena cava (IVC) occlusion. When the ventricular end systolic pressure volume points (point D) from each loop are connected a straight line is created. The slope of this line is ventricular elastance (E_{es}) and it uniquely defines the contractile state of the ventricle (Fig. 2.5).

Afterload in this model can be defined simply as Pes (point D) or as the stress (force per unit area) encountered by ventricular fibers after the onset of shortening as represented by moving from point C to D.

$$\text{Stress} = \frac{\text{pressure} \times \text{radius}}{2h}$$

where h is wall thickness. Afterload, defined as wall stress, is constantly changing during ventricular ejection because ventricular pressure, radius, and thickness are all changing during ejection.

These definitions of afterload are incomplete because they do not directly describe the characteristics of the arterial system. Because the ventricle produces pulsatile ejection of a viscous fluid (blood) into a viscoelastic reservoir (the arterial system), it is worth considering the characteristics of the arterial system and of the blood, both of which constitute impedance to ventricular ejection. Pulsatile and nonpulsatile flow must be considered because both exist in the intact arterial system. The nonpulsatile component of afterload is measured as peripheral vascular resistance. This is a familiar concept and is defined as

$$\frac{\text{Mean arterial pressure} - \text{central venous pressure}}{\text{cardiac output}}$$

Blood viscosity and the caliber of the arterioles are the major determinants of peripheral vascular
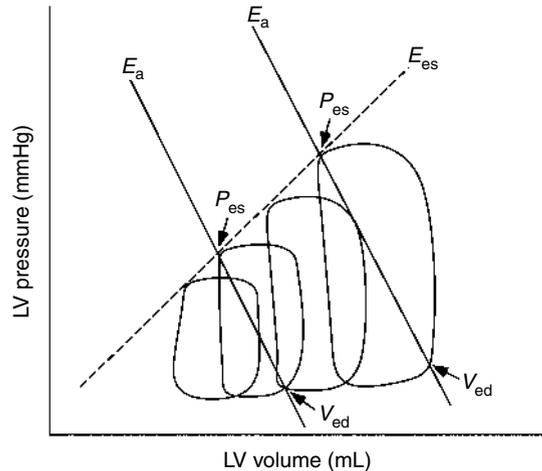
Fig. 2.5 A family of four ventricular pressure–volume loops have been generated by varying preload (ventricular end diastolic volume or V_{ed}) in a ventricle with fixed contractility (E_{es}) and fixed afterload (E_a). Joining the ventricular end-systolic pressure (P_{es}) and volume points from the four loops defines the slope Ees. The ventricular end-systolic pressure and volume points correspond to point D in Fig. 2.4. E_a is the slope of the line defined by joining Ved to Pes for each loop. Since afterload is fixed in this example the slope E_a is the same for each loop. This can be seen in loops 2 and 4. Despite fixed afterload and fixed contractility, augmentation of preload results in an elevation of P_{es}. The intersection point of E_{es} and E_a uniquely define P_{es} for each loop. P_{es} will remain constant with an augmentation of preload only if E_a simultaneously decreases (shallower slope).

resistance. The pulsatile component of afterload is measured as frequency-dependent aortic input impedance, which is determined by the elastic properties of the proximal aorta and by the reflection of pulse waves from the peripheral arterial tree. Effective arterial elastance (E_a) is defined as the ratio of LVESP/SV (P_{es}/SV) and is the line that connects point B to D (see Fig. 2.5). This relationship incorporates peripheral resistance, characteristic impedance, and lumped total arterial compliance. Thus E_a can be used to define the hydraulic load (afterload) of the LV.

In the pressure–volume loop scheme, LVESV and P_{es} (point D) are uniquely determined by the intersection point of the contractile state (E_{es}) and

the afterload (E_a). Normally, the ratio of E_a/E_{es} is 0.7–1.0. In this range, SW (external mechanical work) and efficiency (ratio of SW/myocardial oxygen consumption) are optimized. In heart failure patients the ratio may be as high as 4.0 due to simultaneous decreases in E_{es} and increases in E_a.

For a given E_{es} with E_a constant an increase in preload (LVEDV or V_{ed}) will produce an increase in SV and an increase in LVESP (P_{es}) (see Fig. 2.5). This increase in the area ABCD is known as preload recruitable stroke work (PRSW). In reality the only way in which LVESP (P_{es}) could remain constant for a given E_{es} with an increase in preload would be for the slope of E_a to decrease. Stated another way, an increase in preload for a given E_{es} will cause a parallel (no change in slope) shift in E_a to the right resulting in an increase in P_{es} and LVESV. With enhanced contractility (steep E_{es} slope) the rise in P_{es} will be great and the reduction in LVESP will be small; PRSW will be high. With diminished contractility (shallow E_{es} slope) the rise in P_{es} will be small and the reduction in LVESP will be great; PRSW will be limited. This is consistent with the clinical observation that in the presence of reduced contractility preload augmentation does not substantially improve SV and cardiac output.

For a given contractile state with fixed preload, an increase in afterload (steeper E_a slope) results in an increase in P_{es} and LVESV; represented by moving upward and to the right on the line A decrease in afterload (shallower E_a slope) results in a decrease in P_{es} and LVESV; represented by moving downward and to the left on the line (Fig. 2.6). Increased contractility is represented by an E_{es} that is steeper and shifted upward to the left. An increase in contractility with preload and afterload fixed obviously augments SV because of the marked decrease in LVESV with LVEDV (preload) constant (Fig. 2.7). Decreased contractility is represented by an E_{es} that is shallower and shifted downward to the right. With fixed preload (V_{ed}) and afterload (E_a), SV is diminished when contractility decreases (see Fig. 2.7). It is also obvious that the shallower the E_{es} slope (more depressed contractility) the more sensitive the ventricle will be to
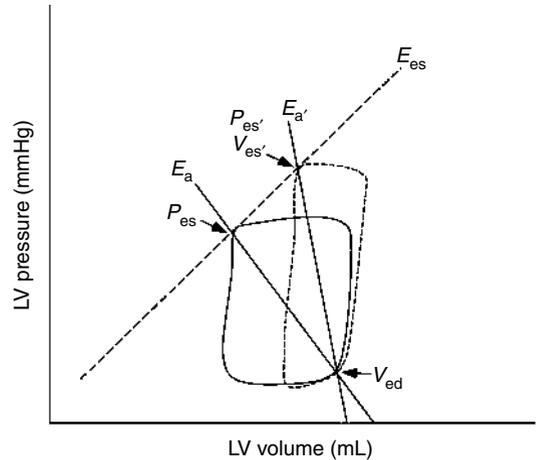
Fig. 2.6 Two ventricular pressure–volume loops illustrating the effect of increased afterload ($E_{a'}$) with preload (V_{ed}) and contractility (E_{es}) fixed. Increased afterload is represented by the line $E_{a'}$ which has a steeper slope than line E_a. Increased afterload ($E_{a'}$) results in an increase in P_{es} (from P_{es} to $P_{es'}$) and an increase in end-systolic volume (from V_{es} to $V_{es'}$), which causes a reduction in SV (from $V_{ed}-V_{es}$ to $V_{ed}-V_{es'}$). EF = $E_{es}/(E_{es} + E_a)$ and therefore EF falls as E_a increases to $E_{a'}$ with E_{es} constant.

an increase in E_a as evidenced by a greater increase in LVESV.

Figure 2.8 serves to unify these concepts. Loop 1 represents the control situation. Loop 2 represents an abrupt increase in afterload with contractility constant. The result is an increased LVESV and an unchanged LVEDV. The result is a reduction in SV. In subsequent beats (loop 3) of a normal heart, LVEDV is increased such that the original SV is now maintained at the new increased afterload. The ability of the ventricle to maintain SV in the face of increasing afterload by increasing preload is defined as preload reserve. Preload reserve is exhausted when the sarcomeres are stretched to their maximum diastolic length. When this occurs, there will be no further augmentation of the velocity of shortening and the ventricle behaves as if preload is fixed. For a given level of contractility, after preload reserve is exhausted, additional increases in afterload will be accompanied by parallel decreases in SV (loop 4). This is defined as a state of afterload mismatch. Afterload mismatch is
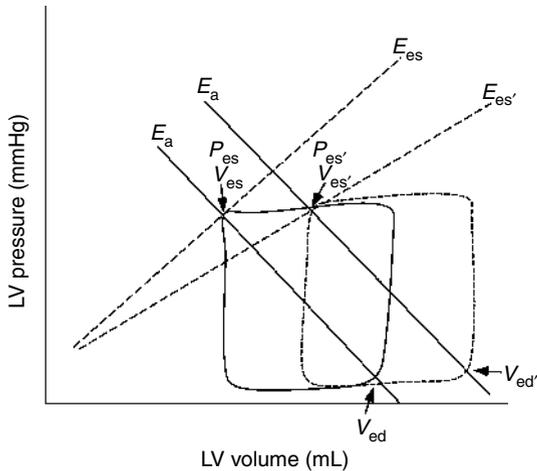
Fig. 2.7 Two ventricular pressure–volume loops illustrating effect of decreased contractility ($E_{es'}$) with P_{es} and afterload (E_a) constant. Decreased contractility is represented by the line ($E_{es'}$) that has a shallower slope than line E_{es} and is shifted downward to the left. Since afterload is fixed in this example, the slope E_a is the same for both loops. Decreased contractility ($E_{es'}$) results in an increase in end-systolic volume (from V_{es} to $V_{es'}$) while $P_{es} = P_{es'}$. Since P_{es} and E_a are constant in this example, stroke volume (SV) must be constant as well as SV = P_{es}/E_a. As a result $V_{ed'}$ increases by an amount equal to the increase in $V_{es'}$. With P_{es} fixed SV will only decrease with a decrease in contractility if afterload (E_a) simultaneously increases (steeper slope). Progressive increases in Ea will result in a greater increase in V_{es} for $E_{es'}$ as compared to E_{es}. Although SV is constant in this example EF decreases because EF = $E_{es}/(E_{es} + E_a)$.

the inability of the ventricle at a given level of contractility to maintain SV in the face of an increased wall stress.

Diastolic function

Normal diastolic function is dependent on normal ventricular diastolic compliance, distensibility, and relaxation. Both extrinsic and intrinsic factors affect ventricular diastolic function. It is necessary to differentiate between compliance, distensibility, and relaxation, and this is best accomplished by examining diastolic pressure–volume diagrams
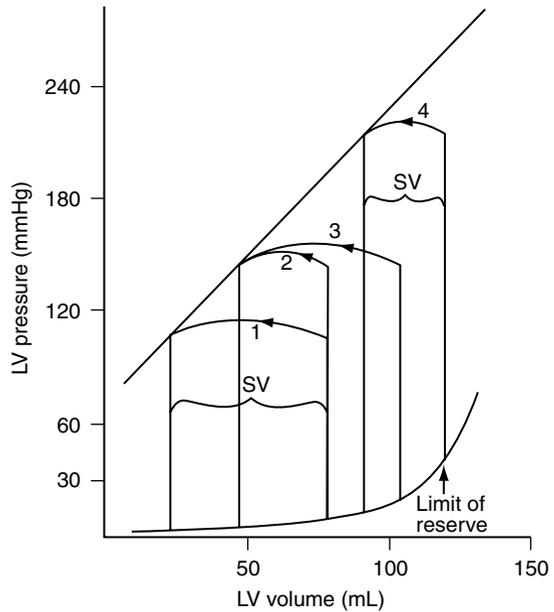
Fig. 2.8 Ventricular pressure–volume loops illustrating the compensation of an intact ventricle for progressive increases in afterload with contractility fixed. Stroke volume (SV) can be maintained in the face of progressive afterload increases until preload reserve is exhausted.

(Fig. 2.9a–d). Any or all of these abnormalities may exist in a given patient.

Compliance

Compliance or distensibility is defined as the ratio of a volume change to the corresponding pressure change or as the slope of the volume–pressure ($\Delta V/\Delta P$) relationship. Elastance or stiffness is the inverse of compliance ($\Delta P/\Delta V$). Decreased compliance or increased stiffness is thus defined as an increase in the steepness of the pressure–volume plot (see Fig. 2.9c). Strictly speaking, diastolic compliance is determined by the intrinsic volume–pressure relationship of completely relaxed myocytes. There are two causes of poor diastolic compliance.

Increased chamber stiffness

This occurs in aortic stenosis or systemic hypertension. In these cases, there is an increase in the amount of myocardial tissue due to concentric
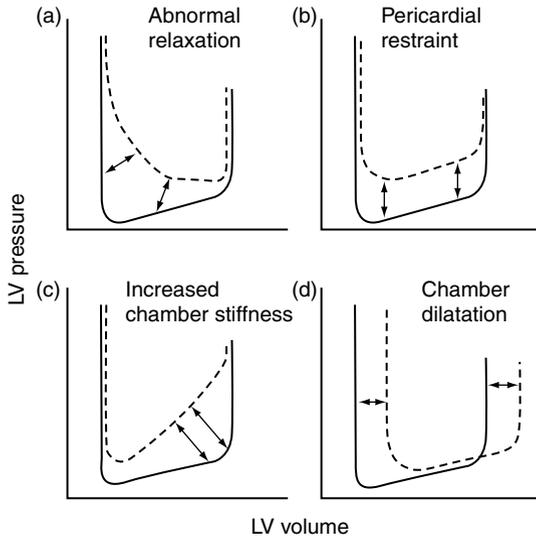
Fig. 2.9 A series of diastolic pressure–volume curves. The solid curve in each example represents a normal diastolic pressure–volume relationship, whereas the dotted curve represents the altered diastolic pressure–volume relationship. (a) The diastolic pressure–volume relationship when ventricular relaxation is impaired. (b) The diastolic pressure–volume relationship when distensibility is reduced as with pericardial restraint. (c) The diastolic pressure–volume relationship when ventricular chamber stiffness is increased or ventricular chamber compliance is reduced. (d) The effect of chamber dilatation on a normal diastolic pressure–volume relationship.

LV hypertrophy. Diastolic compliance of the ventricle is diminished despite that fact that the compliance of the individual muscle units is normal.

Increased muscle stiffness

This occurs in restrictive cardiomyopathies due to amyoidosis and hemochromatosis. In these cases, the compliance of the individual muscle units is diminished due to an infiltrative process.

The diastolic pressure–volume relationship is dynamic. There is high compliance at low volumes and diminished compliance at higher volumes. As a result, reduced diastolic compliance is not limited to ventricles with altered pressure–volume slopes. A ventricle forced to make use of preload reserve to maintain SV may function on the steep portion of an otherwise normal compliance curve (see Fig. 2.9d).

Distensibility

Decreased ventricular distensibility is defined as an increased diastolic pressure at a given volume. This would be represented in a diastolic pressure–volume diagram by a parallel upward shift of the entire pressure–volume relation (see Fig. 2.9b). Decreased distensibility can occur from intrinsic and extrinsic causes.

Intrinsic causes

It has been demonstrated clearly that pacing-induced ischemia in humans with coronary artery disease (CAD) is responsible for diminished diastolic distensibility. Although impaired relaxation certainly plays a role in diastolic dysfunction with ischemia, the pressure–volume relation in ischemia more closely resembles the pattern seen with pericardial restraint (see Fig. 2.9b). This diminished diastolic distensibility often precedes systolic dysfunction. In addition, pacing-induced ischemia elicits diminished diastolic distensibility in humans with aortic stenosis without CAD. Differences in the diastolic behavior of ischemic and non-ischemic segments of the same ventricle subjected to pacing-induced ischemia have been demonstrated. An upward shift (diminished distensibility) in the pressure–length relationship is observed in ischemic segments. For a given diastolic volume this results in an increase in diastolic pressure, which causes the nonischemic segments to move to a steeper (less compliant) portion of their original pressure–length relationship.

Extrinsic causes

Decreased distensibility may be caused by extrinsic limitations to ventricular expansion in diastole. Diminished distensibility occurs due to ventricular interdependence via an intact ventricular septum and the restraining effect of the pericardium (see Fig. 2.9b). For example, distension of the right ventricle with a leftward septal shift will result in diminished distensibility of the left ventricle. In addition, reduced distensibility may occur due to restrictive pericarditis or pericardial

tamponade a diseased or fluid-filled pericardium (see Chapter 7).

Relaxation

Ventricular relaxation is an energy consumptive process. Adenosine triphosphate (ATP) is required for calcium sequestration back into the sarcoplasmic reticulum and for detachment of actin–myosin cross-bridges. When isovolumic relaxation is delayed, early diastolic filling is impeded. When relaxation is incomplete, filling is impeded throughout diastole (see Fig. 2.9a). Relaxation is impaired during myocardial ischemia and in patients with hypertrophic and congestive cardiomyopathies.

Normally, the right ventricular end-diastolic pressure (RVEDP) is 1–2 mmHg greater than the mean right atrial pressure (RAP), and the left ventricular end-diastolic pressure (LVEDP) is 2–3 mmHg greater than the mean PAOP and the LAP. These small differences in pressure are due to the volume added to the ventricle by atrial systole. When LV compliance is poor, the A wave produced by atrial systole will be large and the additional volume provided by the atrial kick in end-diastole will result in a large increase in LVEDP. In these patients, the peak A-wave pressure in the LAP or PAOP trace is a better measure of LVEDP than the mean LAP or PAOP because the mean LAP or PAOP pressure will underestimate LVEDP. Even large A waves only slightly elevate mean LAP because their duration is short. Thus, well-timed atrial contraction results in a large elevation of LVEDV with only a small elevation of mean LAP and limited pulmonary venous congestion. For patients who chronically function on a steep portion of the compliance curve, a large A wave, left atrial enlargement on electrocardiogram (ECG) and an S_4 on physical examination are expected findings.

Analysis of diastolic pressure–volume curves

Ideally, the diastolic pressure–volume curve should be examined over its entire range and under baseline and stress conditions. Unfortunately, this information is not routinely available from cardiac catheterization data. Typically, the A wave, V wave,

and mean pressures of the RAP and PAOP tracing, the RVEDP and LVEDP, and the left ventricular end-systolic and end-diastolic volume indices (LVESVI and LVEDVI) are provided. The LVESVI and the LVEDVI are simply the LVESV and LVEDV obtained by planimetry of left ventricular end-systolic and end-diastolic angiograms divided by the patient's body surface area (BSA). Pressure and volume data from a representative catheterization report are reproduced in Figs 2.10 and 2.11.

One point on the LV diastolic pressure–volume curve is obtained if the pressure and volume measurements are made under identical conditions of preload, heart rate, and ischemia. Thus, incomplete information must be used to draw inferences on overall diastolic performance. Clinically, a dilated heart would be expected in patients who are dependent on a large LVEDV to maintain an adequate forward SV. Patients with chronic volume overload valvular lesions such as mitral regurgitation and aortic insufficiency are good examples. In these patients, a large LVEDV is needed because only a portion of the total SV becomes forward SV. Early in the disease, these patients operate on the flat portion of a diastolic pressure volume curve and have enormous preload reserve. As the disease progresses and systolic function deteriorates, a larger LVEDV is needed to maintain SV. Eventually, these patients operate on the steep portion of the diastolic pressure–volume relationship and are unable to augment preload without large increases in diastolic pressure and subsequent pulmonary congestion. In patients with mitral regurgitation, this analysis of diastolic function is complicated by the presence of regurgitant V waves in the LAP or PAOP trace during ventricular systole. The electronically determined mean LAP or PAOP will be increased in direct proportion to the height and duration of the regurgitant V wave. This will cause the mean LAP or PAOP to overestimate LVEDP. An estimate of the LVEDP can be obtained by examining a calibrated PAOP or LAP trace and determining the A-wave amplitude. In patients without atrial systole, the best estimate of LVEDP will be the PAOP or LAP at end diastole (see Chapter 3).

A normal LVEDV and diminished ventricular compliance is seen most commonly in patients with

CARDIAC CATHETERIZATION REPORT

NAME	AGE	SEX	REPORT #	BIH UNIT #
	61	F		

BODY SURFACE AREA: 1.85 m2
HEMOGLOBIN: 13.4 gms %

HEMODYNAMICS

	NORMALS	
**PRESSURES		
RIGHT ATRIUM (a/v/m)	2-10/2-10/0-8	9/7/6
RIGHT VENTRICLE (s/ed)	15-30/0-8	34/7
PULMONARY ARTERY (s/d/m)	15-30/4-12/9-16	34/16/23
PULMONARY WEDGE (a/v/m)	3-15/3-15/1-10	13/10/9
LEFT VENTRICLE (s/ed)	100-140/3-12	138/13
AORTA (s/d/m)	110-140/60-90/70-105	138/66/97
**CARDIAC OUTPUT		
HEART RATE (beats/min)	60-100	82
RHYTHM	NSR	NSR
O2 CONS. IND (ml/min/m2)	110-150	121
A-V O2 DIFFERENCE (ml/ltr)	30-50	49
CARD. OP/IND FICK (l/mn/m2)	2.5-4.2	4.6/2.5
**RESISTANCES		
SYSTEMIC VASC. RESISTANCE	770-1500	1583
PULMONARY VASC. RESISTANCE	20-120	243
**% SATURATION DATA (NL)		
SVC LOW		65
PA MAIN		65,65
AO		91,93
**ARTERIAL BLOOD GAS		
INSPIRED O2 CONCENTR'N		0.21
pO2		63
pCO2		39
pH		7.46

Fig. 2.10 Reproduction of portion of cardiac catheterization report from 61-year-old woman with severe three-vessel coronary artery disease (CAD) and systolic dysfunction. Right and left ventricular pressure measurements, Fick cardiac output (CO) determination, and derived hemodynamic variables are reported.

CARDIAC CATHETERIZATION REPORT

NAME	AGE	SEX	REPORT #	BIH UNIT #
	61	F		

LEFT VENTRICULOGRAPHY:
Volumetric data:

LV end diastolic volume index (nl 50-90 ml/m2).	58
LV end systolic volume index (nl 15-30 ml/m2).	35
LV stroke volume index (nl 35-75 ml/m2).	23
LV ejection fraction (nl 50%-80%).	40

Qualitative wall motion:
RAO:

1. Antero basal -   normal
2. Antero lateral - hypokinetic
3. Apical -   hypokinetic
4. Inferior -   hypokinetic
5. Postero basal -   normal

Other findings:
   Mitral valve was normal.
   Aortic valve was normal.

TECHNICAL FACTORS:
   Total time (Lidocaine to test complete) = 47 minutes.
   Arterial time = 29 minutes.
   Fluoro time = 16 minutes.
   Total contrast volume (ml) = 105
Premedications:
          Valium 5 mg, P.O.
          Benadryl 25 mg, P.O.
Anesthesia:
          1% Lidocaine subq.
Anticoagulation:
          Heparin 5000 units, IV

Fig. 2.11 Reproduction of portion of catheterization report from the patient described in Fig. 2.10. Section reports information obtained from left ventriculography. Left ventricular end-diastolic volume index (LVEDVI), left ventricular end-systolic volume index (LVESVI), stroke volume index (SVI) and ejection fraction (EF) are reported. In addition, qualitative descriptions of left ventricular wall motion in five wall segments seen in right anterior oblique (RAO) projection are reported.

LV pressure overload valve lesions such as aortic stenosis and, to a lesser degree, in patients with systemic hypertension. In these patients, the LVEDV necessary to maintain an adequate SV is maintained at the expense of a high LVEDP because compliance is poor. The volume contributed by atrial systole represents a larger proportion of the LVEDV than it does in ventricles with normal compliance because the early diastolic filling is compromised by low compliance and is compensated for by a well-timed forceful atrial systole. Loss of atrial systole in these patients is disastrous because LVEDV can only be maintained by large elevations of mean LAP with consequent pulmonary venous congestion.

A ventricle with abnormal LVEDV and diminished distensibility is characteristic of patients with severe CAD in which the energy requirements necessary to guarantee complete ventricular relaxation at rest are not met. Such diastolic dysfunction precedes the development of systolic dysfunction.

Systolic function

Systolic function is not synonymous with contractility. Normal systolic function is the ability of the ventricle to perform external work (generate a SV) under varying conditions of preload, afterload and contractility. Any assessment of systolic function must take the contribution of these three factors into account.

Ejection fraction

Defined as $\{(\text{LVEDV} - \text{LVESV})/\text{LVEDV}\} \times 100$, the EF is an ejection-phase index and the most commonly used assessment of global systolic function. The LVEDV and the LVESV are obtained from planimetry of LV end-diastolic and end-systolic angiograms (see Fig. 2.1). The normal value is 50–80%. Determination of EF is dependent on variations in preload, afterload, and contractility (see Figs 2.5–2.7). This becomes obvious when EF is described mathematically using the concepts of E_{es}, E_a, stroke volume (SV), and LVEDV (V_{ed}):

$$\text{EF} = \text{SV}/V_{ed}$$

$$\text{EF} = 1 - \frac{P_{es}/V_{ed}}{E_{es}} = 1 - \frac{(E_a * \text{SV})/V_{ed}}{E_{es}}$$

$$\text{EF} = E_{es}/(E_{es} + E_a)$$

Normal E_{es} and E_a are 1–3 mmHg/mL

These equations are consistent with a number of clinical observations:
- In the range of normal contractility (E_{es}), EF is largely insensitive to changes in afterload (E_a) and preload (V_{ed}).
- EF is increasingly inversely related to afterload (E_a) as contractility (E_{es}) decreases with fixed preload (V_{ed}). In addition this inverse sensitivity is enhanced in the setting of reduced preload (V_{ed}).
- EF is increasingly inversely related to preload (V_{ed}) as contractility (E_{es}) decreases with fixed afterload (E_a).
- When preload (V_{ed}) is very low, EF will be reduced in presence of normal contractility (E_{es}) and afterload (E_a).
- If the E_a/E_{es} ratio is 1.0 (ideally matched) then EF = 50%.
- EF is most useful as screening tool with low EF identifying those patients most likely to be susceptible to alteration in preload, afterload, and contractility.

As an example, an increase in LVEDVI from 75 to 90 mL/m^2 with LVESVI constant at 25 mL/m^2, as would occur with afterload and contractility constant, would result in an increase in EF from 66% to 72%. Thus, a 20% increase in preload results in a 9% increase in EF.

EF is not a very sensitive index of CAD because areas of regional myocardial dysfunction secondary to ischemia may exist without depression of global systolic function. EF separates patients with normal LV function from those with LV dysfunction and is reliable in following changes in systolic function in individual patients. An EF lower than 40% in the absence of acute afterload elevations represents depressed systolic function and corresponds clinically with New York Heart Association class 3 symptoms. An EF lower than 25% represents severe depression of LV systolic function and corresponds to New York Heart Association class 4 symptoms (see Chapter 1).

EF may overestimate systolic function in mitral regurgitation because of the unique systolic loading conditions in this lesion. The left ventricle is

presented with two outflow tracts in systole: the aortic valve and the incompetent mitral valve. The mitral valve provides a low impedance outflow tract and the aortic valve provides a normal-impedance outflow tract. EF may remain near normal in the face of depressed systolic function due to this low mean afterload state. With mitral valve replacement and the elimination of the low-impedance outflow tract, the ventricle is presented with more normal systolic loading conditions. EF may actually decrease substantially postoperatively in such patients because depressed systolic function is now unmasked.

Stroke work

Another ejection-phase index of systolic function is stroke work (SW), or external LV work, represented by the area ABCD in Fig. 2.4. When the shape of the LV pressure–volume loop is normal, as is true in the absence of pressure or volume overload conditions, left ventricular stroke work (LVSW) is a good measure of systolic function. Chronic volume and pressure overload conditions alter the shape of the pressure–volume loop and the calculated LVSW is increased above the normal value of 60–120 g-m/beat. LVSW is defined as:

(Mean LV systolic pressure

− mean LV diastolic pressure) × SV × 0.0136

When aortic and mitral regurgitation are absent, this can be simplified to:

(Mean arterial pressure − mean pulmonary artery

occlusion pressure) × SV × 0.0136

because mean arterial pressure approximates mean LV systolic pressure and mean pulmonary artery occlusion pressure closely approximates mean LV diastolic pressure. In direct contrast to EF, alterations in afterload have little effect on calculated SW. SV declines or increases in proportion to the afterload elevation or reduction such that the area of the loop remains unchanged. SW, unlike EF, is very sensitive to changes in preload. The area of the loop is increased or decreased by increases or decreases in preload. LVSW can be converted to LVSWI by dividing SV by BSA to get SVI.

LWSW is used in conjunction with Ved to describe PRSW where PRSW = LWSW/Ved. PRSW is a measure on myocardial contractility that is independent of preload and afterload. This method requires the ability to simultaneously record LV pressures and volumes and is not in routine clinical use.

Left ventriculography

Qualitative analysis of regional wall motion by left ventriculography is another index of systolic function. Ventriculography is performed by making cine recordings as contrast material is injected directly into the mid-left ventricle. Left ventriculography is performed in the 30° right anterior oblique (RAO) projection or in the right and 60° left anterior oblique (LAO) projections. The ventricle is divided into segments (Fig. 2.12) and visual analysis of regional wall motion is made by comparison of end-diastolic and end-systolic cineangiograms (see Fig. 2.1). Five segments are generally analyzed in the RAO projection: anterobasal, anterolateral, apical, diaphragmatic (inferior), and posterobasal. Five segments also may be analyzed in the LAO projection: basal septal, apical septal, apical inferior, posterolateral, and superior lateral. These areas are graded qualitatively for wall motion. Normal areas exhibit concentric inward movement in systole. Hypokinetic areas exhibit reduced concentric inward motion in systole. Akinetic areas exhibit no motion with systole. Dyskinetic areas exhibit a paradoxical outward bulging with systole. Aneurysmal areas exhibit characteristic dilation with either hypokinesis or akinesis.

Areas of hypokinesis generally are composed of ischemic myocardium, whereas akinetic areas are composed of infracted or hibernating myocardium. Improvements in wall motion occur in hypokinetic and akinetic areas when ischemic tissue has been salvaged by revascularization or by pharmacologic interventions to improve perfusion. The presence of collaterals, the absence of surface ECG Q waves, and the presence of an associated proximal coronary stenosis less than 90% improve the likelihood that medical or surgical intervention will improve the wall motion abnormalities. Dyskinetic and aneurysmal areas, respectively, represent regions with little or no viable myocardium and rarely
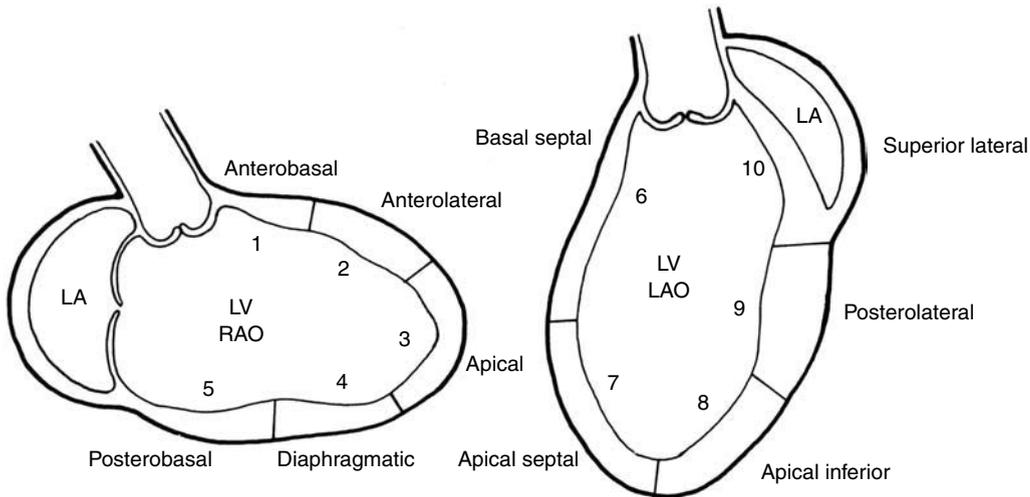
Fig. 2.12   Schematic delineation of the five wall segments seen in right anterior oblique (RAO) and left anterior oblique (LAO) projections during left ventriculography. The following is a summary of coronary arterial supply to these regions:
1. *Anterobasal* – LMCA; proximal LAD; 1st diagonal.
2. *Anterolateral* – LMCA; proximal or mid-LAD; 1st diagonal. **3**. *Apical* – LMCA; proximal, mid, or distal LAD; 2nd diagonal. **4**. *Diaphramatic (inferior)* – proximal, mid, or distal RCA; PDA. **5**. *Posterobasal* – proximal, mid, or distal RCA; PDA. **6**. *Basal septal* – LMCA; proximal or mid-LAD, 1st septal. **7**. *Apical septal* – LMCA; proximal, mid, or distal LAD. **8**. *Apical inferior* – proximal, mid, or distal RCA. **9**. *Posterolateral* – LMCA; proximal or distal CIRC marginals. **10**. *Superior lateral* – LMCA; proximal CIRC marginals. CIRC, circumflex artery; LAD, left anterior descending artery; LMCA, left main coronary artery; PDA, posterior descending artery; RCA, right coronary artery.

show improvement in wall motion with surgical or pharmacologic intervention.

Regional wall motion abnormalities are a more sensitive indicator of CAD than is a reduction in a global ejection-phase index of systolic function such as EF. This is because global systolic function can be maintained in the presence of regional dyssynergy by compensatory increases in wall shortening in areas of normal wall motion as long as large areas of myocardium are not dyssynergic.

Coronary angiography

Coronary angiography delineates the normal and pathologic features of the coronary circulation. Normally, angiography is performed in the 60° LAO projection and the 30° RAO projection with caudal or cranial angulated views if necessary.

Coronary anatomy

Determination of the areas of myocardium at risk with a particular stenotic or vasospastic lesion requires knowledge of the regional blood supply pattern. The right and left coronary anatomy is illustrated in Figs 2.13 and 2.14. Most patients (85%) have a right dominant system of coronary circulation. Here, the right coronary artery extends to the crux cordis in the atrioventricular groove and gives rise to the posterior descending branch, left atrial branch, atrioventricular (AV) nodal branch, and one or more posterior LV branches. In a left dominant system (8%), these branches are supplied by the left circumflex artery and the right coronary artery supplies only the right atria and ventricle. In 7% of patients, the system is balanced, with the right coronary artery supplying the posterior descending, left atria, and AV nodal branches, whereas the left circumflex artery supplies the posterior LV branches.

There is variation in the blood supply to various regions of myocardium, but some generalizations can be made. This information is summarized in Fig. 2.12. Normally, a proximal branch of the left circumflex artery supplies the anterobasal region.
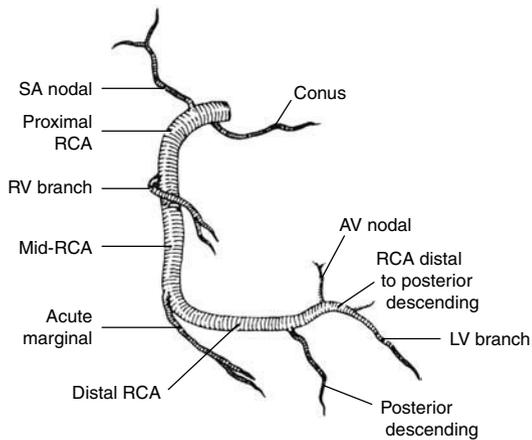
Fig. 2.13 Anatomy of right coronary artery. AV, arterioventricular; LV, left ventricle; RCA, right coronary artery; RV, right ventricle; SA, sinoatrial.
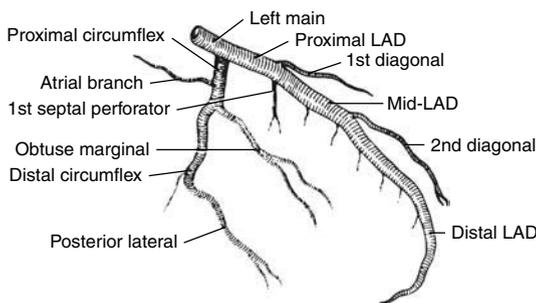
Fig. 2.14 Anatomy of left coronary artery (right oblique). LAD, left anterior descending.

The anterolateral region is supplied by contributions from both the diagonal branch of the left anterior descending (LAD) artery and the obtuse marginal branch of the left circumflex. The terminal portion of the LAD artery supplies the apical region. The inferior region is a combination of the posterior lateral and diaphragmatic regions, which are best seen in an LAO projection. The posterior lateral branch of the left circumflex artery supplies the posterior lateral region. The diaphragmatic region is supplied by the posterior descending artery, which, as previously discussed, is either a branch of the right coronary or left circumflex artery. The posterobasal region is supplied by the proximal right coronary artery. The septal branches of the LAD artery supply the anterior two-thirds of the ventricular septum, and branches of the right coronary and

posterior descending arteries supply the posterior one-third. A branch of the right coronary artery supplies the sinoatrial (SA) node in 55% of patients and by a branch of the left circumflex artery in the other 45%.

The bulk of the right ventricle is located in the diaphragmatic and posterobasal regions supplied by the right coronary artery in a right dominant system. Small portions of the right ventricle also are included in the apical and septal areas. It is for this reason that involvement of the LAD results in compromise of perfusion to the anterior right ventricular wall near the ventricular septum and to the right ventricular apex. Conversely, involvement of the right coronary artery in a right dominant system results in compromise of perfusion to the portions of the left ventricle located in the diaphragmatic and posterobasal regions. How severely the posterior portion of the left ventricle will be compromised in this setting will depend on how much of this region is supplied by the distal branches of the circumflex artery.

Anatomic coronary lesions

Coronary atherosclerotic stenotic lesions are quantitated visually from moving cineangiograms in several projections. Coronary arteriography from a representative catheterization report is reproduced in Fig. 2.15. Stenotic areas of artery are compared with adjacent normal areas and the percent reduction in lumen diameter caused by the stenosis is quantified. Thus, a 90% lesion refers to a stenosis that causes a 90% reduction in lumen diameter. It is generally acknowledged that resting coronary blood flow does not decrease until there is an 85% reduction in lumen diameter. This corresponds to a greater than 90% reduction in lumen cross-sectional area. By contrast, a 50% diameter reduction corresponds to a 75% reduction in cross-sectional area. Maximal coronary flow in response to a stimulus for vasodilation is blunted when there is a 30–45% reduction in lumen diameter and is absent when the lumen diameter is reduced 90%. Inter-observer variability exists in the grading of stenotic lesions. In addition, coronary angiography typically underestimates the severity of stenotic lesions and may not accurately predict the physiologic significance of a particular lesion.

CORONARY ARTERIOGRAPHY

DOMINANCE: BALANCED

ARTERIAL SEGMENT	MORPHOLOGY	% STENOSIS	COLLAT FROM
**RIGHT CORONARY			
1) PROXIMAL RCA	DISCRETE	100	
2) MID RCA	NORMAL		
2A) ACUTE MARGINAL	NORMAL		
3) DISTAL RCA	NORMAL		
4) R-PDA	NORMAL		
4A) R-POST-LAT	NORMAL		
4D) R-LV	NORMAL		
**LEFT CORONARY			
5) LEFT MAIN	NORMAL		
6) PROXIMAL LAD	TUBULAR	70	
6A) SEPTAL-1	NORMAL		
7) MID-LAD	DISCRETE	50	
8) DISTAL LAD	NORMAL		
9) DIAGONAL-1	NORMAL		
10) DIAGONAL-2	NORMAL		
12) PROXIMAL CX	DISCRETE	85	
13) MID CX	DISCRETE	90	
13A) DISTAL CX	NORMAL		
14) OBTUSE MARGINAL-1	NORMAL		
17) LEFT PDA	NORMAL		

Fig. 2.15 Reproduction of a portion of a catheterization report from patient described in Fig. 2.10. This section reports information obtained from coronary angiography. Morphology of stenoses, percent reduction in lumen diameter, and sources of collaterization are reported. A pictorial representation of coronary arterial anatomy also is given.

Coronary spasm

True coronary spasm is diagnosed at the time of coronary angiography with a provocation test utilizing methylergonovine, acetylcholine, or hyperventilation. The test is considered positive if focal spasm occurs in the presence of clinical symptoms or ECG changes.

Coronary thrombus formation

A thrombus superimposed on an obstructive coronary lesion is often the pathogenesis of unstable angina and is the direct cause of an acute transmural myocardial infarction in most patients. Currently, protocols designed to intervene in the early stages of myocardial infarction incorporate thrombolytic therapy, percutaneous transluminal coronary angioplasty, or both.

Coronary collaterals

An extensive network of coronary collaterals is normally present at birth. However, these collaterals are not demonstrable by angiography in normal hearts due to their small diameter. It is only when the collateral channels enlarge secondary to regional myocardial oxygen deprivation that they are visible angiographically. The development of collateral pathways in patients with comparable degrees of coronary insufficiency is variable in both extent and time course. The presence of collaterals has been identified as a determinant of reversible wall motion abnormalities. LV function in the region of an occluded coronary artery is better maintained in the presence of collaterals than in their absence.

Interpretation of coronary angiography data

To properly interpret the coronary angiograms it is necessary to integrate data from the angiograms with data from the right and left heart catheterizations and from the left ventriculograms. Several questions should be answered:
- What is the status of systolic function? Global function in the absence of mitral regurgitation is best evaluated with EF. Regional function is assessed by analysis of the ventriculogram. Patients with an EF greater than 55% would be expected to have limited areas of dyssynergy and no history of a prior myocardial infarct. Patients with a history of prior myocardial infarction or three-vessel coronary disease would be expected to have a reduced EF and more extensive areas of dyssynergy. EFs in the range of 40% are common in this subset of patients. Patients with three-vessel disease and a history of myocardial infarction have EFs in the range of 35%. More extensive areas of dyssynergy would be expected. Patients with an EF lower than 25% have poor ventricular function and will have large areas of akinesis and dyskinesis.
- What is the status of diastolic function? It is necessary to determine whether myocardial ischemia is responsible for diminished ventricular distensibility

as discussed in the section on diastolic function. An elevated LVEDP is characteristic of diastolic dysfunction; although this also may exist in concert with systolic dysfunction, an elevated LVEDP is not synonymous with systolic dysfunction.

• What regions of myocardium are jeopardized? Significant stenotic lesions jeopardize the myocardium in specific regions as discussed previously. A region is at high risk of developing ischemic dysfunction if it is poorly collaterized and distal to a severe stenosis. It also is necessary to determine whether the regional myocardium distal to a stenosis is viable. If the area of myocardium is dyskinetic or aneurysmal with evidence of surface Q waves, pharmacologic and surgical efforts to salvage the area will likely be of no benefit. If the myocardium is viable, however, (hibernating myocardium), then revascularization may lead to a dramatic improvement in regional systolic function.

• What are the consequences of deteriorating function in a given region? Deteriorating function in a given region may cause major management problems. Continued compromise of flow to the AV node may cause progressive heart block with subsequent hemodynamic compromise. A patient with depressed global systolic function whose hypokinetic anterior lateral wall becomes akinetic may develop cardiogenic shock.

Evaluation of valvular lesions

The impressive technological advances in Doppler echocardiography and nuclear cardiac imaging now allow noninvasive assessment of valvular pathology. Evaluation via cardiac catheterization, however, provides important information.

Stenotic lesions

The analysis of stenotic valve lesions is based on obtaining a valve orifice area from flow and pressure–gradient data. The Gorlin equation uses the basic hydraulic formula: area = flow/velocity. Combining this with an equation that relates velocity to mean pressure gradient: velocity = $k \times \sqrt{}$mean pressure gradient, where k is a specific constant for either the aortic or mitral valve

allows a determination of valve area. For the mitral valve, then, the equation is: valve area = flow/$37.7 \times \sqrt{}$mean pressure gradient. For the aortic valve, the equation is: valve area = flow/$44.5 \times \sqrt{}$mean pressure gradient. Obviously, flow occurs across the mitral valve only in diastole and across the aortic valve only in systole. Therefore, cardiac output cannot be substituted for flow in the equations. The time per heartbeat during which blood flows across the mitral valve is defined as the diastolic filling period. The diastolic filling period is measured from mitral valve opening to end diastole. The time per heartbeat during which blood flows across the aortic valve is defined as the systolic ejection period. The systolic ejection period is measured from aortic valve opening to aortic valve closure.

Mitral valve flow (cm^3/sec)

   = {Cardiac output (cm^3/min)}

      $\times$ {diastolic filling period (sec/beat)

      $\times$ heart rate (beat/min)}$^{-1}$

Mitral valve area (cm^2)

   = {mitral valve flow (cm^3/sec)}

      $\times$ {$37.7 \times \sqrt{}$mean pressure gradient (cm/sec)}$^{-1}$

Aortic valve flow (cm^3/sec)

   = {cardiac output (cm^3/min)}

      $\times$ {systolic ejection period (sec/beat)

      $\times$ heart rate (beat/min)}$^{-1}$

Aortic valve area (cm^2)

   = {aortic valve flow (cm^3/sec)}

      $\times$ {$44.5 \times \sqrt{}$mean pressure gradient (cm/sec)}$^{-1}$

The mean pressure gradient for mitral stenosis is obtained by using planimetry to determine the area between simultaneous tracings of the left atrial or PAOP and the LV pressure during the diastolic filling period and then dividing this area by the length of the diastolic filling period. Figure 2.16 illustrates this area during one diastolic filling period. Normally, the pressure gradients for several beats are determined and the average is taken. For aortic stenosis, analogous measurements are made using planimetry to determine the area between simultaneous
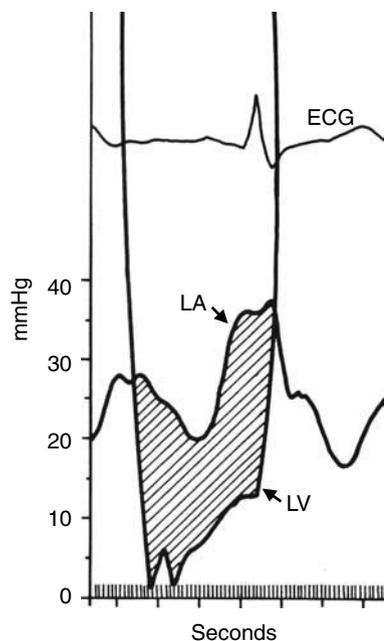
Fig. 2.16 One diastolic filling period in a patient with severe mitral stenosis. Simultaneous tracings of electrocardiogram (EGG), left atrial (LA) pressure, and left ventricular (LV) pressure are shown. The pressure gradient across the mitral valve is crosshatched and seen to vary during diastolic filling period. The length of the diastolic filling period can be seen in seconds.

Fig. 2.17 One systolic ejection period in a patient with severe aortic stenosis. Simultaneous recordings of proximal aortic pressure and LV pressure are recorded. The pressure gradient across the aortic valve is crosshatched and seen to vary during systolic ejection period. Time scale for length of systolic ejection period not shown. Ao, aorta; LV, left ventricular.

tracings of the proximal aortic pressure and the LV pressure during the systolic ejection period. Figure 2.17 illustrates this area during one ejection period. The gradients for several beats are determined and averaged.

It is essential that proper assessment of flow be used for lesions in which stenosis and regurgitation coexist. A thermodilution or Fick cardiac output determination is an assessment of forward flow across a valve orifice. If regurgitation exists, total flow across the valve orifice will be forward flow plus regurgitant flow. If forward flow instead of total flow is used, the valve area for a given gradient will be underestimated and the degree of stenosis will be exaggerated. Total flow is best obtained from angiographic determination of cardiac output. Left ventriculography is used to determine SV (as described previously) and SV is multiplied by heart rate.

It is important when evaluating stenotic lesions that the pressure gradient alone is not evaluated. At low flows (low cardiac output), it is possible for a valve to be critically stenotic with a small transvalvular pressure gradient. Several other relationships should be kept in mind. The mean pressure gradient is directly related to the square of flow. Thus, if cardiac output doubles, the mean pressure gradient will increase by a factor of four. The mean pressure gradient is inversely related to the square of the valve area. Thus, if valve area is reduced by one-half, the mean pressure gradient will increase by a factor of four.

The normal mitral valve area in an adult is $4–6\,cm^2$. The mitral valve area must be reduced to $2.6\,cm^2$ before symptoms occur. A valve area of $1.5–2.5\,cm^2$ is considered mild mitral stenosis, with symptoms occurring during exercise. A valve area of $1.1–1.5\,cm^2$ is considered moderate mitral

stenosis. In these patients an elevated LAP necessary to maintain cardiac output. A valve area of $1.0\,cm^2$ is considered severe mitral stenosis. A LAP of 25 mmHg is necessary to maintain even minimal cardiac output.

The normal aortic valve area is $2.6–3.5\,cm^2$. The aortic valve area must usually be reduced to $0.8\,cm^2$ before angina, syncope, and congestive heart failure occur. A valve area of $0.5–0.8\,cm^2$ is considered moderate aortic stenosis. Severe aortic stenosis exists when the valve area is less than $0.5\,cm^2$.

For adults, valve areas usually are not normalized for body surface area (BSA). As a result, extremes of body size must be taken into consideration when deciding whether a stenotic lesion is significant. A large person with higher cardiac output demands may have a large gradient and symptoms with a valve area that would be adequate for a smaller person with reduced cardiac output requirements. Valve areas commonly are normalized for BSA in infants and children.

Regurgitant lesions

Quantification of regurgitant lesions with catheterization techniques is more difficult and less accurate than for stenotic lesions. Two approaches are available. One method is qualitative; the other is quantitative. Qualitative analysis is based on assessing the amount of contrast material regurgitated into the left atrium during left ventriculography for mitral regurgitation (Fig. 2.18) or into the left ventricle during aortography for aortic regurgitation (Fig. 2.19). The degree of regurgitation is graded from mild to severe (1+ to 4+). In mild aortic regurgitation, a small amount of contrast enters the left ventricle during diastole but clears with each systole. In mild mitral regurgitation, a small amount of contrast enters the left atrium during systole but clears in diastole. In severe aortic regurgitation, the left ventricle is filled with contrast after the first diastole and it remains opacified for several systoles. In severe mitral regurgitation, the left atrium is filled with contrast after the first systole and becomes progressively opacified with each beat. In addition, contrast is seen refluxing into the pulmonary veins. Similar qualitative analysis is used to grade tricuspid regurgitation.
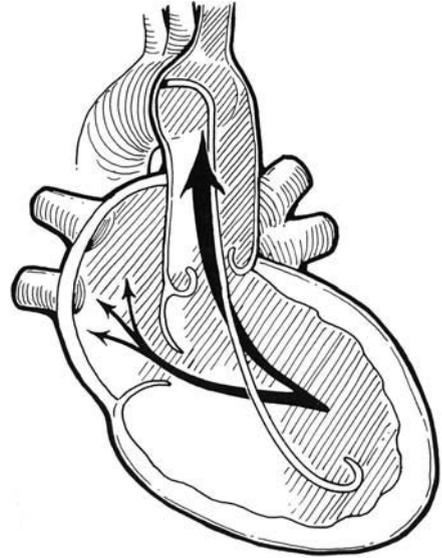
Fig. 2.18 Long-axis cross-sectional view of left atrium, left ventricle, and aorta in severe mitral regurgitation. Injection of contrast material into left ventricle demonstrates regurgitation of contrast into left atrium and pulmonary veins.

The quantitative method of assessing regurgitation is based on calculation of the regurgitant fraction:

$$\text{Regurgitant fraction} = \frac{\text{regurgitant stroke volume}}{\text{total stroke volume}}$$

Regurgitant stroke volume

$$= \text{total stroke volume} - \text{forward stroke volume}$$

Angiographic or total SV is determined from left ventriculography as described previously and forward SV is determined by the Fick method. A regurgitant fraction lower than 30% indicates mild mitral regurgitation, 30–60% indicates moderate mitral regurgitation, and higher than 60% indicates severe mitral regurgitation. A regurgitant fraction of 10–40% indicates mild aortic regurgitation, 40–60% indicates moderate aortic regurgitation, and more than 60% severe aortic regurgitation.

It is important to note that the height and duration of V waves are not a direct assessment of the degree of mitral regurgitation. Severe mitral regurgitation can exist in the absence of a significant
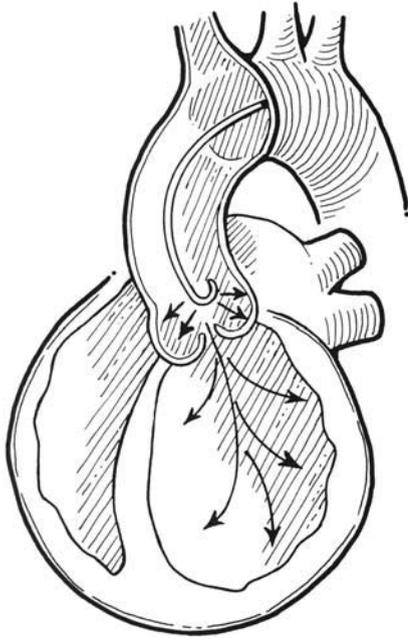
Fig. 2.19 Long-axis cross-sectional view of left ventricle, right ventricle, and aorta in severe aortic regurgitation. Injection of contrast material into proximal aorta demonstrates regurgitation of contrast into left ventricle.

V wave. It has been stated that, for an individual patient, the height of the V wave correlates with the degree of regurgitation under conditions of changing afterload. Such conclusions must be drawn carefully however, as there are several factors that affect the height and duration of V waves:

• The degree of mechanical mitral valve impairment. Mechanical impairment occurs with a ruptured papillary muscle, a torn prosthetic valve leaflet, or a perivalvular leak.

• The degree of functional mitral valve impairment. Functional impairment occurs with papillary muscle ischemia or ventricular dilation with deformation of the valvular annulus.

• The compliance characteristics of the left atrium and pulmonary veins. For a given regurgitant volume, a dilated, compliant left atrium will exhibit a smaller V wave than a small, noncompliant left atrium.

• The relative impedance to ejection through the aortic valve versus that through the incompetent mitral valve. An increase in the impedance to aortic ejection will favor increased outflow through the lower impedance of the incompetent mitral valve. With all other variables constant, this will increase the magnitude of the V wave.

• The inotropic state of the left ventricle. An increase in LV contractility will tend to decrease LV dimensions, decrease the size of the valvular annulus, and thus decrease the amount of regurgitant flow.

• The length of ventricular systole. A decrease in the length of ventricular systole will reduce the time available for regurgitant flow to take place. However, forward SV may be compromised as well.

Analysis of the V wave in tricuspid regurgitation is hampered by similar considerations. Nonetheless, with severe tricuspid regurgitation, the right atrial pressure trace takes on the shape of the right ventricular pressure trace.

Evaluation of cardiac shunts

A comprehensive discussion of the physiology of shunts is provided in Chapter 6. Oxygen saturation measurements in multiple cardiac chambers and the great vessels are used to localize and quantify cardiac shunts. Additionally, angiography during cardiac catheterization may be used to locate cardiac shunts.

Shunt location

Shunt localization is usually accomplished using a combination of angiography and measurement of oxygen saturations in the pulmonary veins, SVC and IVC, right heart chambers, left heart chambers, aorta, and pulmonary artery. Oxygen saturation sampling is used to detect an oxygen saturation step-up in the right heart in the case of a left-to-right shunt or an oxygen saturation step-down in the left heart in the case of a right-to-left shunt. A step-up is defined as an increase in the oxygen saturation of blood in a particular location that exceeds the normal variability in that location; whereas, a step-down is a greater-than-expected decrease in saturation for a given location.

Shunt quantification

Shunt quantification is based on comparison of systemic and pulmonary blood flows. Systemic (Q_S) and pulmonary (Q_P) blood flows are calculated by the Fick method previously described.

$$Q_P = \text{V}_{\text{O}_2}/(\text{PV}_{\text{O}_2}\text{ content} - \text{PA}_{\text{O}_2}\text{ content})$$

PA$_{\text{O}_2}$ content is the pulmonary arterial oxygen content. PV$_{\text{O}_2}$ content is pulmonary venous oxygen content. Sampling blood from the left atrium (when the pulmonary veins return to the left atrium) will provide a weighted average of the four pulmonary veins oxygen content. If a right-to-left atrial level shunt is present this sampling site will not provide an accurate assessment of pulmonary vein oxygen content. Each of the four pulmonary veins can be entered and sampled separately. When this is done segmental areas of intra-pulmonary shunt and V/Q mismatch can be detected. The Pa$_{\text{O}_2}$ or saturation of pulmonary venous blood from a lung segment with V/Q mismatch will improve with an increase in Fi$_{\text{O}_2}$ while there will be no improvement if an intra-pulmonary shunt is present.

$$Q_S = \text{V}_{\text{O}_2}/(\text{SA}_{\text{O}_2}\text{ content} - \text{MV}_{\text{O}_2}\text{ content})$$

SA$_{\text{O}_2}$ is systemic arterial oxygen content. MV$_{\text{O}_2}$ content is mixed venous oxygen content. True mixed venous blood is a mixture of desaturated blood from the IVC, SVC, and coronary sinus. In a normal heart a mixed sample of venous blood from these three locations can be obtained from the pulmonary artery. In the presence of an intra cardiac left-to-right shunt, PA$_{\text{O}_2}$ saturation will overestimate true MV$_{\text{O}_2}$ saturation because pulmonary arterial blood will be a mixture of mixed venous blood and oxygenated pulmonary venous blood from the left heart. In this setting, true mixed venous saturation must be determined from samples taken from the SVC and IVC. If the very low oxygen content low volume blood from the coronary sinus is ignored then a weighted average of oxygen content of SVC and IVC blood can be used to determine MV$_{\text{O}_2}$ content:

$$(3/4 \times \text{superior vena cava O}_2\text{ content})$$
$$+ (1/4 \times \text{inferior vena cava O}_2\text{ content})$$

This formula may be used to determine MV$_{\text{O}_2}$ in the catheterization laboratory when left-to-right shunts exist. More commonly, particularly in children, SVC oxygen content is commonly used as a surrogate for MV$_{\text{O}_2}$ content. SVC blood has a lower oxygen content than IVC blood and a higher content than coronary sinus blood and thus SVC blood provides a very close estimate of the mixture of the three samples. In addition, streaming of blood of varying oxygen contents in the IVC hampers accurate IVC oxygen content sampling.

After Q_P and Q_S have been calculated, shunts can be quantified. For an isolated left-to-right shunt, the magnitude of the shunt is $Q_P - Q_S$. For an isolated right-to-left shunt, the magnitude of the shunt is $Q_S - Q_P$. The ratio Q_P:Q_S is also useful. It can be calculated from content data alone because the V$_{\text{O}_2}$ terms cancel out:

$$Q_P:Q_S = \frac{(\text{SA}_{\text{O}_2}\text{ content} - \text{MV}_{\text{O}_2}\text{ content})}{(\text{PV}_{\text{O}_2}\text{ content} - \text{PA}_{\text{O}_2}\text{ content})}$$

Furthermore, if the blood is sampled using a low $F_{\text{I}_{\text{O}_2}}$, the dissolved oxygen portion of the content equation (P$_{\text{O}_2} \times 0.003$) can be ignored. The hemoglobin $\times$ 1.34 term cancels out and the equation can be simplified to one using just saturation data from the four sites:

$$Q_P:Q_S = \frac{(\text{SA}_{\text{O}_2}\text{ saturation} - \text{MV}_{\text{O}_2}\text{ saturation})}{(\text{PV}_{\text{O}_2}\text{ saturation} - \text{PA}_{\text{O}_2}\text{ saturation})}$$

A Q_P:Q_S >2.0 constitutes a large shunt, whereas a Q_P:Q_S <1.25–1.5 constitutes a small shunt. Obviously, a Q_P:Q_S <1.0 indicates a net right-to-left shunt.

For bidirectional shunts, it is necessary to calculate effective pulmonary blood flow (Q_{Peff}) and effective systemic blood flow (Q_{Seff}). Q_{Peff} is the quantity of desaturated systemic venous blood that traverses the pulmonary capillaries to be oxygenated. Q_{Seff} is the quantity of oxygenated pulmonary venous blood that traverses the systemic capillaries to deliver oxygen to tissue. Q_{Seff} and Q_{Peff} are always equal. This concept is discussed in detail in Chapter 6.

$$Q_{\text{Seff}} = Q_{\text{Peff}} = \text{V}_{\text{O}_2}/(\text{PV}_{\text{O}_2}\text{ content} - \text{MV}_{\text{O}_2}\text{ content})$$

The left-to-right shunt is defined as $Q_P - Q_{\text{Peff}}$ while the right-to-left shunt is defined as $Q_S - Q_{\text{Seff}}$.

The net shunt is the difference between these two calculated shunts.

Evaluation of the pulmonary vasculature

Marked increases or decreases in pulmonary blood flow routinely occur in patients with congenital heart disease. Obstructive pulmonary vascular disease may occur as a consequence of increased pulmonary blood flow in patients with congenital heart disease. The extent of pulmonary vascular disease will greatly influence the type of corrective or palliative operative procedure performed. For patients with diminished pulmonary blood flow, an evaluation of the extent and caliber of the pulmonary vessels is necessary to choose the proper corrective or palliative operative procedure.

Pulmonary artery wedge angiogram

The pulmonary artery wedge angiogram is recorded on cine film while radiocontrast material is injected into a catheter that is in the pulmonary artery wedge position. Generally, the artery to the posterior basal segment of the right lower lobe is studied. As obstructive pulmonary vascular disease progresses, the wedge angiogram demonstrates progressive increases in the diameter and tortuosity of the pulmonary arteries, a diminution in the blush seen as capillaries fill, and the abrupt termination of the dilated, tortuous arteries with a marked decrease in the number of supernumerary arterial branches.

Pulmonary vein wedge angiogram

In many congenital cardiac lesions with reduced pulmonary blood flow, the pulmonary vasculature may be well visualized with injection of contrast into collaterals that arise off the aorta. For patients with pulmonary atresia, pulmonary blood flow is markedly diminished and the pulmonary arteries may not be well visualized with contrast injections into collateral vessels. In this instance, the pulmonary vein wedge angiogram may be used to delineate the pulmonary vasculature. Retrograde filling of the parenchymal pulmonary vessels can be seen on cine recordings when contrast is hand injected into a catheter wedged in a pulmonary vein. When antegrade pulmonary blood flow is severely diminished, retrograde filling of even the main pulmonary artery can occur.

Assessment of pulmonary arterial hypertension

Assessment of pulmonary arterial hypertension (PAH) is defined as a PA systolic pressure >35 mmHg or mean pulmonary artery pressure (PAP) >25 mmHg at rest or mean PAP >30 mmHg with exercise. While the causes of PAH are myriad the etiology of pulmonary hypertension related to cardiac disease can be divided into four general categories:

LA hypertension

Elevated LAP can result from a number of causes (mitral valve disease, LV diastolic dysfunction, LV systolic dysfunction, loss of AV synchrony). This is the by far the most common cause of elevated PAP in adults with acquired heart disease.

Pulmonary venous obstruction

This may be the result of obstruction to pulmonary vein entry into the venous circulation as with total anomalous pulmonary venous return or as with cor triatriatum, or the result of obstructive disease inherent to the veins themselves.

Pulmonary vascular occlusive disease (PVOD)

Chronic exposure of the pulmonary arterial bed to high flow and/or pressure leads to extensive structural changes. There is progressive muscularization of peripheral arteries, medial hypertrophy of muscular arteries and gradually reduced arterial number due to occlusive neointimal formation with fibrosis. Chronic LA hypertension can lead to development of a similar process thru chronic elevation of PAP.

High Q_P:Q_S

When a large nonrestrictive intracardiac communication exists, particularly at the ventricular level, PAP may be systemic or just sub-systemic. The question that must be answered is whether the elevated PAP is due to high flow into a low resistance pulmonary bed (high Q_P:Q_S, normal PVR,

Table 2.1 Characteristics findings in pulmonary hypertension from different etiologies.

Etiology	Pressures	LAP	TPG	PVR	Q_P
LA hypertension	PAD ≈ PAOP ≈ LAP (acute)	↑↑	↔	↔	↔
	PAD > PAOP ≈ LAP (chronic)	↑↑	↑	↑	↔
Pulmonary vein obstruction	PAD ≈ PAOP ≫ LAP	↔	↑↑	↑↑	↔ sl ↓
Pulmonary vascular occlusive disease	PAD ≫ PAOP ≈ LAP	↔	↑↑	↑↑	↔ sl ↓
Large L–R shunt	PAD ≈ PAOP ≈ LAP	sl ↑	↔ sl ↑	↔ sl ↑	↑↑

LAP, left atrial pressure; PAD, pulmonary artery diastolic pressure; PAOP, pulmonary artery occlusion pressure; PVR, pulmonary vascular resistance (TPG/cardiac output) nL < 2 Wood units; Q_P, pulmonary blood flow; TPG, transpulmonary gradient (mPAP–LAP) nL 5–10 mmHg.

large L–R shunt) or normal/low flow into a high resistance pulmonary bed (normal/low $Q_P:Q_S$, high PVR, PVOD).

Determination of the etiology of pulmonary hypertension requires measurement of the PAP, LAP, PAOP, TPG, and PVR as summarized in Table 2.1.

Suggested reading

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CHAPTER 3

Monitoring

Basic monitoring of cardiopulmonary function is essential to the safe conduct of any anesthetic. For patients undergoing cardiac surgery, advanced monitoring of cardiac, pulmonary, renal, and cerebral function will allow measurement of the physiologic variables necessary to make sound clinical decisions. The extent of monitoring required for a given case should be individualized and based upon the relative advantages and risks present. The consideration for advanced monitoring should include patient characteristics, the anticipated surgical procedure, and the postoperative requirements for advanced monitoring. This chapter will provide an overview of the monitoring systems used most commonly in the management of cardiac surgical patients.

Standard American Society of Anesthesiologists (ASA) monitors

The ASA approved the *Standards for Basic Anesthetic Monitoring* in 1986 and last amended the document in 2005. This standard outlines the basic requirements for all anesthetics including cardiothoracic and vascular procedures. There are two essential standards outlined in the text:

- *Standard I*. Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics and monitored anesthesia care.
- *Standard II*. During all anesthetics, the patient's oxygenation, ventilation, circulation, and temperature shall be continually evaluated.

To ensure oxygenation, the standard prescribes that inspired oxygen concentration will be monitored with an oxygen analyzer with a low oxygen concentration limit alarm in use. The patient's oxygenation will be assessed using a quantitative method such as pulse oximetry. Further, when a pulse oximeter is used, the variable pitch pulse tone and a low threshold alarm shall be audible. Adequate exposure and illumination is required to assess patient color.

Ventilation shall be continually evaluated for adequacy. Means to determine adequacy include chest excursion, observation of the reservoir bag, auscultation, expired end-tidal carbon dioxide concentration monitoring and qualitative monitoring of the volume of expired gas. Airway manipulation involving a laryngeal mask airway or endotracheal tube shall have the device position confirmed with carbon dioxide monitoring. When ventilation is controlled by a mechanical ventilator, there shall be a disconnection device in place with an audible alarm. During regional anesthesia or monitored anesthesia care, ventilation shall be evaluated by continual observation of qualitative clinical signs and/or monitoring for the presence of end-tidal carbon dioxide.

Circulation will be assessed with the use of on electrocardiogram (ECG) continuously displayed during the duration of the anesthetic. An arterial blood pressure and heart rate will be determined at least every 5 minutes. Every patient shall further have at least one of the following continually monitored: palpation of a pulse, auscultation of

heart sounds, intra-arterial monitoring, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

Finally, every patient shall have their temperature monitored when clinically significant changes in temperature are intended, anticipated, or suspected.

These monitoring standards form the basis upon which all advanced monitoring of the cardiothoracic patient occurs. Advanced monitoring in the cardiothoracic patient involves both invasive and non-invasive strategies to assess circulation. In addition, the cardiothoracic patient may require advanced cerebral function monitoring. Finally, the cardiothoracic anesthesiologist is required to monitor advanced coagulation function monitoring. The remainder of the chapter will review the various components of this advanced monitoring stratagem.

Advanced electrocardiographic (ECG) monitoring

The Advanced electrocardiographic is a standard monitor during cardiac surgical procedures for monitoring heart rate, rhythm, and ischemia. A five-electrode ECG system capable of monitoring seven leads (I, II, III, aV_R, aV_L, aV_F, and V_5) is typical. In most operating room (OR) environments, leads II and V_5 are simultaneously monitored. The combination of these two leads provides the best surveillance for ischemia and arrhythmia detection (Fig. 3.1).

Dysrhythmia detection

Lead II usually allows P-wave identification and morphology allowing for easy dysrhythmia identification. In some tachydysrhythmias (paroxysmal atrial tachycardia, nodal rhythm, ventricular tachycardia), the P wave may be difficult or impossible to see in any of the standard leads. In other tachydysrhythmias (atrial fibrillation, atrial flutter), the P wave is absent. In some cases of AV nodal block or AV dissociation, the relationship between the P waves and the QRS complex may be difficult to discern with standard ECG leads. In such instances, the bipolar esophageal or intra-atrial ECG may be useful. Two electrodes are incorporated in either
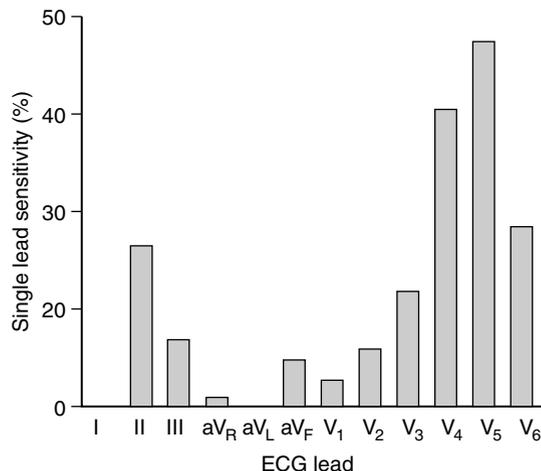
Fig. 3.1 The lead sensitivity in detecting myocardial ischemia is displayed. The combination of lead II and V_5 provides the greatest ability to detect ischemia and rhythm disturbances. (From London MJ, Hollenberg M, Wong MF, *et al*. *Anesthesiology* 1988;**69**:232–41, with permission.)

a 12-French esophageal stethoscope for pediatric patients or a 15-French esophageal stethoscope for adults. Alternatively, two of the three atrial electrodes from a pacing pulmonary artery catheter (PAC) can be used to obtain a bipolar intra-atrial ECG. The two leads from these electrodes are connected to the right arm and left arm jacks of a standard three-lead ECG system. The third lead of the three-lead ECG is connected to the patient via a skin electrode and lead I monitored. Because the esophageal and intra-atrial ECG place electrodes so proximal to the atria, there is augmentation of atrial activity such that the P wave is often larger than the QRS complex.

Ischemia detection

The presence of ECG changes is useful in the detection of myocardial ischemia. Specifically, ischemia alters repolarization causing either downsloping or horizontal ST-segment depression. Transmural ischemia and myocardial injury are associated with ST-segment elevation. In the case of coronary spasm, ST-segment elevations are likely to be the initial manifestation seen on ECG. For ECG monitoring to be effective in detecting ischemia, the appropriate leads must be monitored. Exercise

treadmill testing has demonstrated that 89% of the significant ST-segment depressions occurring during exercise can be detected in lead V_5. The addition of leads II, AV_F, V_3, V_4, and V_6 to lead V_5 increases the sensitivity of ischemia detection to 100% during exercise testing. Combining leads V_5 and II increase the sensitivity for detecting ischemic changes to 90%. This combination allows the most sensitive dysrhythmia and ischemia detection and is therefore the preferred lead selection in most OR environments.

It is important to understand ECG mode selection and ischemia analysis. The monitoring mode (0.5–40.0 Hz) filters out high and low frequency artifacts thereby attenuating the effects of extraneous interference from 60 cycle interference, electrocautery, respiratory variation, and movement. Unfortunately, this mode makes analysis of subtle ST segment changes unreliable. The diagnostic mode (0.05–100.00 Hz) reflects the true extent of ST segment changes but is more prone to interference. The monitoring mode is best selected when there is a low risk of ischemia; whereas, the diagnostic mode should be employed when ischemia is suspected or anticipated.

Automated ST-segment software is currently available on many intraoperative monitoring systems. These ST-segment analysis systems identify the QRS complex and then identify the isoelectric point in the P–R interval and a measurement point along the ST-segment (80 ms from the J-point). Most monitors analyze of two to three leads simultaneously allowing a more complete examination for ischemia. Alarms may be set for specific amounts of ST-segment deviation.

Arterial pressure monitoring

Arterial access allows beat-to-beat monitoring of arterial blood pressure as well as the ability to obtain arterial blood samples for analysis of partial pressure of oxygen (Po_2), partial pressure of carbon dioxide (Pco_2), pH, bicarbonate, and other electrolytes. The most common sites of arterial cannulation are the radial and femoral arteries in adults and children. In newborns the umbilical artery serves as an alternative to the radial or femoral arteries.

Radial artery cannulation

Radial artery cannulation can be accomplished in infants, children, and adults. A 24-gauge Teflon or polyurethane catheter is appropriate for infants <4–5 kg. A 22-gauge catheter is appropriate for infants and children weighing less than 30 kg, whereas a 20-gauge catheter is used in larger children and adults. The wrist is dorsiflexed over a roll of towel or gauze and secured on a short arm board. The thumb is taped back to reduce the mobility of the artery. Neither the dorsiflexion of the wrist nor the taping of the thumb should be so severe as to compromise the radial pulse. The puncture site should be approximately 2 cm proximal to the styloid process of the radius. After appropriate sterile prepping, the area of proposed puncture is anesthetized with 1–2 mL of 1% lidocaine in the awake patient. When using a 22-gauge catheter it is helpful to nick the skin with a needle directly over the artery prior to catheter placement. The skin nick helps prevent deformation of the catheter tip.

The catheter is introduced at an angle of 30° to the artery with the bevel of the needle directed upward. When blood flows freely out the end of the catheter, the angle between the catheter and the artery is reduced and the catheter and needle are advanced approximately 1–2 mm. At this point, both the catheter and needle should be within the vessel lumen, and the catheter can be advanced forward over the needle into the vessel. If there is no blood flow out the needle, it is likely that the posterior wall of the artery has been punctured. The needle and catheter are then intentionally advanced through the posterior wall. The needle is withdrawn partly from the catheter and the catheter is then withdrawn until its tip is located within the lumen of the artery and free flow of blood is noted. At this point, the catheter is advanced into the artery. Alternatively, a small guide wire (0.018) can be passed up a 24-, 22-, or 20-gauge catheter into the artery and often will facilitate advancement of the catheter (Fig. 3.2a–c).

Radial arterial cannulation is associated with a very low incidence of morbidity. An Allen's test to assess collateral circulation to the hand via the ulnar artery and palmar arch is frequently performed before cannulation of the radial artery. There is
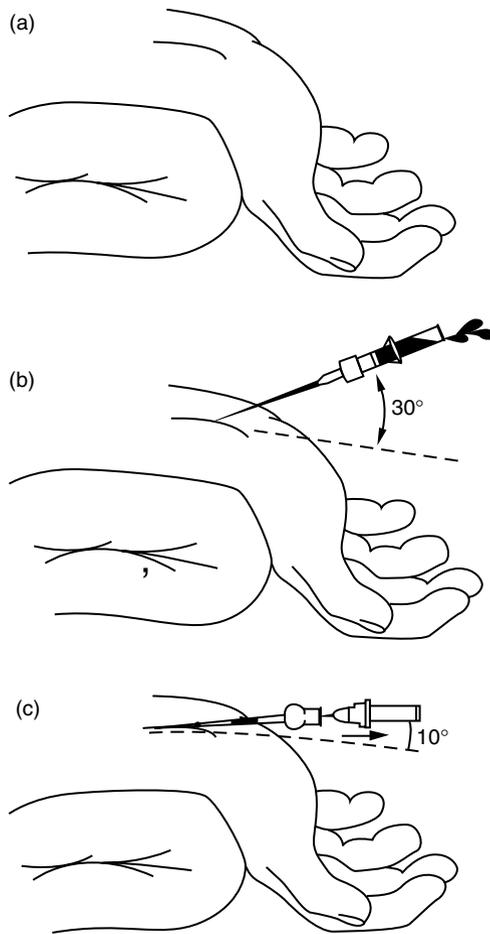
Fig. 3.2 Radial artery cannulation. (a) The wrist is positioned. (b) The artery is cannulated approximately 2 cm proximal to the styloid process of the distal radius. (c) The needle angle is reduced and the catheter advanced. (From Lake CL. *Cardiovascular Anesthesia*. New York, Springer-Verlag, 1985:54, with permission.)

controversy regarding the specificity and sensitivity of an Allen's test, however, and this examination is not universally applied. The radial artery catheter is most often placed into the wrist of the nondominant hand for patient comfort and convenience. In some instances, however, the radial artery catheter must be introduced preferentially into one radial artery or the other, as specified below:

• *Blalock–Taussig shunts*. For children undergoing these subclavian to pulmonary artery shunts, the radial artery contralateral to the subclavian artery being used must be used for monitoring. Likewise, for children with pre-existing Blalock–Taussig shunts, accurate arterial blood pressure will be obtained only in the contralateral arm.

• *Coarctation repair*. Arterial blood pressure is best monitored in the right radial artery for a variety of reasons: arterial blood pressure in the left arm may be lower than that in the right arm in the presence of hypoplasia of the aortic isthmus, a left subclavian artery patch may be used to repair the coarctation, or left subclavian artery circulation may be compromised by placement of aortic cross-clamps during the coarctation repair.

• *Thoracic aortic surgery*. Left subclavian artery flow may be compromised by surgical procedures on the distal arch or descending aorta; therefore, blood pressure should be monitored in the right radial artery. For procedures involving the ascending aorta, the left radial artery is a better choice.

Femoral artery cannulation

A 22-gauge, thin-wall needle to puncture the artery in infants and children weighing less than 30 kg can be used for femoral artery cannulation. After free flow of blood is obtained, a straight wire is passed through the needle up into the artery. For infants, a 2-inch 20-gauge catheter is passed into the artery over the wire. For children, a 3-inch 20-gauge catheter can be employed. For children weighing more than 30 kg, an 18-gauge thin-wall needle for arterial puncture and a 4-inch 18-gauge catheter is appropriate. For larger children and adults, an 18-gauge thin-wall needle for arterial puncture and a 6-inch 16- or 18-gauge catheter is used.

Femoral artery catheters have been used with a low complication rate for infants, children and adults. Hesitation to use femoral artery catheters in children stems from concern that damage to the poorly encapsulated hip joint may occur either directly, from sepsis or arterial occlusion and thrombosis. This does not seem to be a problem for infants and children when proper insertion techniques and catheter sizes are used. However, for infants younger than 1 month of age, the incidence of transient perfusion-related complications

(loss of distal pulse, limb coolness) has been reported to be 25% when a 20-gauge catheter is used. This is higher than the rate associated with radial or umbilical artery catheterization in this age group.

Umbilical artery cannulation

The umbilical artery cannulation may be obtained in the catheterization laboratory or in the intensive care unit (ICU) in neonates requiring invasive arterial pressure monitoring. A 3.5- or 5-French catheter is used for arterial monitoring. The catheter tip should lie just above the aortic bifurcation but below L3, or alternatively, above the diaphragm at the T7–T8 level.

Central venous access

Access to the central venous circulation is essential for cardiac surgical patients for a variety of reasons including secure intravenous (IV) access for volume and medication administration and advanced monitoring of volume status and cardiac function. The internal and external jugular veins and the subclavian veins are commonly used for central venous access in infants, children, and adults. The right internal jugular vein offers fairly constant anatomy with a straight course to the right atrium and a low complication rate. Attempts at left internal jugular venous cannulation may lead to injury to the thoracic duct, and for patients with congenital heart disease, the left internal jugular may drain into a persistent left superior vena cava. The left subclavian vein provides an alternative for patients with difficult or impossible internal jugular cannulation. For patients with communication between the right and left heart chambers, all peripheral and central venous lines must be kept clear of air bubbles to avoid potential systemic air embolization.

A wide variety of central venous catheters are available for use. For adults and large children, 7- and 8-French double- and triple-lumen catheters are available. For infants and children weighing <4 kg, 4-French double-lumen catheters 5 cm in length are available. For children weighing >4 kg, 5-French double-lumen catheters 5 or 8 cm in length are used.

Internal jugular cannulation

Three general approaches to the internal jugular using anatomical landmarks have been described: central, anterior, and posterior. The central approach involves localization of the internal jugular vein at the apex of the triangle formed by the two heads of the sternocleidomastoid muscle. The apex is lateral to the carotid pulse and generally is at the level of the cricoid cartilage (2–3 finger-breadths above the clavicle in adults). This approach applies to infants and children. The anterior approach involves localization of the vein at the lateral border of the medial head of the sternocleidomastoid at a point halfway between the clavicle and the mastoid. The posterior approach involves localization of the vein under the lateral border of the medial head of the sternocleidomastoid at the level of the cricoid cartilage. Regardless of the approach, extreme care must be exercised to ensure that the jugular vein is cannulated and not the internal carotid artery (CA). Ultrasound imaging of the internal jugular vein demonstrates large anatomic variability in the relationship between the jugular vein and the CA (Figs 3.3 & 3.4). In about half of children and adults, more than 75% of the right CA is overlaid by the right internal jugular vein when the head is rotated to the left. This overlap can be reduced somewhat by rotating the head less than 40% from the neutral position. Ultrasonic guidance facilitates catheter placement and may reduce the complication rate of central venous catheter placement. The following is recommended for cannulation of the internal jugular vein:

1 The patient is positioned with the head turned away from the intended cannulation site. Supplemental oxygen is supplied to nonanesthetized patients.

2 For adults and older children, the pillow is removed from beneath the head to produce a slightly extended neck position. For elderly patients with limited neck mobility, removal of the pillow may not be possible. For children, infants, and neonates, it may be necessary to place a small roll under the shoulders to prevent cranial hyperflexion due to the larger head size.

3 The anatomic outline of the clavicle and of the two heads of the sternocleidomastoid muscle are
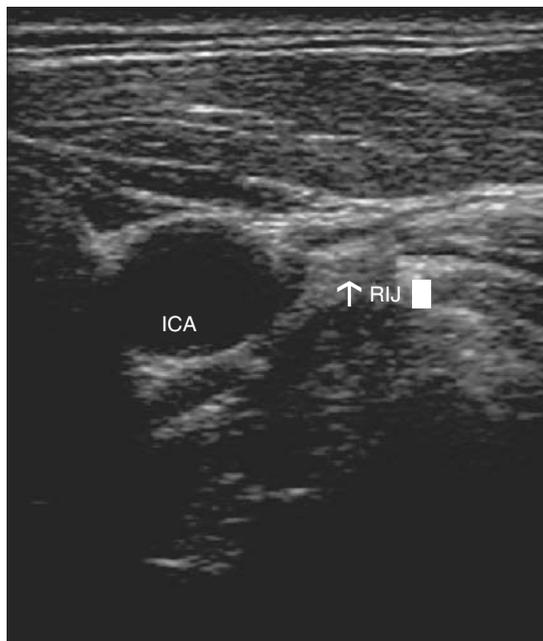
Fig. 3.3 The internal carotid artery (ICA) is well visualized. In this patient with spontaneous respiration, the right internal jugular vein is collapsed (RIJ).

Fig. 3.4 In this same patient with a Valsalva maneuver, the right internal jugular vein (RIJ) is now engorged and prominent, anterior and lateral to the internal carotid artery (ICA).

identified (some prefer to mark these structures with a pen). In nonanesthetized patients, lifting the head off the bed will help define these landmarks. An ultrasonic probe (5.0–7.5 MHz) is placed on the neck using ultrasonic gel. The relationship of the internal jugular and CA relative to each other and to the anatomic markings is noted. The depth of the vein below the skin surface also is determined. Head position can be altered to provide the least amount of overlap of the internal jugular and CA without compromising access to the neck. Ultrasonography further allows one to determine whether the internal jugular is small, absent, thrombosed or compressed from extravascular structures (i.e. hematoma from previous attempts). This may prompt a look at the contralateral internal jugular or move to a subclavian vein cannulation.

4 The neck is prepped and draped using sterile technique. The operator is gowned and gloved. For awake patients, local anesthesia is accomplished with 1% lidocaine in the area of the intended needle puncture. Deeper infiltration should be performed

with caution because the vein is not very deep below the skin. The patient is placed in a 10–15° Trendelenberg position. This positioning increases the size of the internal jugular and reduces the risk of air embolus. It is best to wait until the last minute to do this for patients with pulmonary venous congestion or poor ventricular function because prolonged periods in the Trendelenberg position may exacerbate pulmonary venous congestion and heart failure. In nonanesthetized patients, this may result in patient discomfort, dyspnea, agitation and lack of cooperation.

5 A 25-gauge 5/8-inch needle is used to locate the center of the vein in all but the largest of adults. A $1\frac{1}{2}$-inch 22-gauge needle rarely is needed to localize the internal jugular. There is no need to keep a hand on the CA after the vein position has been localized with ultrasound. This maneuver only serves to compress the internal jugular.

6 After the vein is localized, the finder needle can be left in place or removed. The appropriate-sized

thin-wall needle is inserted through the skin in the same orientation as the finder needle. The thin-wall needle is advanced. If the skin is depressed or dimpled inward, the vein is at least partially compressed. When dimpling occurs, the skin should be allowed to "rebound." This does not mean pulling the needle back out of the skin, it means relieving pressure to allow the skin to return to a neutral position. Some compression of the vein by the larger thin-wall needle is inevitable, but when the needle is advanced without compressing the skin, it is more likely that the vein will be entered on the way in and less likely that the vein will be transfixed and the CA will be punctured. Often, when the skin is allowed to rebound, free flow of internal jugular blood is obtained without any further advancement of the needle.

7 When free flow of internal jugular blood is obtained, the thin-wall needle is fixed in place with the fingers of the left hand while the hypothenar eminence rests on the patient. A flexible J-wire is advanced into the thin-wall needle and vein. If the wire goes a short distance out the end of the needle and resistance is met, advancement of the wire while spinning it with the right hand should be attempted. If resistance is still met, the wire can be left in place and the thin-wall needle can be removed. An appropriate-sized IV catheter is then placed over the wire and advanced into the vein. The guide wire is removed and a syringe is attached to the catheter. The syringe is aspirated and the catheter is withdrawn until free flow of blood is obtained. The catheter is then advanced into the vein and the guide wire is reintroduced.

8 If there is any doubt that the thin-wall needle or catheter is in the internal jugular, the needle or catheter should be connected to the monitor and the venous (or arterial) waveform identified. Checking the color of the blood or the blood flow through the catheter are unreliable indicators of arterial cannulation.

9 When the guide wire is in place in the internal jugular (it is reassuring and common to see some ventricular ectopy as the wire is advanced), a skin nick is made with a knife. The skin nick should be contiguous with the wire; that is, there should not be a skin bridge between the wire and the incision made with the knife. The dilator is passed over the wire. The dilator should only be passed once and only deep enough to pass through skin, soft tissue, platysma, and into the vein. The dilator is removed and gentle pressure is held over the dilated puncture site until the central venous pressure (CVP) catheter or PAC introducer is placed.

10 For instances in which venous access is difficult or large transfusion requirements are anticipated, two catheters can be placed in the same internal jugular. In this "double-stick" technique, one guidewire is placed and then a second guidewire is placed through a second puncture site 1–2 cm above or below the first one. The cannulation process is then the same as described previously.

The most common complication of the internal jugular approach is carotid puncture (4%). Other potential complications of the internal jugular approach include pneumothorax, thoracic duct injury, brachial plexus injury, and air embolism.

External jugular cannulation

The external jugular approach is complicated by the presence of a system of venous valves, which can make the placement of a guidewire and, subsequently, a catheter into the central circulation, difficult. The advantage of this approach is that there is little or no risk of carotid puncture, pneumothorax, thoracic duct injury, or brachial plexus injury. For adults, the use of a guidewire with a flexible J-shaped tip increases the success rate of this approach to 75–95%, compared with 95% for the internal jugular route. In children, the success rate of this approach is approximately 60%. Clinically silent venous thrombosis in pediatric patients is high when the external jugular catheter does not reach the central circulation.

Central circulation pressure monitoring

Pulmonary artery catheter monitoring

PACs are multilumen, multipurpose catheters available in a variety of sizes (5-, 7-, and 7.5-French). A typical PAC contains the following

components:

1 A proximal lumen that terminates in a port located 30 cm (7- and 7.5-French) or 15 cm (5-French) from the distal end of the catheter. When the catheter is positioned properly, this proximal port will be located in the right atrium. This lumen is used to measure right atrial pressure (RAP) and to inject fluid of a known volume and temperature for determination of a thermodilution (TD) cardiac output.

2 A distal lumen that terminates in a port located at the distal end of the catheter. This lumen measures pressures as the catheter is advanced into position and, when the catheter is properly positioned, is used to measure pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure (PADP) and pulmonary capillary wedge pressure (PCWP).

3 A balloon located 1 mm from the distal end of the catheter. This balloon is connected to the proximal end of the catheter by a lumen that runs the length of the catheter. The balloon can be filled with air from a syringe located at the proximal end. The 7- and 7.5-French catheters have a 1.5-mL balloon, and the 5-French catheter has a 1-mL balloon. When the balloon is inflated, the catheter is directed forward in the flow of blood. Balloon inflation is used whenever the catheter is advanced. When the catheter is positioned properly in the pulmonary artery, inflation of the balloon will result in the balloon occluding a branch of the pulmonary artery. The pressure tracing obtained from the distal port at this point will be a measure of the PCWP. As described in Chapter 2 it is technically the pulmonary artery occlusion pressure (PAOP) that is measured.

4 A thermistor is located at the distal end of the catheter just proximal to the distal port and the balloon. The thermistor is connected to one or more plugs at the proximal end of the catheter, which are used to interface the thermistor with a cardiac output computer.

5 The catheter is labeled in 10-cm increments from the distal end of the catheter.

6 Optional features in PACs include:

a An additional lumen for drug infusion.

b An additional lumen for placement of a bipolar right ventricular endocardial pacing wire.

c Atrial and ventricular pacing electrodes for bipolar endocardial atrial, ventricular, and atrioventricular (AV) sequential pacing. These catheters contain three atrial electrodes and two ventricular electrodes. Two electrodes must be in contact with the endocardium for successful pacing. Considering the variations in patient size and the length of catheter necessary to properly position a PAC, the presence of three atrial electrodes increases the likelihood that two electrodes will be in contact with the atrial endocardial surface. These catheters are 80% effective in establishing atrial, ventricular, and AV sequential pacing.

d The addition of fiberoptic bundles, which allow continuous determination of mixed venous oxygen saturation by reflective spectrophotometry. Light of selected wavelengths is transmitted down a fiberoptic bundle, the tip of which is located in the pulmonary artery. This light is transmitted through blood flowing past the fiberoptic bundle and is reflected back to be transmitted down another fiberoptic bundle to be analyzed by a photodetector. The differential absorption of known wavelengths of light by oxyhemoglobin and deoxyhemoglobin is used by a computer to determine mixed venous oxygen saturation. The use of continuous mixed venous oxygen saturation measurements will be discussed in detail later.

e The ability to perform continuous cardiac output determinations using a thermal filament.

f The ability to measure right ventricular ejection fraction using a rapid-response thermistor PAC (discussed in detail later).

PAC placement

In cardiac surgery, PACs usually are introduced percutaneously into the right heart and pulmonary artery via an introducer placed in the right internal jugular vein. For adults and large children, 7-, 7.5-, and 8.0-French catheters are used and are placed through an 8.5- or 9.0-French introducer. The 5-French catheter is used in smaller children (weighing 15–40 kg) and is placed through a 6-French introducer.

During placement, the patient should be monitored with a continuous ECG display. A defibrillator should be in the room and in working order.

The defibrillator should be capable of being synchronized with the ECG signal to allow cardioversion as well as defibrillation. The catheter must be placed under sterile conditions by the operator. The catheter is placed in a sterile sheath, and the proximal end of the catheter is handed off to an assistant, who uses the syringe to test balloon inflation. The fully inflated balloon should protrude out over the distal end of the catheter and inflate symmetrically. The assistant also should connect the proximal and distal lumens to their respective transducer/flush systems. The proximal lumen will be used to measure the RAP while the distal lumen will be used to measure the PASP, PADP, and PCWP. The distal lumen trace must be visible on the monitor screen as the catheter is advanced. Finally, the TD cardiac output computer should be connected to the appropriate jack and the correction factor for the catheter being used should be programmed into the computer.

The catheter is held, loosely coiled, in the operator's hand with the tip pointed toward the patient's left (toward the right ventricle and pulmonary outflow tract). The catheter is placed into the introducer and advanced 20 cm for older children and adults and 10 cm for smaller children. At this point, the balloon is inflated and the catheter is advanced with a smooth motion. For adults and older children, a RAP trace will be seen on the distal lumen trace at approximately 20–30 cm. For smaller children, this will occur at approximately 10–15 cm. Smooth catheter advancement with the balloon inflated continues until the right ventricular trace is seen, followed by the PASP trace and finally the PCWP trace.

Catheter advancement stops when the PCWP trace is seen. For adults and older children, the PCWP trace will be seen at approximately 45–55 cm. In smaller children, the PCWP trace will be seen at approximately 25–35 cm. Deflation of the balloon at this time should result in reappearance of the PASP trace. If the PCWP trace remains after balloon deflation, the catheter should be pulled back. The catheter should not remain in the PCWP position for any longer than it takes to measure PCWP. Excessive balloon inflation can lead to pulmonary artery rupture or pulmonary infarction.

If the catheter is advanced more than 10–15 cm (5–10 cm for smaller children) before the trace from the next expected chamber or vessel is noted, the catheter may be coiling in the right atrium or ventricle. At this point, the balloon should be deflated, the catheter should be drawn back into the sheath. The catheter can then be advanced again after inflation of the balloon. Catheter coiling may ultimately lead to catheter knotting.

If coiling occurs, several things can be tried to advance the catheter out of the RA or RV:
1 Remove the catheter from the introducer and make certain that the balloon inflates properly.
2 Orient the curve of the catheter so that it is more anterior than medial as it enters the introducer. This may help direct it toward the tricuspid valve orifice.
3 After multiple attempts, the catheter may soften. This can be remedied by flushing the distal port with 2–3 mL of iced saline or by gently twisting the catheter as it is advanced.
4 For awake patients, taking a deep breath may enhance blood flow out the RA and the right ventricular outflow track. For anesthetized patients, release of a Valsalva maneuver may accomplish the same thing.
5 Putting the patient in the head-up position and/or rotating the bed left or right may help as well.

Most patients with congenital heart disease are not candidates for percutaneous placement of PACs. Some of the reasons and considerations in these patients include:
1 Some patients (less than approximately 15 kg) are too small for the 5-French catheters.
2 In some patients, percutaneous placement of a PAC may be difficult or impossible. For example, the presence of a large atrial septal defect or a ventricular septal defect may make placement difficult without the use of fluroscopy. Similarly, the presence of tricuspid atresia, pulmonary atresia, or pulmonary stenosis make percutaneous placement impossible.
3 The PAC may interfere with the surgical repair and may have to be removed intraoperatively.
4 If necessary, catheters can be placed directly into pediatric patients by the surgeon immediately before termination of cardiopulmonary

bypass (CPB). A thermistor probe (2.5-French) or a thermistor probe combined with a distal lumen (4-French) may be placed directly into the pulmonary artery via the right ventricular outflow tract. When combined with a directly placed right atrial catheter (3.5-French), these will allow determination of TD cardiac outputs. Because these catheters do not allow determination of PCWP, a left atrial pressure (LAP) line may be placed by the surgeon as well. These lines may be placed directly into the left atrium or into the left atrium via the right superior pulmonary vein. Caution must be exercised with left atrial lines to avoid introduction of air into the systemic circulation.

Central venous and pulmonary artery pressure (PAP) measurements

Right and left atrial pressure

Right atrial pressure (RAP) is monitored directly through the proximal lumen, whereas LAP is not directly measured by the PAC. The PCWP will be an accurate assessment of LAP, except for instances in which there is pulmonary venous obstruction (rare) or in which the pulmonary alveolar pressure exceeds pulmonary venous pressure. In these instances, PCWP will reflect pulmonary alveolar pressure (Palv). Pulmonary alveolar pressure will exceed pulmonary venous pressure (Pv) when the distal port lies in zone one (PAP < Palv > Pv) or zone two (PAP > Palv > Pv) of the lung. Fortunately, most catheters (93%) reside in zone three (PAP > Palv < Pv) portions of the right middle and lower lobes.

The RAP trace usually is of higher quality than the PCWP trace because the LAP changes are damped as they are transmitted through the pulmonary vasculature to be detected by the distal port. The RAP and LAP traces normally contain A, C, and V waves as well as X and Y descents (Fig. 3.5).

A wave

The A wave reflects the atrial pressure increase seen during atrial systole. Atrial systole occurs at ventricular end diastole and is commonly called the atrial kick. The peak of the right atrial A wave
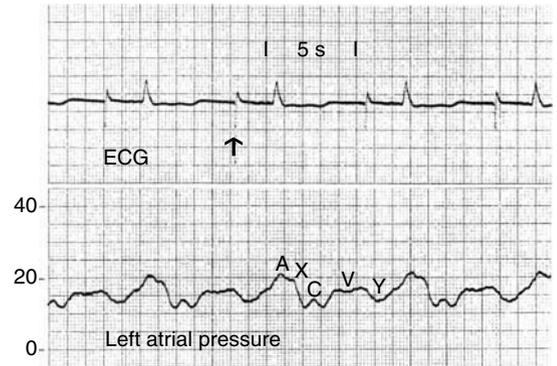
Fig. 3.5 Left atrial pressure (LAP) obtained from a patient undergoing left atrial pacing. Arrow shows pacer spike. The paper speed is 50 mm/s and clearly shows the A, C, and V waves as well as the X and Y descent. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

follows the peak of the P wave on the ECG by 80 ms when simultaneous RAP and ECG traces are compared. The peak of the left atrial A wave follows the peak of the P wave by 240 ms due to the later depolarization of the left atrium compared with the right atrium. The peak A-wave pressure is the best estimate of ventricular end-diastolic pressure, particularly when ventricular compliance or distensibility is poor (Fig. 3.6). Obviously, no A wave will be present when atrial systole is absent, as in atrial fibrillation and atrial flutter. For instances in which atrial systole is not synchronous with ventricular diastole, atrial contraction may occur in the presence of a closed tricuspid or mitral valve during ventricular systole. This will result in production of a large A wave (cannon A wave) because the atrium cannot empty via the closed tricuspid or mitral valve. Cannon A waves may be seen during nodal rhythms with retrograde atrial depolarization (Fig. 3.7), re-entrant supraventricular tachycardia in which ventricular activation precedes atrial activation, and heart block with nonconducted atrial activity occurring during ventricular systole. Cannon A waves also may be seen in instances in which atrial and ventricular contraction are synchronous but in which atrial outflow is prevented by tricuspid or mitral atresia.
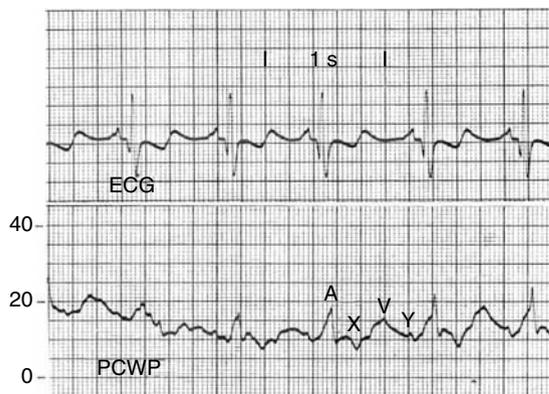
Fig. 3.6 Pulmonary capillary wedge pressure (PCWP) trace from a patient with aortic stenosis and concentric left ventricular hypertrophy. A large A wave is clearly seen. The peak A-wave pressure at end-expiration is 18 mmHg; this is the best estimate of left ventricular end-diastolic pressure. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
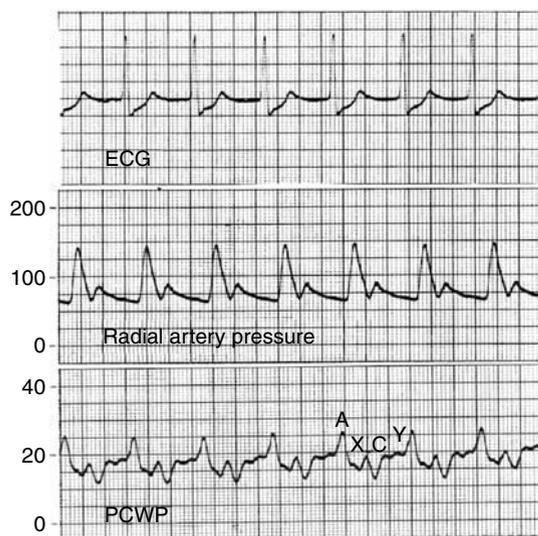
Fig. 3.7 Pulmonary capillary wedge pressure (PCWP) obtained from a patient in a nodal rhythm with retrograde atrial activation. Cannon A waves are present. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

C wave

The C wave reflects movement of the tricuspid or mitral valve annulus into the atrium during the iso-volumic phase of ventricular systole and is often not well seen. The C wave follows the A wave by a time interval equal to the P–R interval and is seen best when the P–R interval is prolonged.

V wave

The V wave represents passive atrial filling while the tricuspid and mitral valves are closed during ventricular systole. The peak V-wave pressure will be determined by the compliance of the atrium and the volume of blood that enters the atrium during passive filling. In the right atrial trace, the V wave peaks near the end of the ECG T wave, whereas the left atrial V wave peaks after the T wave.

A large V wave may be produced by tricuspid or mitral regurgitation (Figs 3.8 & 3.9). In this setting, the V wave represents a combination of passive atrial filling and regurgitation of blood into the atrium via the incompetent valve during ventricular systole. Commonly, the height and duration of the V wave is used to quantitate tricuspid or mitral regurgitation. Such conclusions must be drawn carefully, however, because the duration of systole, the extent of mitral or tricuspid valve impairment, atrial compliance, the systolic performance of the ventricle, and the impedance to ejection via the pulmonary artery or aorta all contribute to the height and duration of V waves.

It is important to note that other factors may be responsible for production of a large V wave. A large volume of blood returning to the atrium and poor atrial compliance will both produce large V waves. For example, in the presence of a ventricular septal defect with a two-to-one left-to-right shunt, left atrial venous return will be twice that of right atrial return. Likewise, in the presence of poor ventricular systolic performance, preload reserve may be exhausted to meet baseline cardiac output demands. In both instances, the large preload requirements will result in atrial distension, with the atrium functioning on the steep portion of its compliance curve. This reduced atrial compliance will result in the production of a large V wave during passive atrial filling.

Fig. 3.8 Pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) from a patient with mitral regurgitation. The presence of the large V wave may make distinguishing PAP from PCWP difficult. Close examination shows that the peak of the PAP trace occurs much earlier in the electrocardiogram (ECG) cycle than the V wave in the PCWP trace. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
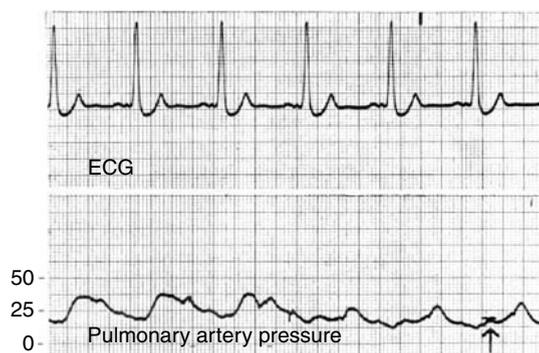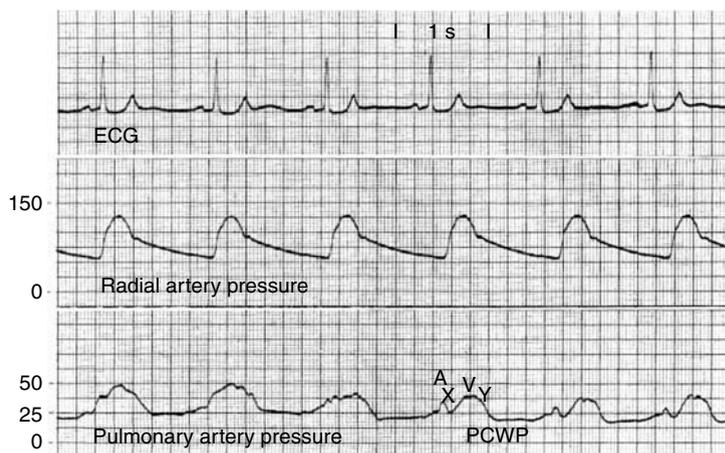
Fig. 3.9 Pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) in a patient with mitral regurgitation. The PCWP V wave is clearly seen. The arrow points to the end-diastolic pressure in the PCWP trace. This pressure is approximately 18 mmHg and is the best estimate of left ventricular end-diastolic pressure (LVEDP). (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

Differentiating the PAP trace from the PCWP can be difficult in the presence of large V waves because of the similarity of the two traces. Failure to recognize the V wave of the PCWP can result in over advancement of the PAC into a distal pulmonary artery, increasing the likelihood of a catheter-induced pulmonary artery perforation. Use of simultaneously obtained PAP and systemic artery pressure or ECG traces can be used to differentiate the two traces. It has been demonstrated that the peak of the pulmonary artery trace normally occurs approximately 130 ms after the upstroke of a simultaneously recorded systemic arterial trace, whereas the peak of the V wave occurs approximately 350 ms after the systemic arterial upstroke. Similarly, the peak of the V wave will occur later in the ECG cycle than the peak of the PAP wave.

X and Y descent

The X descent follows the A and C waves and reflects a combination of the downward displacement of the tricuspid and mitral valve with the onset of ventricular systole and atrial relaxation following atrial systole. The Y descent follows the V wave and reflects rapid atrial emptying after opening of the tricuspid and mitral valves. Thus, the Y descent also reflects early diastolic filling of the ventricle. In the presence of pericardial tamponade, the X descent usually will remain visible while the Y descent will be attenuated. In pericardial tamponade, diastolic filling of the heart chambers is impeded because the potential space available for expansion of the heart in the pericardium is largely eliminated when the pericardium is filled with fluid. For this reason, passive filling and expansion of the ventricle as reflected in the Y descent is attenuated. To the contrary, the X descent is preserved because it reflects a decrease in pericardial volume as atrial relaxation and ventricular systole begin.

For patients with constrictive pericarditis, early diastolic filling of the ventricle is not compromised as it is in pericardial tamponade. Constrictive pericarditis is characterized by impairment of ventricular filling in late diastole. Because early diastolic filling is not impaired and because atrial pressure is elevated, the Y descent is more prominent than normal in constrictive pericarditis. As in pericardial tamponade, the X descent remains prominent. This combination of prominent X and Y descents gives a characteristic shape to the atrial pressure curve, which is often referred to as the M or W sign.

Pulmonary artery pressure

A determination of systolic, mean, and diastolic PAP can be made with a PAC. In the presence of normal pulmonary vascular resistance, the diastolic PAP will overestimate the PCWP by 2–3 mmHg. In the presence of increased pulmonary vascular resistance, the diastolic PAP will overestimate PCWP and cannot be used as a substitute measurement.

Limitations

There are major limitations to accurate measurement and interpretation of intracardiac and PAPs. Common errors include a failure to properly zero the transducers, placement of the transducer at an inappropriate level relative to the patient (transducer too low reports a spuriously high pressure), catheter whip, and catheter dampening.

Determination of mean pressure

Monitor systems designate systolic, diastolic, and mean pressures as the average highest, lowest, and mean pressures obtained during a preset time interval or a series of such intervals. The electronically determined mean RAP and PCWP will be skewed upward by the presence of large V waves. This will cause mean RAP or PCWP to overestimate ventricular end-diastolic pressure. A device to provide calibrated paper printout of pressure traces is useful in analysis of pressure traces. These paper traces can be used for accurate determination of A- and V-wave pressures as well as systolic and diastolic PAP. The best estimate of ventricular end-diastolic pressure will be the peak A-wave pressure. For patients without an atrial systole, the best estimate of ventricular end-diastolic pressure will be the RAP or PCWP at end diastole. This can be determined by obtaining simultaneous ECG and RAP or PCWP paper traces. End-diastolic pressure in the RAP trace is determined at a point approximately 40 ms before the start of upstroke of the QRS complex. End-diastolic pressure in the PCWP trace is determined at the QRS ST-segment junction.

Changes in pleural pressure

Transmural pressure, i.e. the pressure acting to distend a heart chamber, is determined by the pressure–volume relationship of the chamber. Intracardiac pressures (such as RAP and PCWP) are equal to the transmural pressure plus the juxtacardiac pressure. Transmural and intracardiac pressure will be equal as long as juxtacardiac pressure is zero. Pleural pressure is a major determinant of juxtacardiac pressure. Pleural pressure will be negative during spontaneous inspiration and positive during controlled inspiration and forced exhalation. Large fluctuations in pleural pressure will cause intracardiac pressure to over- and underestimate transmural pressure and preload. Ideally, all intracardiac pressure determinations should be made at passive end-expiration, when pleural pressure is close to zero (atmospheric pressure).

If positive end-expiratory pressure (PEEP) is added to the ventilation circuit, the juxtacardiac pressure at end expiration may be greater than atmospheric pressure; this will cause intracardiac pressure to overestimate transmural pressure and preload. How much a given quantity of PEEP will elevate juxtacardiac pressure depends on the relationship of lung and thoracic compliance. Under normal circumstances, the juxtacardiac pressure is expected to rise by approximately one half the value of the added PEEP. Thus, if 10 cm H_2O of PEEP is added, the juxtacardiac pressure can be expected to increase by 5 cm H_2O. When lung compliance is high (emphysema) and thoracic compliance is low (obesity), a larger proportion of the added PEEP will be added to the juxtacardiac pressure. A smaller proportion will be added in cases where lung compliance is poor (acute respiratory distress syndrome) and thoracic compliance is high (muscle relaxation).

Ventricular preload and pressure measurements

Ventricular preload is defined as the ventricular end-diastolic volume. Unfortunately, methods of obtaining measurements of ventricular end-diastolic volume are not possible in a clinical environment. In the absence of tricuspid or mitral stenosis, the A wave of the RAP and LAP (as measured by PCWP) traces are good estimates of the right and left ventricular end-diastolic pressures. If we assume that the ventricular pressure–volume relationship does not vary, then measurement of ventricular end-diastolic pressure is as good an assessment of preload as ventricular end-diastolic volume. Unfortunately, the shape of the ventricular pressure–volume relationship is not linear. Furthermore, changes in ventricular distensibility and compliance alter the relationship between ventricular pressure and volume. It is not surprising, then, that changes in PCWP and LAP have been shown to correlate poorly with changes in left ventricular end-diastolic volume in both the pre- and post-CPB periods.

Thermodilution cardiac output determination

Thermodilution (TD) cardiac output is a modification of the indicator dilution method in which flow is determined from the following relationship:

Known amount of indicator injected

    × time/measured concentration of indicator

In the bolus TD method, the indicator is a crystalloid injectate (usually 5% dextrose in water or isotonic saline) at a temperature lower than the blood temperature. Blood temperature is measured by a thermistor in the pulmonary artery. Crystalloid temperature is measured by separate thermistor. A predetermined volume of crystalloid is injected into the right atrium. Adequate mixing of the crystalloid and blood occurs before passage into the pulmonary artery, and the change in blood temperature over time after injection of the crystalloid is measured by the thermistor in the pulmonary artery. Cardiac output in liters per minute can be calculated with the aid of a computer and

the equation:

$$\text{Cardiac output} = V_1 \times S_1 \times C_1 \times (T_B - T_1)$$
$$\times\, 60/S_B \times C_B \int \Delta T_B(t)\, dt$$

where V_1 is the volume of the injectate; S_1 and S_B are the specific gravity of the indicator and the blood, respectively; C_1 and C_B are the specific heat of the indicator and the blood, respectively; and T_1 and T_B are the temperature of the indicator and the blood, respectively. $(S_1 \times C_1)/(S_B \times C_B) = 1.08$ when isotonic saline or 5% dextrose is injected. $\Delta T_B(t) dt$ is the temperature–time curve measured by the pulmonary artery thermistor after indicator injection. $\int \Delta T_B(t)\, dt$ is the area under the temperature–time curve.

A computer extrapolates the exponential down slope of the temperature–time curve to the baseline and then determines the area under the curve. With all variables thus known or measured the computer solves the equation for cardiac output.

Two recent modifications of the bolus TD technique deserve attention: continuous cardiac output (CCO) monitoring and RV ejection fraction (EF) catheters.

The CCO technique makes use of a thermal filament located between the 15- and 25-cm gradations on the PAC. No injectate is necessary. This filament infuses, on the average, 7.5 W of heat, heating the blood as it passes by. Although warmed, the blood temperature always remains below 44°C. The resulting temperature change is detected downstream in the pulmonary artery and cross-correlated with the input sequence to produce a TD washout curve. This requires use of a signal processing system with an enhanced signal-to-noise ratio because the thermal input is low relative to the background PA thermal activity. The monitor displays the average cardiac output from the previous 3–7 minutes updated every 30 seconds. In the Stat mode, a new cardiac output can be obtained every 45–60 seconds. In this mode, fast trend estimates of cardiac output can be obtained when an unstable thermal signal is present. These catheters also can be used to obtain standard bolus injectate cardiac outputs.

Clinical studies have demonstrated a close correlation between TD cardiac output determinations made with the bolus and CCO techniques in a relatively stable ICU environment. A major advantage of the CCO technique would be the ability to monitor acute changes in cardiac output (CO) as they occur in real time. In the Stat mode, these changes can be tracked approximately every minute; in the standard mode, changes are averaged over time and show data more consistent with a trend over time. In either mode, the changes in CCO lag behind those seen with mixed venous saturation monitoring.

Right ventricular ejection fraction (RVEF) catheters are another modification of the bolus injectate catheter. RVEF catheters incorporate:

• a rapid response thermistor, which has a reaction time of 50 ms compared with the 300–1000 ms response time of standard bolus injectate PACs.

• a multi-hole injectate port located 21 cm from the catheter tip to ensure complete mixing of the injectate in the RV.

• two ECG electrodes, which enable the computer to detect the R wave.

• This arrangement allows beat-to-beat determination of PA temperature changes. The injectate mixes and equilibrates with RV blood within two beats. There is an exponential decrease in the amount of indicator ejected with each subsequent beat. PA concentrations of indicator for each beat are equal to the RV end-diastolic concentration of indicator for that beat. This produces a series of diastolic temperature plateaus that are identified by the computer. The RVEF is calculated as follows from three diastolic plateaus using the equation:

$$EF = 1 - RF_{mean}$$

where

$$RF_{mean} = (RF_1 - RF_2)/2$$

$$RF_1 = (T_2 - T_B)/(T_1 - T_B)$$

$$RF_2 = (T_3 - T_B)/(T_2 - T_B)$$

where T_1, temperature at first diastolic plateau; T_2, temperature at second diastolic plateau; T_3, temperature at third diastolic plateau; and T_B, blood temperature.

• Stroke volume (SV), right ventricular end-diastolic volume (RVEDV), and right ventricular end-systolic volume (RVESV) are calculated as follows:

$$SV = CO/HR$$

$$RVEDV = SV/EF$$

$$RVESV = RVEDV - SV$$

The normal RVEF = 0.4. Good correlations between PAC determined RVEF and radionuclide determined RVEF have been reported.

• Several points regarding TD CO techniques (bolus, RVEF, and CCO) are worth emphasizing:

a TD CO is a measure of pulmonary blood flow, which in the absence of shunting (both intracardiac and systemic to pulmonary artery), is equal to forward right heart output.

b Cardiac output is inversely proportional to the area under the pulmonary artery temperature time curve.

c There are large cyclical variations in the TD determination of cardiac output during the different phases of mechanical ventilation. This seems to be due to cyclic variations in pulmonary blood flow and temperature. For this reason, bolus measurements obtained at random during the ventilatory cycle will exhibit a great deal of variability, whereas those obtained during the same phase of the ventilatory cycle will have the greatest reproducibility. It has been demonstrated that multiple cardiac output values obtained at end expiration or peak inspiration in ventilated patients have high reproducibility. The highest measured TD CO occurs at peak inspiration, whereas the lowest occurs at end expiration. Triplicate TD CO determinations are commonly made at end-expiration because end-expiration is the easiest phase of respiration to detect clinically. This practice provides excellent reproducibility but tends to underestimate the average cardiac output over one full cycle of mechanical ventilation.

d Injectate temperatures from 0°C to room temperature are used. The lower temperatures are obtained by placing the injectate in an ice bath. The accuracy and variability of TD CO in adults is similar with either 10 mL of room temperature or iced injectate. Sinus bradycardia and atrial fibrillation have been

reported in conjunction with iced injectate for cardiac output determination. The slowing of the sinus rate is likely due to cooling of the sinus node.

- TD cardiac output is inaccurate in the presence of:

a Low cardiac outputs. Cardiac output is overestimated because low flow allows the cold injectate to warm and reduces the area under the TD curve.

b Left-to-right intracardiac shunts (atrial septal defect, ventricular septal defect). Computer analysis of the temperature–time curve often is not possible due to recirculation of indicator (cold water) through the pulmonary vasculature, which results in interruption of the exponential downslope of the temperature–time curve with a prolonged, flat deflection. The larger the shunt, the earlier the recirculation curve interrupts the normal downslope. Manual planimetry has been used to determine the area under the two portions of these curves. The ratio of the area under the terminal deflection of the curve to the area under the entire curve has been shown to be an accurate estimate of the ratio of pulmonary to systemic blood flow.

c Tricuspid regurgitation. Regurgitation of a fraction of the cold injectate results in delayed clearance of the indicator from the right heart. This causes the TD curve to be broad and of low amplitude, which results in inaccurate assessment of forward cardiac output. In the presence of TR TD cardiac output tends to underestimate true cardiac output at high cardiac outputs and to overestimate it at low cardiac outputs. Similar problems are encountered with CCO catheters.

d Rapid infusion of volume via peripheral IV catheters. Abrupt increases in the infusion rate of IV solutions within 20 seconds of a bolus TD CO determination have been shown to result in variations of up to 80% in TD CO. The precise timing of the infusion rate increase relative to the TD CO measurement determines whether the output will be an over- or underestimate. It is recommended that volume infusions be terminated or held at a constant rate for at least 30 seconds before a TD CO determination. Likewise, rapid infusions of cold IV solutions affect the accuracy of CCO catheters.

The accuracy of bolus TD CO determinations in the period immediately following termination of CPB is questionable. Bolus TD COs have been shown to underestimate true cardiac output by approximately 0.5 L/min in the first 10 minutes after termination of CPB due to a downward drift of the temperature baseline in the pulmonary artery. Another source of bolus TD CO error in the first 30 minutes after termination of CPB is the presence of respiratory variations or thermal noise in the pulmonary artery blood temperature. These thermal variations in pulmonary artery blood temperature may cause large variations in the bolus TD CO determinations made at the various points in the respiratory cycle. This problem can be minimized by measuring bolus TD CO at the same point in the respiratory cycle or eliminated by holding ventilation during bolus TD CO determination.

Similar considerations may exist for the CCO technique. In theory, the data processing of the CCO system should minimize the effects of baseline temperature shift and of thermal noise and improve performance. There is a poor correlation between bolus TD CO and CCO during the first 45 minutes after termination of CPB. The "stat" mode should be used during this interval.

Continuous mixed venous oxygen saturation (Svo_2) monitoring

Svo_2 monitoring is available with some PACs. The Svo_2 is measured in the main pulmonary artery by oximetry. The main pulmonary artery is the location of the most reliable site of true mixed venous (SVC, IVC, and coronary sinus) blood. In infants and children where SVC saturation is used as a surrogate for mixed venous saturation surgically placed oximetric SVC catheters can be used. In either case, the Svo_2 is used to determine total tissue oxygen balance. It will not reflect regional oxygen imbalance (Table 3.1). Several definitions are in order:

- Oxygen (O_2) delivery (Do_2) = cardiac output (CO) × O_2 content.
- Arterial oxygen content (Cao_2) = (hemoglobin (Hgb) × 13.8) (Sao_2) + (0.003 × Pao_2).
- Mixed venous oxygen content (Cvo_2) = (Hgb × 13.8) (Svo_2) + (0.003 × Pvo_2).
- Oxygen consumption (Vo_2) = the metabolic rate or the amount of oxygen consumed by the body.

Table 3.1 Limitations of mixed venous oxygen saturation monitoring. (From Marx G, Reinhard K. *Curr Opin Crit Care* 2006;**12**:263–8, with permission.)

SvO$_2$ level	Consequences
SvO$_2$ > 75%	Normal extraction; O$_2$ supply > O$_2$ demand
75% > SvO$_2$ > 50%	Compensatory extraction; increasing O$_2$ demand or decreasing O$_2$ supply
50% > SvO$_2$ > 30%	Exhaustion of extraction; beginning of lactic acidosis; O$_2$ supply < O$_2$ demand
30% > SvO$_2$ > 25%	Severe lactic acidosis
SvO$_2$ < 25%	Cellular death

This is equal to the amount of oxygen delivered systemically (CO) (CaO$_2$) minus the amount of oxygen returned to the heart (CO) (CvO$_2$).

• If we ignore the small dissolved component of oxygen in arterial (0.003 × PaO$_2$) and venous blood (0.003 × PvO$_2$) then (CO) (CaO$_2$) − (CO) (CvO$_2$) = [(Hgb × 13.8) (SaO$_2$) (CO)] − [(Hgb × 13.8) (SvO$_2$) (CO)] = (Hgb × 13.8) (CO) × (SaO$_2$ − SvO$_2$). This is simplified to:

$$SvO_2 = SaO_2 - [VO_2/(Hgb \times 13.8)(CO)]$$

Thus, mixed venous oxygen saturation as measured continuously by a mixed venous saturation PAC varies directly with CO, Hgb, and SaO$_2$ and varies inversely with VO$_2$. If SaO$_2$, Hgb, and VO$_2$ remain constant, then SvO$_2$ will directly reflect changes in CO. Under these circumstances, continuous measurement of SvO$_2$ is analogous to a continuous CO measurement. The response time of SvO$_2$ to acute changes in CO under conditions of constant SaO$_2$, Hgb, and VO$_2$ has been demonstrated to be more rapid than CCO measurements. This is a reliable and sensitive indicator of function in the cardiac surgical patient.

A normal SvO$_2$ is 75%, which corresponds to a mixed venous PO$_2$ of 40–45 mmHg. SvO$_2$ is a reflection of the adequacy of systemic oxygen delivery. A reduced SvO$_2$ indicates inadequate systemic oxygen delivery and increased peripheral oxygen extraction and should prompt an evaluation of SaO$_2$, Hgb, VO$_2$, and CO. Similarly, a low CO in the setting of a normal SvO$_2$ indicates that systemic oxygen delivery is adequate to meet present metabolic needs and that, in reality, the CO is not low for the metabolic demand. Although a high CO is reassuring, it does not guarantee adequate systemic oxygen delivery under conditions of reduced Hgb and SaO$_2$ or increased VO$_2$. A SvO$_2$ measurement allows this determination to be made.

Hemodynamic profiles

The information obtained from a PAC can be used in conjunction with arterial blood pressure monitoring to obtain a number of derived hemodynamic parameters. The most commonly used parameters, their formula, and their units of measurement are given in Table 3.2.

Efficacy and complications of pulmonary artery catheterization

Remarkably, demonstrating the efficacy of pulmonary artery catheterization is difficult. There are several studies indicating that PAC is not associated with improved outcome. Unfortunately, each study carries certain limitations making a broad recommendation against use in specific patient populations impossible. Published guidelines for PAC use indicate that PAC risk and benefit must be weighed in each patient in view of the specific patient characteristics, intended surgical procedure, and the practice setting. PACs are indicated in patients at increased risk of hemodynamic disturbance, clinical evidence of cardiovascular disease, pulmonary dysfunction, hypoxia, renal insufficiency, or other conditions associated with hemodynamic instability. Surgical procedures associated with increased risk include those with anticipated hemodynamic instability, damage to the heart, vascular tree, kidneys, liver or brain. The decision to use a PAC should be based upon the individual hemodynamic risk characteristics of the individual case rather than the type

Table 3.2 Hemodynamic parameters, derivation, and measurement. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

Formula	Units	Normal value
$SV = CO/HR \times 1000$	mL/beat	60–90
$SI = SV/BSA$	mL/b/m^2	40–60
$LVSWI = [1.36 \times (MAP - PCWP)/100] \times SI$	[g-m/m^2]/beat	45–60
$RVSWI = [1.36 \times (PAP - CVP)/100] \times SI$	[g-m/m^2]/beat	5–10
$SVR = (MAP - CVP/CO) \times 80$	dynes s/cm^5	900–1500
$PVR = (PAP - PCWP/CO) \times 80$	dynes s/cm^5	50–150

BSA, body surface area; CO, cardiac output; CVP, central venous pressure; HR, heart rate; LVSWI, left ventricular stroke work index; MAP, mean arterial blood pressure; PAP, pulmonary artery; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary venous return; RVSWI, right ventricular stroke work index; SI, stroke index; SV, stroke volume, SVR, systemic vascular resistance.

of procedure. Finally, PAC use may be indicated for postoperative management depending upon the practice setting which should consider factors such as technical support and nursing training and skills.

PAC insertion carries all the risks of central line placement. There can be arterial injury, pneumothorax, arrhythmias, pulmonary artery hemorrhage, thromboembolism, sepsis, and endocardial damage. In addition, there may be misinterpretation of information resulting in inappropriate patient care. Finally, unnecessary PAC placement is expensive.

The incidence of catheter-induced transient premature ventricular contractions (PVCs) during advancement of PACs is approximately 65%; whereas, the incidence of persistent PVCs during catheter advancement is only approximately 3.0%. These persistent PVCs are generally self-limited. Removal of the catheter nearly always stops the persistent PVCs. If persistent, pharmacologic therapy with lidocaine (1.0–1.5 mg/kg) may suppress these PVCs. The prophylactic use of lidocaine does not reduce the incidence of these benign, transient catheter-induced PVCS. The incidence of catheter-induced right bundle branch block is less than 0.05%. Although frequently mentioned, the risk of complete heart block in a patient with a pre-existing left bundle branch block is rare. If concerned about arrhythmias, the PAC can be floated after the sternum and pericardium are opened and direct access to the heart obtained.

The incidence of pulmonary artery rupture, a potentially lethal complication, is less than 0.07%. The risk of pulmonary artery rupture is increased by anticoagulation, pulmonary hypertension, distal catheter placement, and eccentric balloon inflation. Pulmonary infarction is rare (<0.07%) and can be avoided by preventing the catheter from remaining in a continuous wedge position. Placement of pulmonary catheters has resulted in direct tricuspid and pulmonary valvular damage as well as tricuspid and pulmonary valvular endocarditis.

Transesophageal echocardiography

Transesophageal echocardiography (TEE) is an intraoperative diagnostic and monitoring modality with wide use among cardiovascular anesthesiologists. The esophagus lies in direct proximity to the heart and great vessels allowing extraordinarily clear imaging windows. Furthermore, TEE allows intraoperative use without disrupting the surgical procedure. It is a valuable tool in the ICU and in the evaluation of trauma or other hemodynamically unstable or poorly responsive patients. Every cardiovascular anesthesiologist should be familiar with the basic applications, advantages, and limitations of TEE.
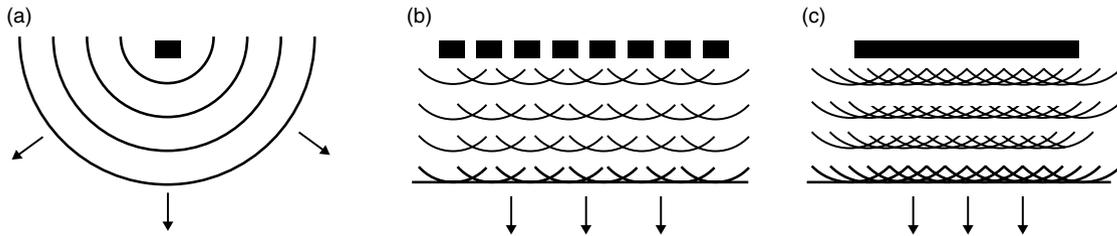
Fig. 3.10 Generation of longitudinal ultrasound wave front production. (a) Single small element. (b) Multiple small elements (phased array). (c) Single large element. The ultrasound waves travel in circular fashion away from a single element. Transesophageal echocardiography (TEE) imaging typically employs phased array ultrasound wave generation. (From Feigenbaum H. *Echocardiography*, 5th edn. Philadelphia: Lea & Febiger (Lippincott Williams & Wilkins), 1994:4, with permission.)

Basics of ultrasound

Ultrasound is defined as sound waves above the audible range in humans (above 20 000 cycles/s). In echocardiographic equipment, piezoelectric crystals in the distal transducer head generate and receive the ultrasound waves (Fig. 3.10a–c). A high frequency electrical current is applied to the crystal causing vibration and sound wave formation. As the generated sound waves pass through tissue, they are either absorbed, reflected, refracted, or scattered. The degree of ultrasound wave reflection (return to the transducer) is enhanced when the structure of interest is perpendicular to the ultrasound wave. In order to identify two contiguous structures, there must be a difference in density and impedance between them altering beam absorption, reflection, refraction and scattering.

The frequency of the ultrasound waves produced by the piezoelectric crystals is important. Recall that wavelength equals velocity (V) divided by frequency (F): $1 = V/F$. Because ultrasound travels at 1540 m/s through soft tissue, there is a constant relationship between frequency and wavelength. As the frequency of the vibrations of the piezoelectric crystals increases, the length of the waves produced decreases. A smaller wavelength signal allows better image resolution but is prone to greater signal attenuation with increasing distance from the transducer. Likewise, greater wavelength will reduce resolution, but will enhance visualization of structures at greater depth from the transducer.

When the piezoelectric crystal receives a reflected sound wave, it vibrates and generates an electrical signal. Because the wavelength, the frequency, and the speed of the transmitted and reflected waves are known, the time it takes for the signal to be transmitted and reflected back can be used to determine the depth of the reflecting object (remember, ultrasound travels at a constant 1540 m/s through soft tissue). With proper amplification and processing, these signals are converted to display the real-time reflected wave activity (the image).

Doppler echocardiography is based on the Doppler principle, which states that when a wave of a given frequency strikes a moving target it will be reflected with a frequency shift proportional to the velocity of the target parallel to the path of the emitted wave. If the target is moving toward the emitted wave, the frequency of the returning reflected wave will be higher. If the target is moving away from the emitted wave, the frequency of the reflected returning wave will be lower. Red blood cell mass is an excellent reflector in the heart and vascular system. Measuring the red blood cell flow velocity in the heart is the application of Doppler technology in echocardiography. The Doppler principle, when used to calculate the velocity of red blood cell mass, can be summarized in the following equation:

$$V = c f_{\mathrm{d}} / 2 fo \cos \theta$$

where V, velocity of red cells; c, speed of sound in tissue (1540 m/s); f_{d}, shifted or Doppler frequency; fo, transmitted frequency; θ, the angle of incidence between the transmitted wave and the velocity vector being interrogated.

Recall that cosine 90° and cosine 270° = 0, the cosine 0° = 1 and cosine of 180° = −1; therefore, detection of velocity is most accurate when the transmitted beam and the velocity vector are parallel (cosine 0° and 180°). The detection of velocity is impossible when the transmitted beam and the velocity vector are perpendicular (cosine 90° and 270°). In practice, aligning the Doppler beam and the velocity vector within 20° produces acceptable results (6% underestimation of velocity). By convention, flow away from the transducer (cosine 180°) has a negative value and flow toward the transducer (cosine 0°) has a positive value.

M-mode echocardiography

M-mode echocardiography is the simplest echocardiographic imaging technique. Ultrasonic waves of known frequency and wavelength are transmitted in a single beam path and recorded over time. This provides a linear ("ice pick") view of the imaging sector through which the beam passes (Fig. 3.11). M-mode is used in conjunction with two-dimensional (2-D) imaging and the cursor line is used to direct the beam path through the desired area. The reflected waves are displayed in real time as a time-motion study. The vertical axis displays the distance and intensity of the reflected from

the transducer, and time is on the horizontal axis. Blood-filled chambers with little or no reflected wave activity appear black, whereas valve tissue and myocardium with high wave reflectivity are gray or white.

Ultrasound waves through a single beam path are transmitted and received in 0.001 seconds. As a result, the display is a real-time repetitive display of cardiac activity along this single beam line at 1000 frames/see. This M-mode feature allows very high-resolution images of moving cardiac structures.

Two-dimensional (2-D) echocardiography

Two-dimensional imaging is the display of reflected images obtained for transmission of waves not along a single beam line but across a multiple beam line sector. This sector usually is 60–90° wide (Fig. 3.12). Sector scanning is accomplished most frequently by use of a phased-array technology. In 2-D imaging, a set of piezoelectric crystals are activated in phased sequences to create a single beam through a defined sector. An analogy may help: For M-mode, imagine a man holding a flashlight in one position, looking at one object; in 2-D, imagine the same man moving the flashlight beam back and forth across the horizon and putting the combined images together to create a picture of the objects in the night. The resulting sector sweep in

Fig. 3.11 M-mode image through the left ventricle with a measurement of fractional shortening (FS). The left ventricular internal dimension is measured in both systole (LVIDs) and diastole (LVIDd). The FS = LVIDd − LVIDs/LVIDd. Normal is 0.25–0.45.

Fig. 3.12 Two-dimensional (2-D) mid-esophageal four chamber view of the heart. There is left ventricular septal hypertrophy.

2-D contains approximately 100 single scan lines. The computer assembles these scan lines and displays the processed information as the echocardiographic image. Obviously, obtaining 100 scan lines is more time consuming than obtaining one scan line, as in M mode (hence, diminished spatial resolution). Two-dimensional images are presented in real time with the sector scan updated 30–60 times/s as opposed to the 1000 times/s of M mode. As with M mode, distance of the reflected wave from the transducer is displayed from the top of the scan down and the displayed brightness of the reflected wave is proportional to its amplitude.

Pulsed-wave (PW) Doppler

PW Doppler analyzes frequency shifts in a time-gated manner. The transducer intermittently transmits and then waits a specified time (t) to receive reflected ultrasonic signals. This pulse and receive pattern allows depth localization because the distance of the reflecting object from the transducer is defined by:

$$d = ct/2$$

where d, distance of the reflecting object from the transducer; c, 1540 m/s; t, time between emission and reception of signal.

In practice, the PW Doppler cursor and sample volume are positioned on an updated 2-D image. After the Doppler cursor and sample volume are positioned, only reflected signals from that position are analyzed (Fig. 3.13). The sample volume also can be selected (usually from 2 to 6 mm). This allows the interrogated area to be expanded or contracted. Data are displayed as spectra, which are a real-time presentation of velocity over time.

There are limitations with PW Doppler. In order to reliably detect the frequency shift (and hence the velocity) of a reflecting object, the reflected ultrasound wave must be sampled at a frequency at least twice that of the object (Nyquist criterion). The sampling frequency of PW Doppler is the pulse repetition frequency (PRF). Thus, the maximal detected velocity for a given PRF is PFR/2. This is the Nyquist limit. Thus, the maximum velocity that can be detected is limited. An additional problem is that the
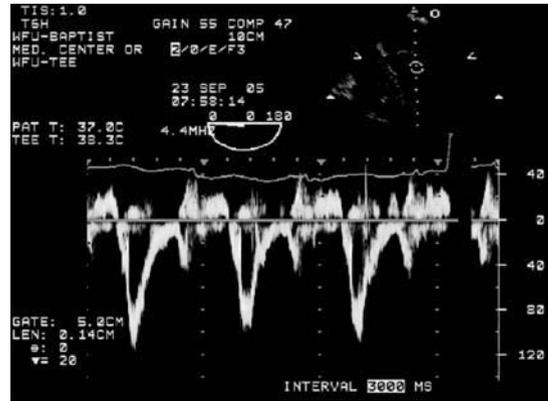
Fig. 3.13 Pulse wave Doppler at the distal tips of the mitral valve demonstrating an E and A wave.

PRF must decrease as the distance from the transducer to the sampling site increases. This must occur because it takes longer for the emitted wave to reach the increased depth and for the reflected wave to return.

Exceeding the Nyquist limit causes aliasing or wraparound. The signal literally wraps around the velocity scale in the other direction. It then becomes difficult or impossible to determine red cell velocity or direction. The trade-off is unambiguous distance information but ambiguous velocity and direction information. An analogy may help: recall old Western movies in which the wagon wheels appear to be rotating backwards as the wagon moves forward. This is due to the frame capture rate of the film as the spokes on the wagon wheel turn. Appropriate film capture (altering the PRF) will capture the forward progression of the spokes allowing the image to portray the reality. There are two strategies to deal with aliasing during PW Doppler interrogation. The first is to increase the available scale. The second is to shift the baseline. If wraparound still occurs, then continuous-wave (CW) Doppler must be used to determine peak velocity and direction.

PW Doppler is useful for measuring low velocities at very specific locations such as mitral and tricuspid inflow or in the pulmonary and hepatic veins.

Continuous-wave Doppler

In CW Doppler, one transducer continuously emits signals and a separate transducer continuously

receives reflected signals. These transducers are not the same ones used to obtain 2-D images. This arrangement allows reliable measurement of very high velocities because there is no lag between emission and reception of signals. In other words, the PRF is extremely high. Because reflected signals returning from all points along the Doppler beam are recorded, the location of returning signals is ambiguous. In addition, lower velocity signals are buried in the higher velocity signals. Therefore, CW Doppler provides unambiguous peak velocity and direction information but ambiguous distance information.

In practice, the CW Doppler cursor is positioned on an updated 2-D image just like PW except that there is no sample volume. A spectrum of data is displayed demonstrating a real time presentation of object velocity over time. CW Doppler is useful for measuring high velocities such as those seen with aortic stenosis (Fig. 3.14) or with intracardiac shunts. With the baseline shifted, velocities up to 600–800 cm/s are obtainable.

Color-flow Doppler
Color-flow CF Doppler is a modification of PW Doppler called multigated PW Doppler. Sampling of object velocity occurs at several locations along many lines in a sector. The sample volumes are called packets. The average velocity and direction for the spectra in a sample volume are determined and assigned a predetermined color. Generally, 8–16 samples per frame determine the average object velocity. The set of velocities that are averaged in a sample volume for a single frame is called a packet or packet size. Object velocities are assigned specific colors. A popular presentation is BART (blue away, red toward). In this scheme, velocities toward the transducer are red and those away are blue. As velocity increases, the intensity of color increases as well. The CF Doppler image is presented in real time as a sector displayed over a real-time 2-D image (Fig. 3.15).

CF Doppler has some of the same limitations as PW Doppler. There is no position ambiguity, but the peak velocity is limited and decreases with the distance from the transducer. Aliasing occurs and is presented as a color mosaic. Because the color image is presented over the real-time 2-D image, the direction of the aliased signal can be determined easily. This is an obvious advantage when comparing CF to PW Doppler. Because the averaging process loses valuable spectral data, CF Doppler is useful for detection of abnormal flows and the direction and spatial extent of these flows. Reliable determination of peak velocities requires PW or CW Doppler spectral analysis.
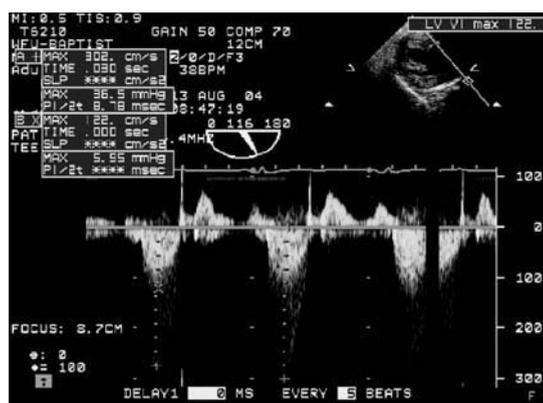
Fig. 3.14 Continuous wave Doppler across the aortic valve in the deep transgastric long-axis view. The peak velocity is approximately 3 m/s yielding a peak gradient of 36 mmHg.
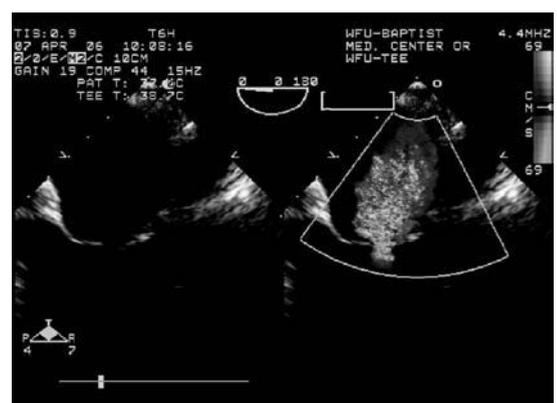
Fig. 3.15 This color compare image shows the two-dimensional (2-D) image on the left and the color-flow Doppler image on the right. There is a central jet of mitral regurgitation that is severe.
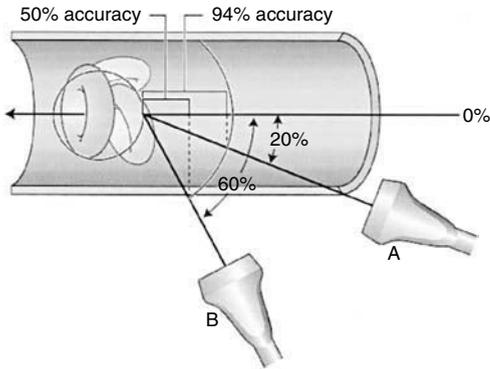
Fig. 3.16 The angle of interrogation has a great impact on the accuracy of Doppler measurement. (From Obeid AI. *Echocardiography in Clinical Practice*. Philadelphia: Lippincott Williams & Wilkins, 1992, with permission.)

Doppler spectra measurements

As discussed previously, Doppler spectra represent object velocity data over time. Velocities toward the transducer are presented above the zero velocity line or baseline and are assigned positive values. Velocities away from the transducer are presented below the zero line or baseline and are assigned negative values. Accurate Doppler measurements are dependent on the Doppler beam being parallel (or within 20° of parallel) to the interrogated flow (Fig. 3.16). Several important Doppler spectra measurements are discussed below.

Pressure gradients

A velocity measurement (m/s) can be converted to a pressure gradient (mmHg) using a modification of the Bernoulli equation $4V^2$ where $V =$ velocity in meters per second. Peak instantaneous pressure gradients are determined by identifying the peak velocity (Max V) of the desired Doppler spectra and using the equation $4V^2$. In practice, machine software will calculate the peak pressure gradient using a peak velocity identified by the operator (see Fig. 3.14). Peak instantaneous gradients are always greater than the peak-to-peak gradients determined at catheterization.

Velocity–time integral

Velocity–time integral (VTI) is determined by tracing (planimetry) the entire Doppler spectra over the desired portion of the cardiac cycle (systole or diastole). Machine software integrates the area under the traced spectra to determine VTI in centimeters. VTI can be used to determine the mean gradient, the stroke volume, and orifice area using the continuity equation.

Mean velocity (cm/s) is determined by the machine software by dividing the VTI (cm) by the duration of flow (seconds). Mean velocity cannot be used to calculate the mean gradient because the mean gradient is actually the average of multiple instantaneous gradients within the VTI trace. Machine software determines, totals, and averages these individual pressure gradients to determine the mean gradient.

Stroke volume and cardiac output are determined using the VTI as follows. The VTI can be used to determine stroke volume (cm^3) by multiplying the VTI (cm) obtained at a given location by the area of the location (cm^2). Cardiac output is then stroke volume multiplied by heart rate (HR). This determination can be done in the main pulmonary artery, in the right ventricular outflow tract (RVOT), at the mitral valve annulus, in the left ventricular outflow tract (LVOT), or at the level of the aortic valve. The feasibility depends on two factors:
- obtaining a Doppler spectra from the desired area with the Doppler beam within 20° of parallel to blood flow, and
- obtaining an accurate measure of the area from which the Doppler sample was obtained.

Diameter (D) is easily measured with ultrasound can be converted to area using the equation:

$$\text{Area} = \pi(r)^2 = \pi(D/2)^2 = 0.785(D)^2$$

Alternatively, a direct measurement of area can be obtained using planimetry.

The continuity equation makes use of the VTI to calculate valve areas. The conservation of mass demands that a stroke volume remain equal immediately upstream and downstream of a stenotic valve. Although the velocities may be different, the mass of ejected blood must be the same. Thus,

$$(A_1) \times (\text{VTI}_I) = (A_2) \times (\text{VTI}_2)$$

where A_1, area of region 1; A_2, area of region 2; VTI$_1$, VTI from area 1; VTI$_2$, VTI from area 2.

The concept can be extended to state that the flows across all valves in the heart must be equal, but this is true only in the absence of regurgitant lesions or shunts. Thus, in theory, the continuity equation could be used to determine aortic valve area using mitral valve or pulmonary artery flows or vice versa.

Deceleration time, acceleration time, pressure half-time

Deceleration time (D1) is the time it takes (ms) for the peak velocity of a Doppler spectra to fall to the zero baseline (Fig. 3.17). In instances in which the zero baseline is not reached, the natural slope of the Doppler spectra is extended to the baseline.

The acceleration time (A1) is the time it takes (ms) for the Doppler spectra to reach peak velocity from the zero baseline.

The pressure half-time (PHT) is the time it takes (ms) for the peak velocity gradient of a Doppler spectra to decrease by one-half. In other words, it is the time it takes for the peak velocity to decline to the peak velocity divided by $\sqrt{2}$. In addition, the PHT (ms) is always $0.29 \times DT$. The PHT is important because it can be used to calculate mitral valve area (MVA) over a wide range of values using the formula: $MVA = 220/PHT$.

TEE probes

TEE probes consist of an echocardiographic transducer or combination of transducers fitted to the distal, flexible end of a gastroscope. The transducer consists of an array of piezoelectric crystals. Most current adult TEE transducers have a 64-crystal element, whereas pediatric probes have a 48-crystal element. Adult TEE transducers generally operate at 5 MHz, whereas pediatric probes operate at 7.5 MHz. Some adult TEE probes possess frequency agility or the ability to function at 3.7 and 5 MHz, whereas some pediatric probes can function at 7.5 and 5.5 MHz. The higher frequency transducers can be used without significant signal attenuation because of the proximity of the transducer to the heart. TEE probes allow 2-D, M-mode, PW Doppler, CW Doppler, and CF Doppler imagining.

Hand controls allow flexion of the transducer both side to side and anterior and posterior. These controls allow 70° of lateral mobility in each direction (right and left) and 90° of anteflexion and retroflexion (Fig. 3.18). Presently, there are single-plane, biplane, and multiplane adult TEE probes available. Pediatric single plane and biplane probes can be used for neonates and infants as small as 2–3 kg. With care, adult probes can be used for children as small as 15–20 kg.

Fig. 3.17 Schematic of a CW Doppler spectra across a stenotic mitral valve. The velocity–time integral (VTI) is the shaded area inside the spectra. The values calculated from the VTI are shown in the upper left hand corner. The deceleration time is obtained by extending the slope of the spectra to the zero baseline. The pressure half time (PHT) can be determined by calculating V_2 and measuring the time between V_1 and V_2. The values calculated from the DT are shown in the bottom right corner. DT, deceleration time; MVA, mitral valve area. (From DiNardo JA. Monitoring. In: DiNardo JA (ed) *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

Max V = 250 cm/s
Mean V = 185 cm/s
VTI = 200 cm
Max PG = 25 mmHg
Mean PG = 13.7 mmHg

DT = 600 ms
PHT = 174 ms
MVA = 1.26 cm^2

Fig. 3.18 Movement of the transesophageal echocardiography (TEE) probe allows extensive sectioning and imaging of the heart in a two-dimensional (2-D) plane. (From Shanewise JS, Cheung AT, Aronson S, *et al. Anesth Analg* 1999;**89**:870–84, with permission.)

Single-plane probes have a single transducer that transmits and receives ultrasonic signals in the 0° plane (transverse or horizontal plane). Biplane probes have two transducers mounted one above the other. One transducer transmits and receives ultrasonic signals in the 0° plane and the other transmits and receives ultrasonic signals in the 90° (longitudinal or sagittal) plane. Changing planes requires switching from one transducer to the other. Because the transducers are at different levels, subtle (1.0–1.5 cm) advancement or withdrawal of the probe is necessary after transducers are switched to ensure imaging at the same anatomic level. Multiplane (omniplane) probes have the ability to transmit and receive ultrasonic signals in any plane from 0 to 180°. These probes use either mechanical rotation or phased-array activation (varying sequential activation of the piezoelectric crystals in the transducer) of a single transducer to accomplish

this. Activation of multiplane capability is obtained with a switch on the handle of the probe.

Insertion of the TEE probe

Insertion of the TEE probe in the anesthetized adult or pediatric patient with an endotracheal tube (ET) in place is usually easy. The patient should have an orogastric tube placed and the stomach should be emptied as well as possible. Even a small volume of air in the stomach can interfere with imaging from the transgastric position. The orogastric tube should be removed before probe insertion. The presence of a tube in the esophagus will interfere with imaging. The endotracheal tube should be well secured. The TEE probe is left in the unlocked position and is lubricated with ultrasonic gel. A bite block is essential for TEE examinations in nonanesthetized patients, but in anesthetized patients it is only required in patients with jagged teeth or at the operator's discretion.

The operator stands in the same position as if to perform direct laryngoscopy. The patient's head and neck should be in a neutral position. There should be no positioning rolls under the patient's shoulders. The thumb of the left hand is placed on the patient's tongue and the left hand is used to pull the jaw upward. The right hand is used to insert the probe into the pharynx to the left side of the ET with the probe transducer facing anterior. The remainder of the probe can be looped around the operator's neck and shoulder, held by an assistant, or rested on the head of the bed near the patient. The probe is advanced with steady gentle pressure using a slight left to right rotating motion. The unlocked probe will follow the natural curve of the pharynx. At the pharyngeal-esophageal junction (10 cm from the lips in neonates, 20 cm from the lips in adults), some mild resistance will characteristically be met. This can be overcome with gentle, steady pressure. If undue resistance is encountered, it is possible that the probe is in the piriform sinus or the vallecula. It should be withdrawn and advancement tried again. If there is any doubt regarding probe position, the probe should be placed under direct vision using a laryngoscope. In some rare instances, it is impossible to place the TEE probe.

TEE views

The American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists recommended views for a comprehensive TEE examination are shown in Fig. 3.19.

Views available with a single-plane probe are those obtained in the 0° plane. The basic views available with a biplane probe are those obtained in both the transverse (0°) and longitudinal (90°) planes. Multiplane views are all of the views from 0 to 180°. In fact, most of the views obtainable with a multiplane probe are obtainable with a biplane probe. The difference is that use of a biplane probe requires significantly more probe manipulation than a multiplane probe. The following is useful when using a biplane
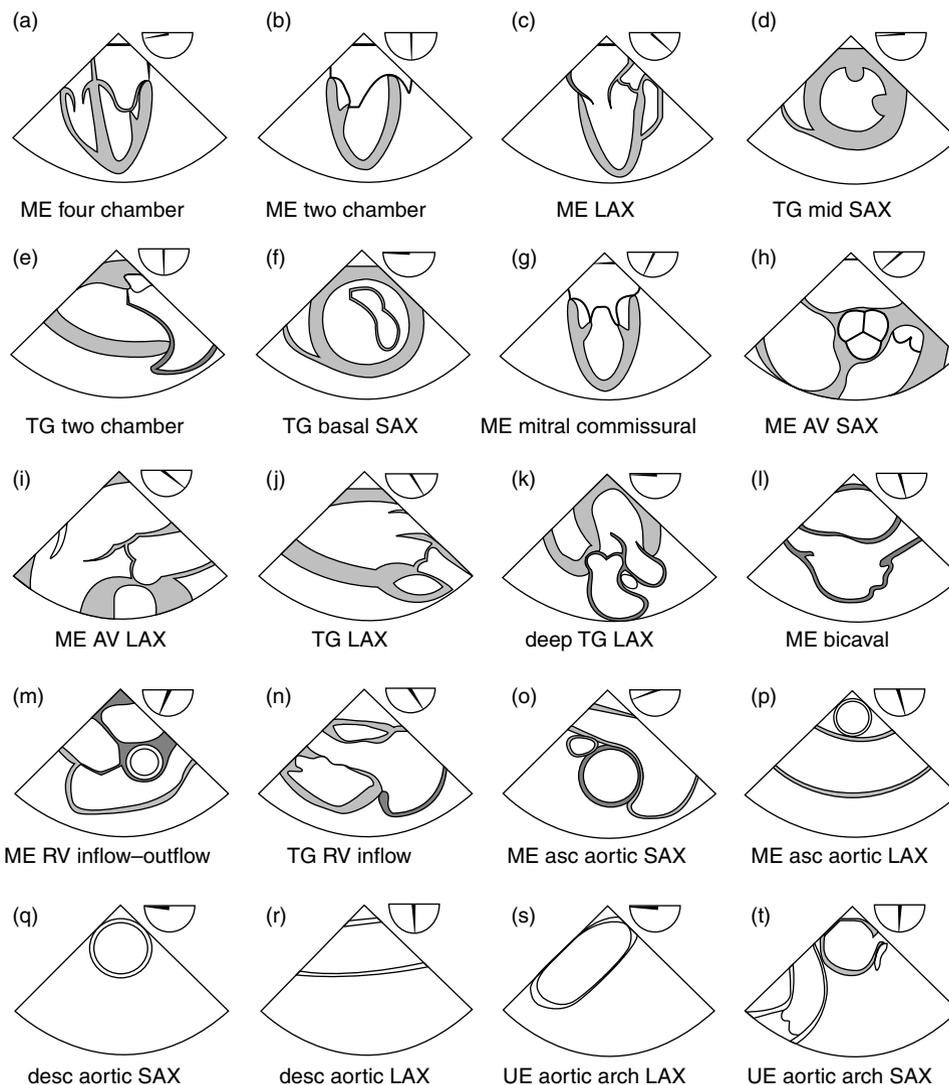
Fig. 3.19 The 20 recommended views for a comprehensive transesophageal echocardiography (TEE) examination by the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. (From Shanewise JS, Cheung AT, Aronson S, *et al*. *Anesth Analg* 1999;**89**:870–84, with permission.)

probe:

- Angles 0–45°: flex the transverse probe to the patient's left.
- Angles 45–90°: flex the longitudinal probe to the patient's right.
- Angles 90–135°: flex the longitudinal probe to the patient's left.
- Angles 135–180°: flex the transverse probe to the patient's right.

In this text, rotation to the right always means to the patient's right (clockwise) and rotation to the left always means to the patient's left (counterclockwise).

Figure 3.20 shows views from the upper esophagus. At this level, there can be interference from air in the right and left main stem bronchi. Good views of the proximal ascending aorta can be obtained. The view at 0° is useful for Doppler interrogation of the main pulmonary artery. For some patients, the pulmonic valve and a small portion of the RVOT can be seen as well.

CF Doppler interrogation just above this level but at a level just below the aortic arch is useful for
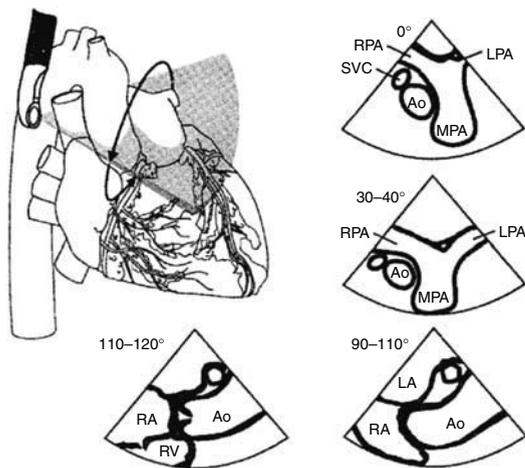
Fig. 3.20 Transesophageal echocardiography (TEE) views at the base of the heart. Ao, aorta; LA, left atrium; LPA, left pulmonary artery; MPA, main pulmonary artery; RA, right atrium; RPA, right pulmonary artery; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

detection of a patent ductus arteriosus (PDA). Gentle anteflexion may be necessary to get good contact with the esophagus at this level.

Figure 3.21 shows views obtained with slight advancement of the probe from the previous level. This level provides excellent views of the pulmonary veins and allows Doppler interrogation. At 0° the left lower pulmonary vein (LLPV) is lateral to and seen at a slightly deeper level (10–50 mm) than the left upper pulmonary vein (LUPV). The LLPV usually is seen in conjunction with the descending aorta. At 0°, the right lower pulmonary vein is posterior to and at a slightly deeper level (10–50 mm) than the right upper pulmonary vein (RUPV). The RUPV is seen in conjunction with the superior vena cava (SVC). The LUPV and LLPV usually can be seen in the same image at 100–110° while the RUPV and RLPV can usually be seen in the same image at 50–60°. A persistent left superior vena cava would appear as a vascular structure (circular in the sulcus between the left atrial appendage and the LUPV).

Figure 3.22 shows views obtained at a slightly deeper level in the upper esophagus. Some of the most valuable views are obtained at this level. Both long- and short-axis views of the aortic valve are seen. In the short-axis views, the right coronary cusp is anterior, the noncoronary cusp is next to the right atrium, and the left coronary cusp is next to the left atrial appendage (LAA). In the long-axis views, two cusps are seen: the right coronary cusp is anterior and the noncoronary cusp is in continuity with the anterior mitral valve leaflet. A good long-axis view of the main pulmonary artery and two leaflets of the pulmonic valve are seen. Views of the tricuspid valve suitable for Doppler interrogation are seen as well.

Figure 3.23 shows views obtained at the midesophageal level. Varying amounts of retroflexion are needed to prevent foreshortening of the left ventricle (LV) and right ventricle (RV). The classic four-chamber view is seen at 0°. These views allow good alignment for Doppler interrogation of the mitral valve. The anterior mitral valve leaflet is seen in continuity with the ventricular septum at 0° and in continuity with the noncoronary cusp of the aortic valve at 130–150°. The LAA also

Fig. 3.21 Transesophageal echocardiography (TEE) views of the pulmonary veins at the base of the heart. Ao, aorta; LA, left atrium; LAA, left atrial appendage; LLPV, left lower pulmonary vein; LPA, left pulmonary artery; LUPV, left upper pulmonary vein; MPA, main pulmonary artery; RA, right atrium; RLPV, right lower pulmonary vein; RPA, right pulmonary artery; RUPV, right upper pulmonary vein; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
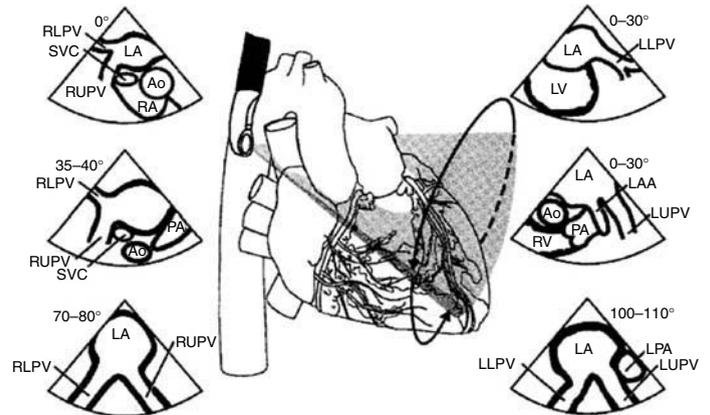
Fig. 3.22 Transesophageal echocardiography (TEE) views obtained from the upper esophagus. Ao, aorta; AV, aortic valve; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; PV, pulmonic valve; RA, right atrium; RV, right ventricle. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
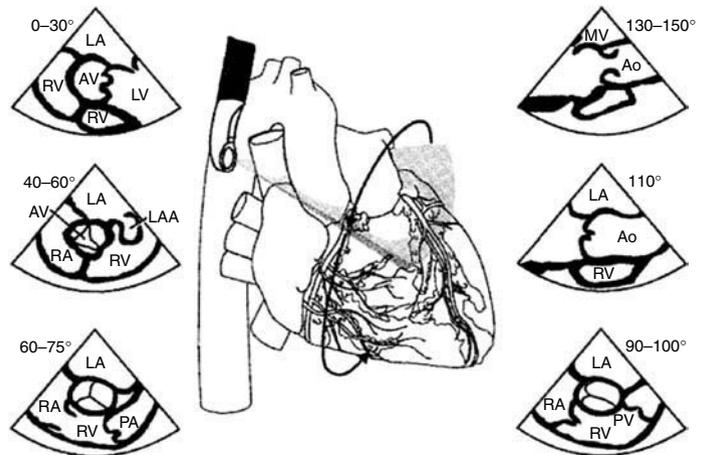
is seen. Slight withdrawal and anteflexion will give a short-axis view of the aorta. The coronary arteries can be seen at this level. The left coronary artery often can be seen dividing into the left anterior descending (LAD) and circumflex branches in the area near the LAA. The right coronary artery is anterior and usually requires very slight probe advancement to be seen. Slight off angles (20–30°) often will allow better visualization.

Figure 3.24 shows views also obtained at the midesophageal level. The probe is rotated to the patient's right to obtain these views from the previous angles. These views provide excellent visualization of the atrial septum, which makes them useful for detection of a patent foramen ovale or atrial septal defect. Good visualization of the right atrium/superior vena cava and right atrium/inferior vena cava (IVC) junctions also is obtained.

Figure 3.25 shows views obtained at the gastroesophageal junction (36–38 cm from the teeth). Gentle anteflexion usually is needed to obtain these views. The coronary sinus (CS) is seen entering the right atrium. A large CS should alert one to the possibility of a persistent left superior vena cava or anomalous pulmonary venous return. The right atrium/inferior vena cava junction and eustachian valve are seen as is the right atrial appendage.

Figure 3.26 shows transgastric views of the left heart structures. Varying degrees of anteflexion are required to obtain these views. These provide the
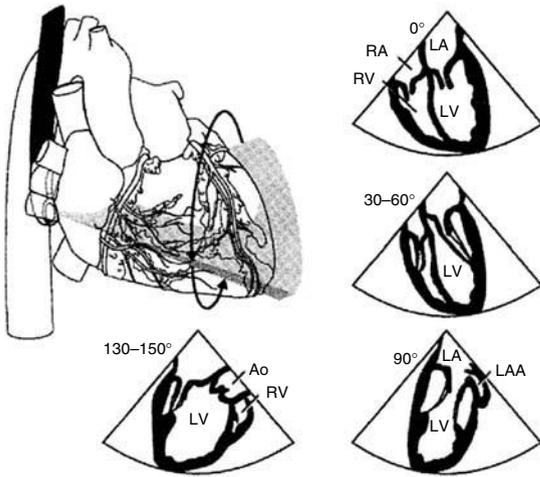
Fig. 3.23 Transesophageal echocardiography (TEE) views obtained from the mid-esophagus. Ao, aorta; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
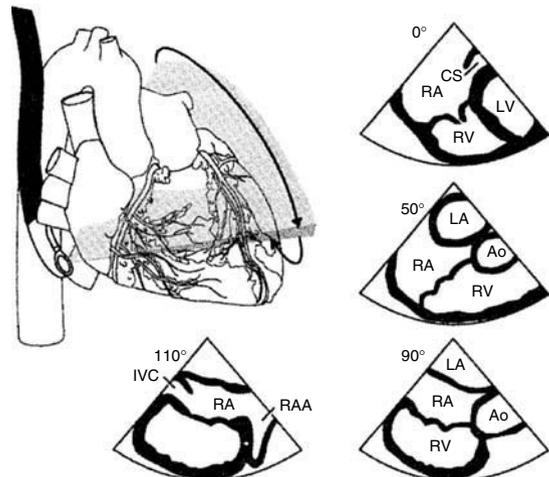
Fig. 3.25 Transesophageal echocardiography (TEE) views obtained at the gastroesophageal junction. Ao, aorta; CS, coronary sinus; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; RA, right atrium; RAA, right atrial appendage; RV, right ventricle; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
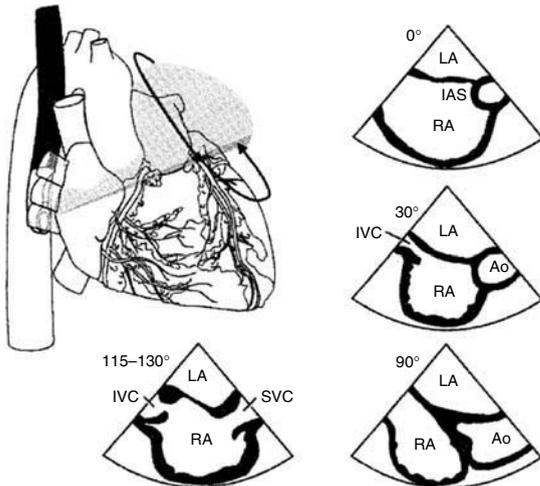
Fig. 3.24 Transesophageal echocardiography (TEE) views obtained from the mid esophagus. Ao, aorta; IAS, interatrial septum; IVC, inferior vena cava; LA, left atrium; RA, right atrium; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
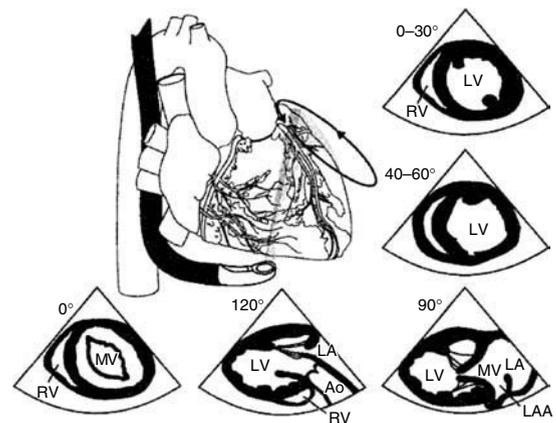
Fig. 3.26 Transesophageal echocardiography (TEE) views at the transgastric position. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; MV, mitral valve; RA, right atrium; RV, right ventricle; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
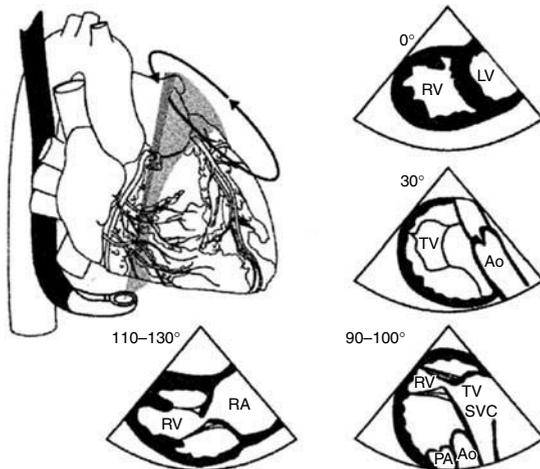
Fig. 3.27 Transesophageal echocardiography (TEE) views of the right ventricle from the transgastric position. Ao, aorta; IVC, inferior vena cava; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava; TV, tricuspid valve. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
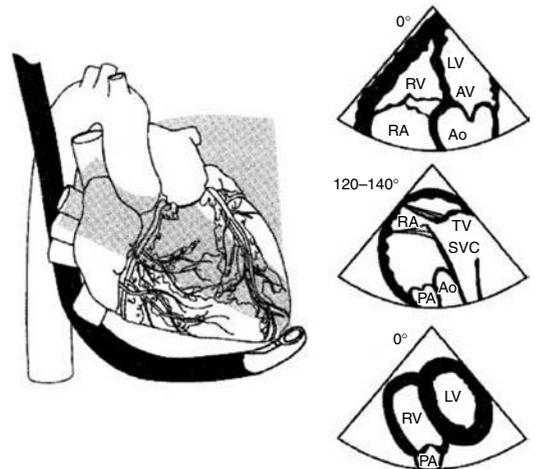
Fig. 3.28 Transesophageal echocardiography (TEE) views from the deep transgastric position. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

short-axis views of the LV and RV used in regional wall motion analysis. The anterior and posterior papillary muscles are seen. With manipulation, the view at or around 1200 can provide views of the LVOT and aortic valve amenable to Doppler interrogation. A short-axis view of the mitral valve suitable for planimetry often is obtainable either by withdrawing the probe slightly or ante-flexing it to a greater degree.

Figure 3.27 shows transgastric views of the right heart structures. Varying degrees of anteflexion are required to obtain these views. They are obtained by rightward rotation of the probe from the previous position. These views provide excellent visualization of the RVOT, which is very useful in the congenital heart disease patient. They also provide good visualization of wall motion in the RV inferior wall and free wall.

Figure 3.28 shows the deep transgastric views. These views are obtained by passing the probe in a neutral position all the way into the stomach. At this point, the probe is maximally flexed and withdrawn until contact is made and resistance is

felt. Flexion of the probe to the left and rotation to the patient's right helps align the image so that the LVOT, aortic valve, and proximal ascending aorta are vertical. This location reliably provides views of the LVOT and aortic valve and of the RVOT and pulmonary valve amenable to Doppler interrogation. These views also provide images equivalent to the those obtainable with subcostal transthoracic imaging which are valuable in children with congenital heart lesions.

Figure 3.29 shows the probe set in the transverse plane and positioned as depicted in Fig. 3.23. Next, the probe is rotated 90–100° to the patient's left and the descending thoracic aorta is visualized. Once it is located, it can be viewed from the arch (see below) to just below the diaphragm. Inability to see the descending aorta to the left should arouse suspicion that there is a right aortic arch. This can be localized by rotating the probe to the patient's right from the original position.

Figure 3.30 shows, with the descending thoracic aorta visualized, the probe being withdrawn, keeping the image of the aorta in the center of
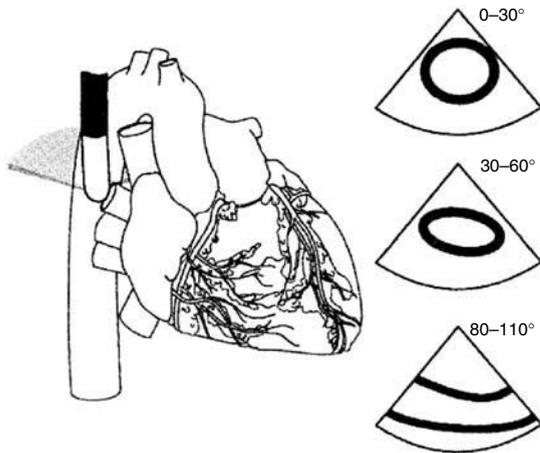
Fig. 3.29 Transesophageal echocardiography (TEE) views of the descending thoracic aorta. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)
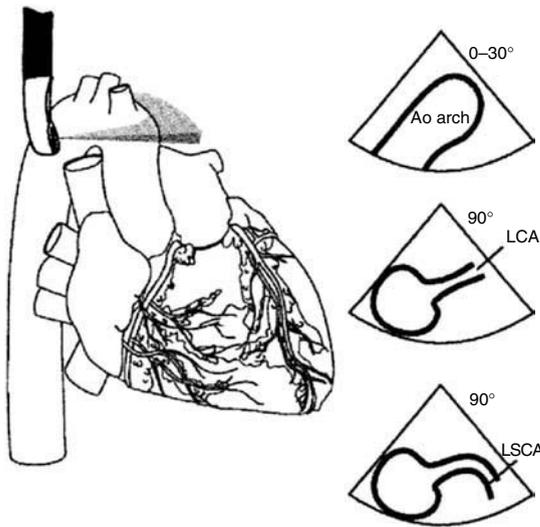
Fig. 3.30 Transesophageal echocardiography (TEE) views of the aortic arch. Ao, aorta; LCA, left carotid artery; LSCA, left subclavian artery. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

the screen. As the arch is approached in the upper esophagus, the probe is rotated slightly to the patient's right. At this point, the inferior portion of the aortic arch is seen. At 90°, a short-axis view of the arch is obtained. With slight further withdrawal and rotation to the patient's right, the left CA can be seen. With rotation to the left, the left subclavian artery can be seen curving off inferiorly.

TEE examination

There is no one way to conduct a comprehensive TEE examination. Each examiner has a particular protocol. What is important is that the examiner conducts the same examination on every patient in a consistent format. This is the only way to avoid missing what may turn out to be critical findings. The examiner should concentrate on known diseases, but not to the exclusion of a complete examination. This should include complete 2-D imaging with a comprehensive Doppler examination. When the TEE probe is not being used, it should be left in the unlocked position and the image should be frozen. Freezing the image will terminate ultrasound transmission. Some examiners advocate advancing the probe to the stomach when it is not being used to prevent undue pressure on the esophagus from the probe tip.

LV systolic function, ejection fraction, and preload

One of the most powerful applications of perioperative TEE is the quick assessment of LV systolic function and regional wall motion abnormalities. LV systolic function can be determined by gross observation or it can be calculated using several different parameters.

Intraoperative changes in the shape and position of the LV pressure–volume relationship make the traditional pressure measurements used to assess LV preload unreliable, whereas hemodynamic assessment of LV ejection fraction is not possible. Both qualitative and quantitative assessment of LV end-diastolic area (EDA), end-systolic area (ESA), and fractional area change (FAC) are possible using TEE.

Quantitative assessment of EDA using TEE provides an accurate assessment of preload in adults

and children. Quantitative assessment of LV EDA is frequently performed using the short-axis view of the LV at the mid-papillary muscle level, although the most accurate assessments are derived from a combination of several views. EDA is determined by one of two ways:

1 Computer planimetry – this method requires freezing the LV end-diastolic TEE image and tracing the endocardial border using a trackball. The computer then calculates EDA. The short-axis EDA for several cardiac cycles are obtained and averaged. This method also can be used to determine ESA using the frozen end-systolic echocardiographic image. ESA and EDA can be used for the FAC, which is analogous to EF.

$$FAC\% = (EDA - ESA)/EDA \times 100$$

2 Automated border detection (ABD) – also called acoustic quantification (AQ), this method makes use of backscattered signals from the blood–tissue interface to outline the endocardial borders in real time. When the data are gated to the ECG, a beat-to-beat display of EDA, ESA, and FAC is provided. Both methods can be performed online, but obviously, the first method is more time consuming and is not a continuous real-time assessment. ABD is a continuous real-time assessment but is cumbersome and, for 20–30% of patients, is unreliable because of poor image quality. FAC obtained by both methods has been shown to correlate well with EF obtained by radionuclide angiography.

Qualitative assessment of EDA, ESA, and FAC requires no special techniques except a trained eye. In practice, clinicians must often make quick judgments for treatment plans based on limited information. TEE allows the ability for clinicians to quickly look at the heart and determine if it is hypokinetic, normal or empty and hyperdynamic is invaluable. It is quick and can be as continuous as desired. Several cautions are in order, however. The development of end-systolic cavity obliteration commonly is used as one of the visual signs of a reduced EDA. However, it has been demonstrated that although many of the episodes of end-systolic cavity obliteration are associated with reduced EDA, end-systolic cavity obliteration does not always indicate reduced EDA. End-systolic cavity obliteration may be caused

by increases in contractility or decreases in afterload. The clinician may also be fooled if using only one view to render an opinion or form judgment. Remember that the TEE slice represents only a limited view of the heart. One area may appear grossly hypokinetic, while the remainder of the heart functions normally. With experience, clinicians can estimate FAC or ejection fraction area (EFA) to within 10% of offline values in 75% of cases. The assessment of EDA as either low or normal corresponds well with offline assessment of EDA as well.

Regional wall motion analysis

TEE analysis of regional wall motion abnormalities (RWMA) can be used to detect myocardial ischemic and has predictive value concerning adverse clinical outcomes.

Intraoperative assessment of RWMA involves imaging the heart in several planes to view all of the 17 wall segments (Table 3.3). The most popular view for general surveillance, perhaps, is the transgastric short-axis view of the LV at the level of the mid-papillary muscle level. This view is obtained easily and contains regions of myocardium supplied by all three coronary arteries. Most data regarding intraoperative use of TEE to monitor for ischemia uses this view with analysis that has been performed offline. One should not forget to assess RV wall motion. The RV is imaged in many planes including the RV inflow–outflow view, the four-chamber view, and the transgastric short axis view.

Wall motion is graded both on excursion and wall thickening. Excursion is defined as inward movement along an imaginary radius to the center of

Table 3.3 Left ventricular 17 segment anatomic model.

Base	Mid	Apex
Anterior	Anterior	Anterior
Anterio-lateral	Anterio-lateral	Lateral
Infero-lateral	Infero-lateral	Inferior
Inferior	Inferior	Septal
Infero-septal	Infero-septal	Apical cap
Anterio-septal	Anterio-septal	

the ventricular cavity. Both assessments are necessary because it is possible for an infarcted segment of myocardium to move passively by surrounding areas of normal myocardium; however, the infarcted myocardium will not thicken. By concentrating on both excursion and thickening, it is possible to account for the translation (lateral motion of the entire heart) and rotation of the echocardiographic image during contraction. Wall motion is graded as follows: 1, normal; 2, hypokinetic; 3, akinetic; and 4, dyskinetic.

A new wall motion abnormality is defined when the wall motion score changes two or more grades. The recognition of a new RWMA is more difficult than it sounds, particularly in the presence of a preexisting RWMA. Furthermore, recognition of mild degrees of RWMAs are more difficult than recognition of normal wall motion or severe RWMA.

LV diastolic function

LV diastolic function is characterized using an integrated approach, involving analysis of the mitral inflow pattern, the pulmonary venous blood flow pattern and tissue Doppler. Diastole commences with isovolumic relaxation. As ventricular relaxation continues, LV pressure falls. LAP eventually exceeds LV pressure and the mitral valve opens, allowing early (E) rapid filling of the LV. Next, a period of diastasis occurs as LA and LV pressure equilibrate. Finally, atrial contraction (A) occurs and augments LV filling as diastole terminates. All of these events are detectable with Doppler spectra.

Isovolumic relaxation time

Isovolumic relaxation time (IVRT) is the time from aortic valve closure to the commencement of flow across the mitral valve. IVRT can be detected by placing the CW Doppler cursor across the mitral inflow and aortic outflow tracts. The time from the aortic valve closure click to the commencement of mitral flow is the IVRT.

Mitral inflow

Mitral inflow can be assessed with the PW Doppler sample volume placed at the tips of the mitral
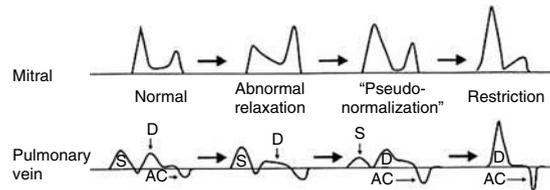
Fig. 3.31 Schematic of the relationship between mitral inflow and pulmonary venous flow patterns. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

Table 3.4 Normal values for mitral inflow parameters as well as those encountered with impaired relaxation and restriction. (From DiNardo JA. Monitoring. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:37–80, with permission.)

	Abnormal relaxation	Normal	Restriction
DT	>240 ms	160–240 ms	<160 ms
E	↓	0.8–1.5 M/s	↔↑
A	↑	0.75 M/s	↓
E/A	E < A	E > A (>1.0)	E ≫ A
IVRT	↑	55–90 ms	<70 ms

leaflets. The spectra will contain E and A velocities, which correspond to passive (E) and atrial (A) filling of the LV (Fig. 3.31). Normal values for the parameters derived from the spectra are shown in Table 3.4.

Pulmonary venous flow

Pulmonary venous flow is measured by placing the PW sample volume 1.0–2.0 cm into the pulmonary vein from its junction at the left atrium. Typically, the LUPV or LLPV is used. A typical pulmonary vein spectra is shown in Fig. 3.31. The systolic (S) velocity occurs as a result of LA filling during LV systole, whereas the diastolic (D) velocity occurs as the result of LA filling during LV diastole. There is flow reversal seen with atrial systole (A). The D velocity usually mirrors the E velocity of mitral inflow. The S velocity often is seen to have an early (S1) and

late (S2) velocity with S1 < S2. S1 is the result of LA relaxation, whereas S2 is the result of movement of the mitral annulus toward the LV apex during LV contraction.

Abnormalities of LV diastolic function

The range of LV diastolic abnormalities is summarized in Fig. 3.32. With impaired relaxation, the E velocity is reduced, the A velocity is increased, and the mitral DT and IVRT are increased. The pulmonary venous spectra mirror these changes with a reduction in the velocity and an increase in the DT of the diastolic component (D) of pulmonary venous return. These changes all are a consequence of prolonged ventricular filling during early diastole. This pattern is very common in patients with coronary artery disease and in patients with left ventricular hypertrophy.

Pseudonormalization occurs due to an elevation in mean LAP. This normalizes the passive mitral filling, mitral DT, and IVRT by increasing the pressure gradient between the LA and LV and masking the impaired relaxation. This pattern is distinguished from the normal pattern by analysis of the pulmonary venous blood flow and the tissue Doppler pattern. The systolic component (S) of pulmonary venous return is reduced because of the elevated LAP. In addition, the flow reversal with atrial contraction is more prominent because of enhanced atrial contraction in the expanded atrium and reduced ventricular compliance.

Rapid mitral DT and IVRT characterize the restrictive pattern. In this pathology, ventricular filling is restricted resulting in rapid equilibration of LAP and LV pressure. The velocity of early filling (E) is high because of an elevated LAP. There is little
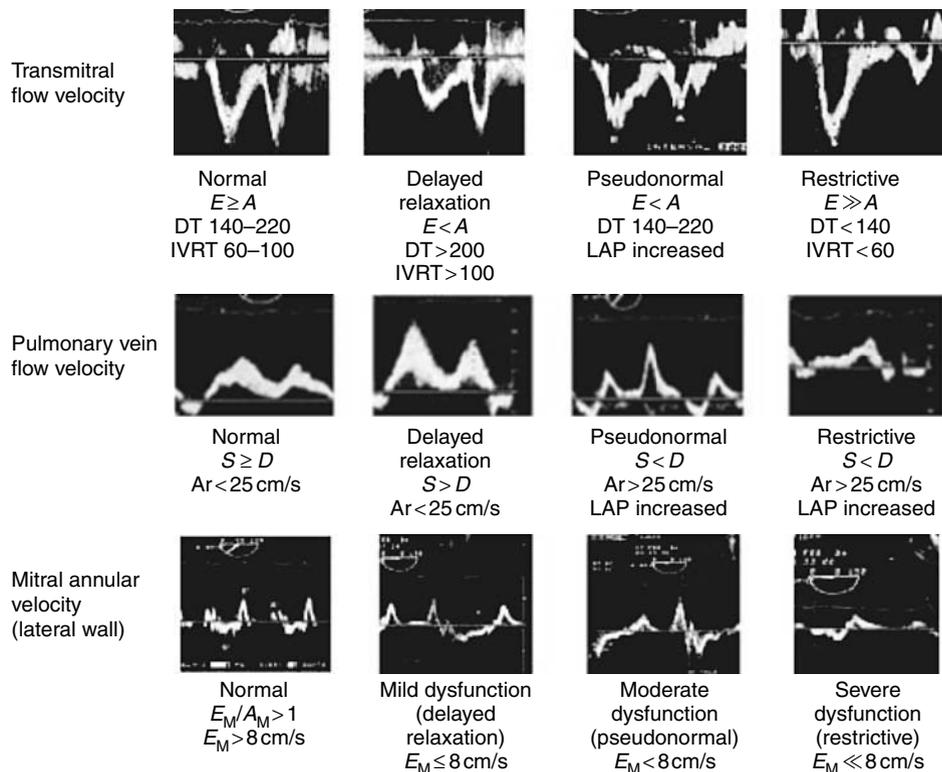
Fig. 3.32 Transmitral Doppler imaging, pulmonary view Doppler imaging, and tissue Doppler imaging profiles corresponding to normal, delayed relaxation, pseudonormal, and restrictive filling patterns. (From Groban L, Dolinsky SY *Chest* 2005;**128**:3652–63, with permission.)

contribution to LV filling from atrial contraction, and thus, atrial filling velocity (A) is low The pulmonary veins exhibit marked reduction of the systolic component (S) of filling due the high LAP. The velocity of the diastolic component (D) is high as it corresponds to the early filling (E) velocity across the mitral valve. There is pronounced flow reversal with atrial contraction because of enhanced atrial contraction and minimal antegrade flow across the mitral valve with atrial systole. This restrictive pattern is common in patients with dilated cardiomyopathies and in patients with ventricular volume overload.

Unfortunately, the velocity patterns are load dependent, which can make application difficult. A normal pattern can be converted to an impaired relaxation pattern with hypovolemia or afterload increases. Similarly, an impaired relaxation pattern can be pseudonormalized with volume expansion.

Tissue Doppler

Tissue Doppler is the application of a PW Doppler in the annular ring of the mitral valve and sampling for the velocity of the heart tissue during relaxation. There are two measured components: the early diastolic movement (E') and the atrial contraction component of ventricular filling (A'). The E' and A' correspond to the mitral inflow velocities of E and A. An E' less than 8 cm/s is abnormal and indicates diastolic dysfunction.

Figure 3.33 provides an easy step-by-step algorithm to determine the degree of diastolic dysfunction.

Right ventricular function

Global RV function is assessed using the same techniques as described for the LV to determine EDA, ESA, and FAC. This usually is performed in a short-axis view, the four-chamber view, and the transgastric view. This allows all five wall segments of the RV to be analyzed: inferior wall, septal wall, lateral wall, anterior wall, and anterior wall of the RVOT. Use of the biplane and multiplane probes allows a long view of both the RV inflow and outflow tracts and of the RV inferior wall and anterior wall of the RVOT. This view is valuable for assessing RV size and systolic function.

Valvular heart disease

All four heart valves are well visualized with TEE. Although most cardiac surgical patients will present to the operating room with a complete diagnostic work up of anatomic structure, a comprehensive examination is required in all patients when a TEE is performed. Heart valve structure and function must be observed and documented. It is not uncommon to find new pathology or new information that will help steer the planned operative procedure. There are many excellent textbooks detailing the various techniques and anatomic findings seen with TEE. In this next section, disease of the mitral, aortic and tricuspid valve are briefly reviewed.

Mitral valve

The mitral valve separates the LV from the left atrium, pulmonary circulation and entire right side of the heart. The valve is bicuspid with an anterior and posterior leaflet. The anterior leaflet is the larger of the two leaflets, accounting for two-thirds of the surface area of the valve. The posterior leaflet wraps around the anterior leaflet, accounting for only one-third of the valve's surface area and two-thirds of the annular circumference. The mitral annulus is a fibrous ring surrounding the mitral valve. During ventricular systole, the contraction of the papillary muscles prevent mitral leaflet prolapse. Ruptured chordae are a common cause of mitral insufficiency. The Carpentier classification divides the three scallops of the posterior leaflet into P1, P2, and P3; and the anterior leaflet into the three segments A1, A2, and A3, which oppose the corresponding scallops of the posterior valve. The coaptation of A1/P1 at the annulus form the anterolateral commissure. The coaptation of A3/P3 at the annulus form the posteromedial commissure.

Mitral stenosis (MS)

Normal mitral valve areas range from 4–6 cm^2, and symptomatic stenosis is seen when the valve approaches 1.5 cm^2. Rheumatic heart disease is a common cause of MS and it is characterized by commissural fusion with doming of the valve leaflets. Leaflet tip thickening and chordae tendineae thickening, fusion, and calcification result in restricted
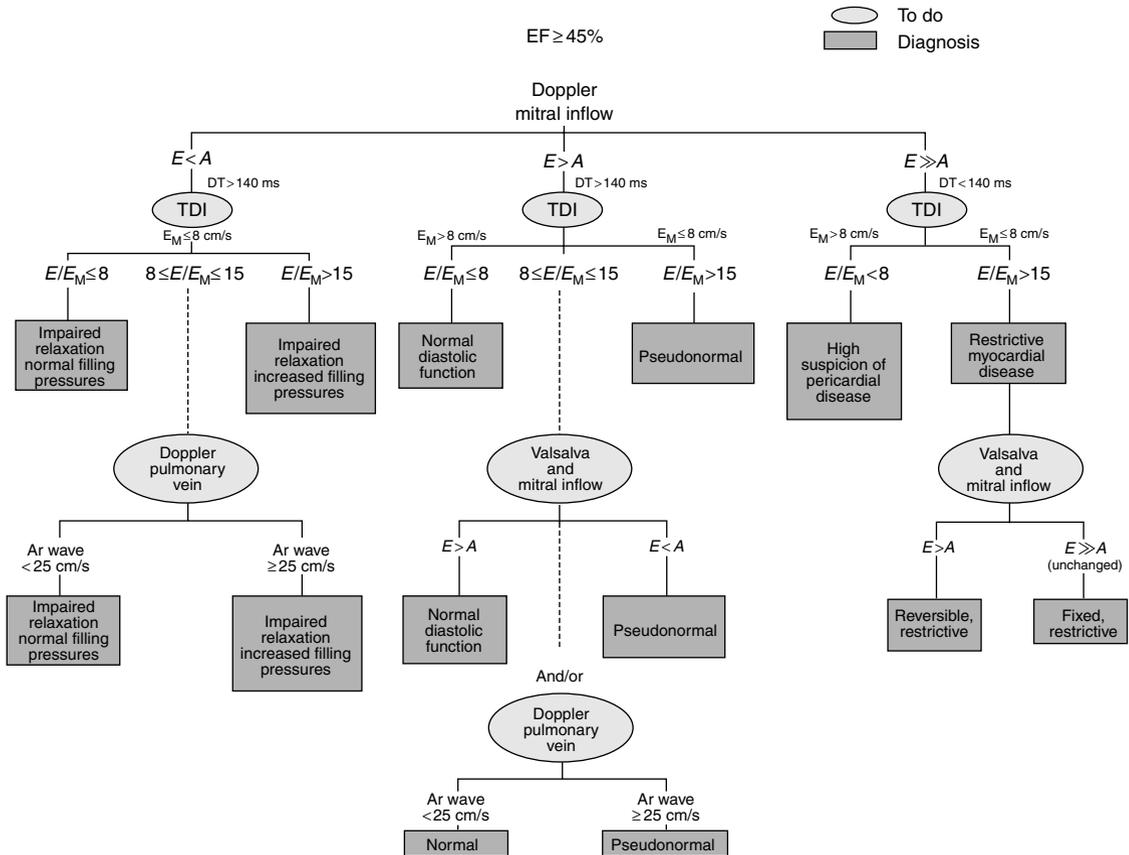
Fig. 3.33 An algorithm to determine the degree of diastolic dysfunction using transesophageal echocardiography (TEE). A, atrial peak velocity; Ar, retrograde velocity; E, early filling peak velocity; E_M, early filling; TDI, tissue Doppler imaging. (From Groban L, Dolinski SY. Transechocardiographic evaluation of diastolic function. *Chest* 2005;**128**:3652–63, with permission.)

leaflet motion. MS increases transvalvular pressure gradients leading to increased left atrial (LA) pressures and LA distention. Increased LA pressures can lead to pulmonary hypertension with right ventricular dysfunction and tricuspid regurgitation. The left atrium will be enlarged and hypokinetic and may be filled with spontaneous contrast (swirling, smoke-like contrast). Spontaneous contrast is indicative of a low flow state and is predictive of subsequent development of left atrial thrombus. The left atrium should be examined carefully for thrombus, particularly in the left atrial appendage. If there is atrial fibrillation or flutter, the atrium will appear akinetic.

Two-dimensional (2-D) anatomy

Two-dimensional imaging of the stenotic mitral valve typically demonstrates thickening and fibrosis of the mitral valve leaflets, restricted leaflet motion, and mitral annular calcification. The MV area can be estimated directly with planimetry in the transgastric basal short-axis view.

Doppler

CW Doppler is used to determine the mean velocity and mean grade using the VTI. Because the mean gradient can underestimate the severity of MS with low cardiac outputs and overestimate the severity in the presence of mitral regurgitation, the valve

Table 3.5 Severity estimation of mitral stenosis.

Grade	Mild	Moderate	Severe
Mean gradient (mmHg)	<6	6–10	>10
PHT (ms)	100	200	>300
DHT (ms)	<500	500–700	>700
MVA (cm^2)	1.6–2.0	1.0–1.5	<1.0

area should be determined. MVA can be calculated using the PHT method. The summary of mean gradients, PHT, deceleration time, and MVA in MS are seen in Table 3.5. Color flow Doppler can be used to calculate valve area using the proximal isovolemic surface area (PISA) equation. The PHT will overestimate MVA (underestimate severity) in conditions in which LV pressure rises quickly in diastole, such as aortic insufficiency (AI) or reduced LV compliance. PHT is unreliable when there is merging of the E and A waves or an alteration in the E wave decay pattern due to tachycardia, atrioventricular (AV) block, or atrial flutter. In these instances, the continuity equation using the MV_{VTI} and the $LVOT_{VTI}$ and $LVOT_{AREA}$ can be used to calculate MVA assuming there is no MR. Details of the use of $LVOT_{VTI}$ and $LVOT_{AREA}$ are explained in the section on aortic stenosis.

Mitral regurgitation

Mitral regurgitation is commonly seen in the cardiac surgical patient. There are a myriad of causes including has including myxomatous degeneration, rheumatic disease, endocarditis, Marfan syndrome, infiltrative diseases (amyloid, sarcoid, mucopolysaccharidosis), collagen-vascular disorders (SLE, rheumatoid arthritis), papillary muscle rupture or dysfunction (ischemia), and cardiomyopathies. General anesthesia, changing hemodynamic conditions and volume status greatly affect measured mitral regurgitation. It is important for the echocardiographer to quantify the degree of MR under physiologic conditions if possible. It may be necessary to use phenylephrine to elevate afterload and attempt to duplicate preoperative conditions for patients in whom the intraoperative assessment of MR is significantly different from the preoperative assessment.

Two-dimensional (2-D) anatomy

Mitral leaflet motion is well visualized with TEE and will direct the echocardiographer to the correct diagnosis. There can be excessive leaflet motion, restricted leaflet motion, or normal leaflet motion with poor coaptation. Excessive leaflet motion can be classified as billowing, prolapse or flail. A billowing mitral leaflet demonstrates bowing of part of the mitral valve leaflet above the level of the mitral annulus. The leaflet edge, however, still coapts well, and there is no MR. Prolapse occurs when the leaflet edge extends above the level of the annulus. Flail leaflet occurs when the supporting structures, the papillary muscle or chordae tendinae rupture, allowing leaflet movement into the left atrium during systole. MR due to excessive leaflet motion will result in a regurgitant jet directed away from the affected valve leaflet. Conversely, MR caused by restricted leaflet motion results in a regurgitant jet directed towards the affected valve leaflet. Severe MR is associated with a dilated left atrium and elevated pulmonary pressure.

Doppler

Comprehensive quantitative evaluation of MR should be performed intraoperatively. Color flow (CF) Doppler analysis of the regurgitant jet (see Fig. 3.15) is performed in combination with PW Doppler interrogation of the pulmonary veins. The area of the regurgitant jet relative to the area of the LA is a useful CF Doppler technique. This should be performed in as many planes as possible to gain a good understanding of the extent of the MR. It should be performed at the level of the mitral valve using a full 180° sweep with a multiplane probe or at multiple angles using a biplane probe. Table 3.6 lists several measures one can use to assess MR severity.

Regurgitant jets, which hug the atrial wall (Coanda effect), are considered constrained jets and will be 30–40% smaller than a free jet (such as a central jet) under the same conditions of regurgitation. Jets that exhibit the Coanda effect usually are associated with moderate to severe MR. When

Table 3.6 Grading of mitral regurgitation severity.

Method	Mild	Moderate	Severe
Jet area (cm^2)	<3	3–6	>6
Vena contracta (cm)	<0.3	0.3–0.55	>0.55
Regurgitant fraction (%)	<30	30–50	>50
Mitral orifice area (cm^2)	<0.2	0.2–0.39	≥0.4
Regurgitant volume (mL)	<30	30–59	≥60
Pulmonary vein flow	Blunted S wave	S wave < D wave	Systolic reversal

the MR jet width at the mitral leaflet (vena contracta) is greater than 0.6 cm, MR usually is severe. Quantitative methods to classify MR exist, such as regurgitant fraction calculations and proximal isovelocity surface area (PISA), but they generally are cumbersome and time consuming.

Technical factors such as CF Doppler gain and Nyquist limit will affect the imaging of the regurgitant jet. Proper technique calls for turning the color gain up all the way, then reduce it until the "sparkling" disappears, and starting with the velocity scale peak at 50–60 cm/s. Both right and left pulmonary veins should be examined because eccentric jets may reverse flow in the pulmonary veins on only one side of the atrium.

The aortic valve

The aortic valve consists of three semilunar valves named according to their relationship to the coronary arteries: the right coronary cusp, the left coronary cusp, and the noncoronary cusp. At the center of the free-edge of each cusp is a tiny, elevated nodule commonly referred to as the nodule of Arantius. The aortic valve complex is composed of the sinotubular junction, the sinuses of Valsalva, the valve cusps, the junction of the aortic valve with the ventricular septum, and the anterior mitral valve leaflet. All of these structures are imaged easily with TEE.

Aortic stenosis

Aortic stenosis occurs when there is a fixed obstruction to left ventricular ejection of blood into the aorta. Normal aortic valve area is 2.5–3.5 cm^2. The severity of aortic stenosis is divided into

three categories by valve area as follows: mild (1.5–1.0 cm^2), moderate (1.0–0.8 cm^2), or severe (<0.8 cm^2). The classic triad of syncope, angina and congestive heart failure are associated with the late stages of aortic stenosis and are ominous signs at their onset.

Two-dimensional (2-D) anatomy

A number of views of the aortic valve are available, but the short- and long-axis views of the aortic valve are most useful. Leaflet mobility should be observed. A stenotic valve will have limited opening and heavy calcification may be present in the leaflets and commissures. A bicuspid aortic valve can be identified easily in a short-axis view. Unfortunately, 2-D imaging is limited by the occasional inability to evaluate the stenotic valve in the correct plane, thereby underestimating the true area of valvular stenosis. Therefore, it is imperative to examine the valve until the narrowest area of stenosis is identifiable and the stenotic area is reproducible with multiple measurements. A secondary sign of aortic stenosis is left ventricular hypertrophy.

Doppler

Severity can also be quantified using Doppler measurements of the peak and mean gradients and the calculated aortic valve area. The mean gradient and peak instantaneous gradient are determined with the VTI obtained by using CW Doppler aligned parallel (or within 20°) to the LVOT, aortic valve, and proximal ascending aorta. If the peak aortic velocity is greater than 4.5 m/s, the aortic stenosis is severe. Either the peak or the mean aortic velocity can be substituted into the simplified Bernoulli

equation that is used to calculate the transvalvular pressure gradient. The simplified Bernoulli equation for the peak gradient is calculated with the following equation: Peak Gradient (mmHg) = 4 (Aortic Peak Velocity)^2. Based on the peak aortic gradient value, the severity of aortic stenosis is graded as mild (<36 mmHg), moderate (>50 mmHg), or severe (>80 mmHg). The simplified Bernoulli equation for the mean gradient is calculated with either of the following equations: Mean Gradient (mmHg) = 4 (Mean Velocity)^2 or 2.4 (Vmax)^2. The value of the mean aortic velocity grades the severity of aortic stenosis as mild (<20 mmHg), moderate (20–50 mmHg), or severe (>50 mmHg). Unfortunately, this technique is sometimes difficult because the deep transgastric long-axis view can be very elusive even for an experienced echocardiographer. Remember that gradients will underestimate the severity of the stenosis when output is low and may overestimate it when output is high. If there is suspicion that the gradient is misleading, the aortic valve area should be calculated or the dimensionless index (DI) should be used:

DI = peak velocity LVOT/peak velocity AoV or

$\quad$ LVOT$_{VTI}$/AoV$_{VTI}$.

A DI < 0.2 indicates severe aortic stenosis. Because the peak velocity in the LVOT and across the aortic valve will change proportionally, this index is independent of cardiac output.

Doppler information can be used to calculate the aortic valve area using the continuity equation: AoV$_{AREA}$ = (LVOT$_{AREA}$) × (LVOT$_{VTI}$)/AoV$_{VTI}$. The LVOT area is determined using the diameter method. The long-axis view of the aortic valve can be used to measure the diameter at the point at which the aortic valve cusps abut the LVOT. AoV$_{VTI}$ is obtained with CW Doppler across the aortic valve in systole with the views used to obtain VTI. LVOT$_{VTI}$ is obtained with PW Doppler in the LVOT just below the aortic valve leaflets in systole with the views used to obtain VTI.

Aortic regurgitation (AR)

TEE can identify the presence of regurgitation, quantify its severity, determine the etiology, and examine the secondary effects on other heart structures (i.e. left ventricle, mitral valve). In general, the etiology of aortic regurgitation is classified into two major groups: leaflet abnormalities and aortic root abnormalities. Leaflet abnormalities include congenital bicuspid valves, calcific valve disease, rheumatic valve disease, myxomatous valve disease, endocarditis, and nonbacterial thrombotic endocarditis. Aortic root abnormalities are the most common cause of aortic regurgitation. Aortic root abnormalities include annular dilatation, hypertensive aortic root dilation, cystic medial necrosis, Marfan syndrome, and aortic dissection.

Two-dimensional (2-D) anatomy

Similar to the evaluation of aortic stenosis, 2-D examination of the aortic valve will yield information on the etiology and extent of aortic regurgitation. In severe AR there may be fluttering of the anterior mitral valve leaflet in diastole when the AR jet is directed along it. There may be enlargement of the ascending aorta and aortic root causing poor coaptation of the aortic leaflets and AR. Retrograde aortic dissection can cause mechanical deformation of the aortic valve annulus and AR. The AR may be associated with vegetations and leaflet perforation. The presence of AR may alter the manner in which cardioplegia is delivered as infusion into the aortic root may not be effective when moderate or severe AR is present. The LV may exhibit eccentric hypertrophy.

Doppler

CF Doppler imaging of the aortic valve in the long axis is used to measure the minimum width of the regurgitant jet (usually at the origin of the jet at the leaflets) relative to the width of the LVOT. AR is graded, based on this assessment, as follows:
- Trace: jet area/LVOT width <0.25
- Mild: jet area/LVOT width 0.25–0.46
- Moderate: jet area/LVOT width 0.47–0.64
- Severe: jet area/LVOT width >0.65

CF Doppler imaging of the aortic valve in the short axis at or just below the level of aortic valve leaflets is used to measure the regurgitant jet area relative to the circular LVOT area at this level (Fig. 3.34).
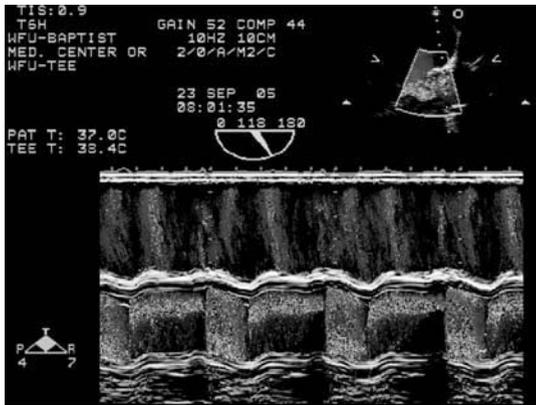
Fig. 3.34 M-mode color Doppler image just below the aortic valve in the left ventricular outflow track demonstrating aortic regurgitation.

Fig. 3.35 Pulse wave Doppler in the hepatic veins of a patient with severe tricuspid regurgitation (TR). There is reversal of hepatic venous flow indicating severe TR.

AR is graded, based on this assessment, as follows:
- Trace: jet area/LVOT width <0.20
- Mild: jet area/LVOT width 0.20–0.40
- Moderate: jet area/LVOT width 0.40–0.60
- Severe: jet area/LVOT width >0.60

CW Doppler is useful for quantifying AR by determining the PHT of the regurgitant spectra. A PHT <300 ms is indicative of severe AR; whereas, a PHT >800 ms is associated with mild AR. This occurs because, in severe AR, there is more rapid equilibration between aortic and LV pressure in diastole and thus a more rapid decay in the velocity of the regurgitant spectra. In severe AR, the CW Doppler spectra will be dense, whereas in mild AR, it will be faint. CF Doppler will help guide positioning of the CW cursor.

PW Doppler of the mitral inflow will reveal a restrictive pattern in severe or acute AR. PW Doppler of the proximal descending thoracic aorta will reveal holodiastolic flow reversal in severe AR. It is impossible to align the Doppler beam parallel to the descending aorta, but it still may be possible to detect diastolic flow reversal.

Tricuspid and pulmonic valves

The tricuspid valve consists of anterior, posterior and septal cusps tethered by chordae tendinae and papillary muscles all suspended by a fibromuscular annulus. The commisures of the tricuspid valve are not as well defined as those of the mitral valve. The orifice is larger than that of the mitral valve and is triangular in shape, as compared to the saddle-shape of the mitral valve. The pulmonic valve is anterior and superior to the aortic valve. Similar to the aortic valve, it is trileaflet and semilunar, consisting of anterior, left and right leaflets. The plane of the valve is roughly perpendicular in orientation to the aortic valve. The pulmonic valve is isolated from the other three heart valves by the infundibulum.

Insignificant tricuspid insufficiency is very common and is often seen in patients with transvenous pacemaker leads and/or PACs. Moderate to severe tricuspid insufficiency is most frequently the result of dilation of the right ventricle and the tricuspid annulus. Any condition resulting in elevated right ventricular pressure (>55 mmHg) or right ventricular dilation can cause tricuspid insufficiency. Common causes observed in surgical patients include myocardial ischemia, cor pulmonale, pulmonary embolism, left heart failure, pulmonic valve stenosis and pulmonary hypertension. Significant mitral insufficiency is a common cause of right ventricular dilation and secondary tricuspid insufficiency. Reversal of flow in the hepatic veins is associated with more severe tricuspid regurgitation (Fig. 3.35).

Tricuspid stenosis is much less common than tricuspid insufficiency. Rheumatic heart disease

is the most common cause of tricuspid stenosis and results in thickened, immobile valve leaflets with commissural fusion. Diastolic doming of the leaflets is usually present. In these cases, the mitral valve is usually also involved. Other causes of tricuspid stenosis, although rare, include congenital anomalies, endocarditis, carcinoid heart disease and endomyocardial fibrosis. Tricuspid valve area is estimated by the pressure half-time method or planimetry.

Pulmonary insufficiency is commonly observed in cardiac surgical patients, especially if a PAC is in place. Severe pulmonary insufficiency is always pathologic and usually the result of dilation of the main pulmonary artery as seen in patients with pulmonary hypertension from any etiology. The causes of pulmonary insufficiency include fenfluramine–phentermine valvulopathy and carcinoid syndrome. These lesions result in short and thickened valves which fail to properly coapt. Infectious endocarditis can affects the tricuspid and pulmonic valves and presents as mobile masses attached to the valve leaflets.

Pulmonic stenosis is categorized as valvular, sub-valvular, or peripheral (supravalvular). Ninety percent of the lesions are valvular in nature and the majority of pulmonary stenosis in the adult population is from untreated or recurrent congenital disease, such as tetralogy of Fallot. Pulmonary stenosis is more commonly seen as individuals with complex congenital heart disease increasingly survive into adulthood. Pressure gradients using CW Doppler across the stenotic valve allow the quantification of pulmonary stenosis as follows: Peak gradients <30 mmHg are associated with mild stenosis, peak gradients between 30 and 65 mmHg indicate moderate stenosis, and gradients >65 mmHg are seen with severe pulmonary stenosis. The continuity equation can be used to determine the area of the pulmonary valve to further assess disease severity.

TEE after valve repair or replacement

After any valvular surgery, the repair or replacement must be assessed for both regurgitation and stenosis. The presence of trace to mild MR after MV repair does not confer increased morbidity or mortality. The valve should be evaluated for stenosis
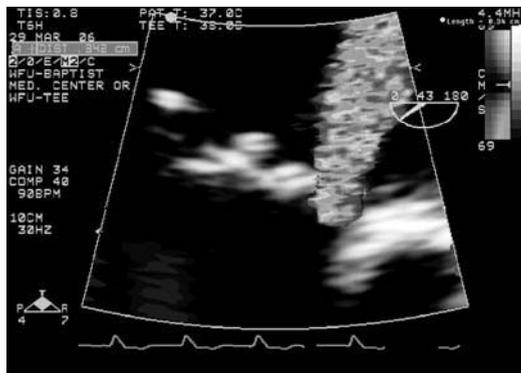
Fig. 3.36 Zoom view of a perivalvular leak after a mitral valve replacement. Transesophageal echocardiography (TEE) evaluation after all valve repair and replacement procedures must include an examination for regurgitation, perivalvular leak, and gradients across the valve.

either directly by planimetry or indirectly with the PHT method. Systolic anterior motion (SAM) leading to LVOT obstruction should be evaluated. Discussion of all types of prosthetic valves is beyond the scope of this presentation. However, several important points deserve discussion. All mechanical valves have some small quantity of regurgitant flow built into their design to prevent thrombus formation. This regurgitant flow is characterized by low velocity, small area, and location within the annulus of the valve. If a leaflet is stuck in the open position, the amount of regurgitation present will be large. Tissue valves are not regurgitant unless they have degenerated. Perivalvular leaks generally have a high velocity and are located at the outer margin of the annulus or sewing ring (Fig. 3.36).

Prosthetic valves should have transvalvular gradients that are physiologic for the particular position. If the gradient across a prosthetic valve is high, an aggressive examination to determine whether the leaflets are opening is warranted. A leaflet may be stuck closed because of impingement on surrounding tissue.

Removing air from the heart

All procedures in which the heart is opened have potential to introduce air into the systemic circulation. In addition, closed procedures have

the potential to introduce air because of the placement of vents to decompress the left side of the heart. TEE can detect intracardiac air and guide air evacuation before termination of CPB. Air is particularly likely to be retained in the LV apex, left atrium, right coronary sinus, and the pulmonary veins, particularly the right upper pulmonary vein.

Estimation of intracardiac pressures

Peak pressure gradients

This method requires the presence of a regurgitant valve or a communication between cardiac chambers. It is based on the premise that the peak velocity of a regurgitant jet can be used to determine the pressure gradient between two cardiac chambers during either systole or diastole. Peak velocity is converted to the peak pressure gradient using $4V^2$.

For example, if there is a TR jet with a peak velocity of 3.0 m/s, then a peak pressure gradient of 36 mmHg exists between the RV and RA during systole because TR is a systolic event. If we measure the central venous pressure (CVP) to be 10 mmHg (or assume that it is 10 mmHg), then RV systolic pressure must be $36 + 10 = 46$ mmHg. If we know (or assume) that there is no RVOT obstruction, then PA systolic pressure is also 46 mmHg.

Pulmonary regurgitation (PR) Doppler spectra can be used in the same way. The peak PR velocity (velocity at the beginning of diastole) is used to calculate the pressure difference between the pulmonary artery (PA) and the RV at the time of pulmonary valve closure in diastole which gives a good estimate of mean PA pressure (PAP).

Mean PAP = 4(peak PR velocity)^2 + RV end-diastolic pressure (EDP); RV EDP = CVP, which again is measured or assumed. If the PR velocity at the end of diastole is used, PA EDP can be calculated. PA EDP = 4(end-diastolic PR velocity)^2 + RV EDP; RV EDP = CVP, which again is measured or assumed.

The same arguments can be used with MR and AR velocities.

Movement of the atrial septum

The shape of the atrial septum is determined by the atrial pressure gradient. Normally, LAP is greater than RAP and the atrial septum is bowed toward the RA. During the passive, expiratory phase of mechanical ventilation, there is a transient mid-systolic reversal of inter-atrial septum position with bowing of the atrial septum into the LA from the RA. This finding is highly predictive of a pulmonary capillary wedge pressure (PCWP) less than 15 mmHg. Conversely, absence of this finding is highly predictive of a PCWP greater than 15 mmHg.

The observation of an atrial septum continuously shifted to the left would predict elevated RAP.

Pulmonary and hepatic venous blood flow velocities

Reductions in the systolic portion of the hepatic venous Doppler spectra relative to the diastolic portion are strongly correlated with increases in RAP. In fact, progressive decreases in the ratio VTIsystolic/(VTIsystolic + VTIdiastolic) are associated with increasing RAP. Similar observations have been made regarding pulmonary venous Doppler spectra and PCWP and LAP. When LVEDP >15 mmHg the flow duration of pulmonary versus atrial flow reversal is more than 30 ms longer than the duration of the mitral A wave.

Thoracic aorta

TEE is useful for examination of the ascending aorta, aortic arch, and descending thoracic aorta. The distal ascending aorta and proximal aortic arch are poorly visualized because of interposed interference from air in the trachea and/or left main stem bronchus. Unfortunately, this area encompasses the region in which the aortic cannula, aortic cross-clamp, and proximal ends of the saphenous vein grafts are typically placed. Because of the higher incidence of stroke seen in patients with atheroma in the ascending and descending aorta undergoing undergo cardiac surgery with CPB, there is concern about manipulation of the aortic if it contains atheroma. Presently, only epiaortic scanning (placement of a transducer directly on the aorta) can reliably visualize this area.

Atheromatous disease of the aorta is graded I to V as follows: I, normal; II, extensive intimal thickening; III, sessile atheroma protruding <5 mm
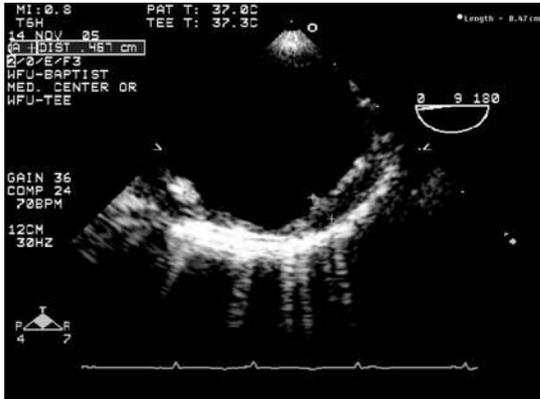
Fig. 3.37 Moderate plaque in the descending aorta. Such an image may prompt an epiaortic examination of the ascending aorta.

Fig. 3.38 An epiaortic scan of the ascending aorta reveals grade III atheromatous disease.

into the aorta; IV, sessile atheroma protruding >5 mm into the aorta; and V, mobile atheroma (Figs 3.37 & 3.38).

Observation of atheroma in the aorta should prompt attention to placement of the aortic cannula. Although TEE can rarely be used to visualize the site of aortic cannulation, it can be used to visualize the jet out of the aortic cannula. This is accomplished using CF Doppler in conjunction with a 2-D image of the aortic arch. The direction of the jet out of the aortic cannula is important because the jet can dislodge plaque. Misdirection of the cannula jet down the left subclavian artery or left CA also

can be detected using CF Doppler in conjunction with 2-D images of those vessels. TEE also is used extensively to diagnosis aneurysm, dissection, and disruption of the ascending aorta, aortic arch, and descending aorta. Ultrasound artifacts are found in 50–60% of patients and may result in misdiagnosis. There are two classes of artifacts: linear and mirror image. Linear artifacts occur in the ascending aorta and are the result of reflections from either the left atrium (LA) or right pulmonary artery (RPA). They can be distinguished from intimal flaps because they do not display rapid oscillatory motion, do not disrupt the CF Doppler flow pattern, are parallel to the posterior aortic wall, have movement (best seen with M mode) parallel to that of the posterior aortic wall, and are located twice as far from the posterior wall of the LA or RPA as from the posterior wall of the aorta. Mirror image artifacts occur in the arch and descending aorta and give the appearance of a double barrelled aorta. They are caused by reflections from the lung–aorta interface. They can be distinguished from intimal flaps or false lumens by the double-barrelled mirror image appearance and by the lack of interruption of the CF Doppler flow pattern.

Congenital heart disease

A comprehensive treatment of the use of TEE of the wide variety of congenital lesions the pediatric cardiac anesthesiologist is likely to encounter is beyond the scope of this chapter. However, by becoming familiar with some basic principles, the reader should be able to begin conducting a good quality examination in patients with congenital heart disease. With a biplane or multiplane probe, a comprehensive 2-D and Doppler examination of the heart, including the LVOT and RVOT can be obtained. The LVOT and RVOT are not well-oriented for performance of a Doppler examination with standard single-plane imaging. If only a single-plane probe is available, the deep transgastric position will allow visualization of the LVOT and RVOT and the ventriculo-arterial connections. In some situations, deep transgastric imaging may provide superior delineation of anatomy than biplane examination. From a practical point of view, deep transgastric imaging with a biplane probe is difficult and much

less satisfactory because the extra transducer element makes the distance from the tip of the probe to the flexion point longer. This makes good tissue contact difficult, particularly in small infants. The following issues should be addressed while performing an examination of a patient with congenital heart disease.

Atrial identity and location

Identity of the atrial chamber by examining the appendage is helpful. The right atrial appendage (RAA) is best seen in the transverse plane at the level demonstrated in Fig. 3.22. Flexion of the probe will allow better visualization. The RAA has a broad junction to the RA which is short and blunt (Snoopy's nose). The LAA is seen in multiple views. The LAA has a narrow junction to the LA, it is long, narrow, and crenulated (Snoopy's ear). The IVC almost always returns to the RA; whereas, the return patterns of the SVC and pulmonary veins are much less reliable. The RA will have a eustachian valve and the LA septal surface has the flap of the fossa ovalis. The atrial situs solitus is the normal condition: the RA on the right side of the heart, LA on the left side of the heart. Atrial situs inversus occurs when the RA is on the left side of the heart, and the LA on the right side of the heart.

Ventricular size and identity

A chamber is considered a ventricle if it receives more than 50% of the ventricular inlet or fibrous ring of an AV valve. The AV valve need not be patent for the chamber to be considered a ventricle, as is the case with tricuspid or mitral atresia. Likewise, the chamber does not need to be large to be considered a ventricle, as is the case with hypoplastic left heart syndrome. The right and left ventricles have different morphologies:

1 RV:

a has the tricuspid valve (three leaflets) with one the leaflets having a chordal attachment to the septum; there are three papillary muscles that are located apically.

b the septal leaflet of the tricuspid valve inserts slightly lower on the intraventricular septum than the anterior leaflet of the mitral valve.

c the RV has a triangular shape and a trabeculated endocardial surface.

d the RV has the moderator band, a band of tissue that stretches from lower intraventricular septum to the anterior RV wall and is best seen in the four-chamber view with retroflexion of the TEE probe.

2 LV:

a has the mitral valve (two leaflets) with no chordal attachment to the septum; there are two papillary muscles that are located at the junction of the apical and middle two-thirds of the chamber.

b has an ellipsoidal shape and a smooth endocardial surface.

Great vessel orientation and identity

Normally, the great vessels are oriented at 45° to each other when they leave the heart with the pulmonary artery (PA) anterior to the aorta. When they are viewed with echocardiography, one vessel will be observed in the short axis and the other will have a sausage shape. This is seen in the transverse plane image. When the great vessels are transposed, they are oriented parallel to each other when they leave the heart. When they are viewed by TEE, both vessels will be observed in the same axis. The rule of thumb when viewing transposed vessels in the short axis is that the anterior vessel is invariably the aorta. When the vessels are aligned side to side, the determination is more difficult and usually requires finding the arch of the aorta or the branch pulmonary arteries to make the determination.

After the great vessels are identified, their relationship to the ventricles must be delineated. This requires creativity in finding the views that allow this to be seen. This is an instance in which deep transgastric views are useful, although biplane imaging also works well.

Presence of intracardiac shunts and obstructive lesions

CF Doppler is indispensable in identifying intracardiac shunts, including those not seen with 2-D imaging. CW Doppler is useful in determining velocities and gradients across restrictive communications or valves, whereas PW Doppler assesses less restrictive orifices as well as hepatic and

pulmonary venous blood flow. The RVOT must be examined carefully for both dynamic and fixed obstructive lesions. Two-dimensional echocardiography in combination with Doppler will clearly delineate dynamic obstructive lesions. The use of CW Doppler to determine intracardiac pressures as described previously is also valuable.

Evaluation of the surgical repair

A comprehensive preoperative intraoperative study is the foundation of repair assessment. This allows the operator to focus the examination on the repaired lesions. Look for the common things:

1 Patch leaks. After ventricular septal defect (VSD) and atrial septal defect (ASD) repairs, detection of residual VSD leaks can be more difficult than it sounds, because the VSD patch produces areas of echo attenuation in the RV and RVOT that may mask leaks. The use of multiplane imaging improves detection but does not completely resolve this problem.

2 Regurgitant valves. After valvuloplasty but also after transvalvular approaches to the lesion (such as approach to a VSD via the tricuspid valve).

3 Stenotic anastomoses. Pulmonary vein anastomosis to LA in total anomalous pulmonary venous return (TAPVR). SVC to PA in bidirectional cavopulmonary connections (bidirectional Glenn) and total cavopulmonary connections (Fontan). PW Doppler interrogation of these cavopulmonary connections will reveal a phasic venous blood flow pattern with respiratory variation.

4 Residual outflow tract gradients. After tetralogy of Fallot repairs and repair of subaortic membranes.

5 Residual gradients across ASD or VSD left open in the course of a staged repair (tricuspid atresia, double outlet RV, hypoplastic left heart syndrome).

6 Ventricular function assessment. After all repairs. Particular attention paid to patients with reimplanted coronary arteries such as vessel switch for transposition of the great vessels or Ross procedure (transplantation of the pulmonic valve to the aortic position and creation of an RV-to-PA conduit) and to patients who may have had air in the coronary arteries during the surgical process.

7 Patency of aortopulmonary shunts. CW Doppler will detect a high velocity signal with flow in systole and diastole. CF Doppler will help position the CW Doppler beam.

Saline-contrast echocardiography

Saline-contrast echocardiography is a technique that can be used to detect intracardiac shunting. The basis of the technique is opacification of the right heart chambers using agitated saline injected rapidly into a catheter. Microbubble formation occurs as the solution leaves the catheter orifice as dissolved gas escapes from solution. The presence of micro bubbles in high concentrations opacifies the RA and RV. The amount of opacification with a properly performed procedure is impressive.

Saline-contrast studies are used most commonly in conjunction with a provocative maneuver to detect right-to-left flow patency of the foramen ovale. Agitated saline is produced by vigorously transferring 10 mL of saline with a small amount of air between two syringes connected by a stopcock. Alternatively, 8 mL of saline and 2 mL of the patient's blood can be used. The agitated mixture can be injected peripherally or centrally.

Detection of the right-to-left flow patency of the patent foramen ovale (PFO) is dependent on transiently increasing RAP above that of LAP. The easiest way to accomplish this is by applying a Valsalva maneuver (actually sustained positive inspiratory pressure) during positive-pressure ventilation. This transiently impedes venous return to the right heart and subsequently to the left heart. Upon release of the Valsalva, the rapid increase in venous return to the right heart will precede the increase in return to the left heart and the result will be a transient elevation in RAP above that of LAP. The atrial septum must bow into the LA for the test to be effective. The test is accomplished by injecting the saline contrast during the Valsalva maneuver. After opacification of the RA occurs, the Valsalva is released and the TEE is observed for appearance of saline contrast in the LA. Appearance of three or more microbubbles in the LA within three cardiac cycles is indicative of a flow-patent PFO.

Intracardiac and endovascular catheters

TEE can be used in a wide variety of ways to image intracardiac and endovascular catheters and

devices. A few of the most common and important are summarized here:

● *Intra-aortic ballon pump (IABP).* TEE views of the descending thoracic aorta can and should be used to document that the tip of the IABP is below the level of the aortic arch and the takeoff of the left subclavian artery. In addition, inflation and deflation can be observed, which may aid in detection of a ruptured balloon.

● *Coronary sinus cannula for cardioplegia.* The coronary sinus is easily seen in most patients and is obliterated when the catheter is placed properly.

● *Ventricular assist devices.* The inflow and outflow cannulas to the devices can be seen and should be checked to rule out obstruction.

● *Venous cannulas for CPB.* Position in the IVC and SVC can be checked. In particular, the IVC cannula should not impinge on any hepatic veins. Difficulty in placing an IVC cannula can be caused by a prominent eustachian valve.

● *PACs.* The position of a PAC can be documented by sequential views of the RA, RV, and PA. This may have some use if catheter placement is difficult.

Contraindications and complications

The relative and absolute contraindications to use of a TEE probe are summarized below:

● Relative:

a Recent gastroesophageal operation

b Esophageal varicies

c Upper gastrointestinal bleed

d Cervical disk disease

e Severe cervical arthritis

f Unexplained dysphagia or odynophagia

● Absolute:

a Esophageal obstruction (stricture, neoplasm)

b Esophageal fistula, laceration, or perforation

c Esophageal diverticulum

d Cervical spine instability

A number of complications have been reported in association with use of TEE probes. Most complications in adults involve trauma to the upper gastrointestinal (GI) tract ranging from minor lacerations to perforation of the esophagus. The incidence of swallowing complications after cardiac surgery in adults having undergone intraoperative TEE also may be higher.

The complications reported in infants and children involve hemodynamic or respiratory compromise. Vigilance is required when using TEE probes in a small child, even with the availability of pediatric probes. Airway obstruction may occur due to compression of the small trachea or bronchus between surrounding tissue and the rigid probe. Likewise, aortic or aortic arch vessel compression may occur.

Prophylactic antibiotic coverage for patients undergoing TEE examinations is debated because it carries a risk of inducing bacteremia like any other endoscopic procedure. Most patients undergoing cardiac surgery receive prophylactic antibiotics of some kind, and many consider this sufficient prophylaxis for endocarditis.

Coagulation monitoring

By necessity, cardiac anesthesiologists must be familiar with coagulation monitoring. CPB requires anticoagulation, and reversal of the anticoagulated condition. In addition, the patient is often prone to bleeding disorders wither through their preoperative medication regimen, thrombocyptopenia or the inflammatory response associated with surgery. Whether at the beginning of the case with heparinization or at the end of the case when there may be excessive bleeding from an unknown cause, the anesthesiologist must be familiar with the tools to treat the patient.

Activated coagulation time

The Activated coagulation time (ACT) is most commonly used to monitor for heparin effect. Whole blood is added to a test tube containing either diatomaceous earth (celite) or kaolin. This activator induces thrombosis which is measured in seconds. Normal ACT values range between 80–120 seconds. When aprotinin is used as an antifibrinolytic agent, kaolin ACT cartridges should be used; celite ACT cartridges are associated with falsely elevated ACT values (thereby making the patient appear fully anticoagulated when, in fact, this is not the case). The ACT test can be modified by adding heparinase to one of the chambers. In this situation, heparin is revered with the heparinase, and therefore any abnormality in ACT value is likely due to

some factor other than inadequate heparin reversal with protamine. The ACT is subject to variability, and there are elevated ACT values seen with both hemodilution and hypothermia. Nonetheless, the ACT is the standard monitor of coagulation in most operating rooms. The ACT should be checked at least every half-hour while on CPB.

Heparin dose–response test

The Heparin dose–response test (HDR) allows the clinician to fine tune the patient variability in response to a heparin dose by constructing an individualized heparin dose–response curve. The HDR uses a known quantity of heparin in an ACT determination, and an algorithm using the baseline ACT and the estimated blood volume to construct a dose–response curve. The advantage of this system is the greater accuracy in dosing eliminating both under and over dosing with heparin. Further, this test provides information on individualized protamine doing at the termination of CPB.

Heparin concentration testing

Heparin concentration can be measured using a device that automatically titrates protamine in known quantities in whole, heparinized blood. Protamine neutralizes heparin in the ratio of 1 mg/100 units of heparin. With this information, a protamine–heparin titration can yield the circulation concentration of heparin. When monitoring heparin concentration, higher doses of heparin are typically administered than when the ACT is monitored likely because of the effects of hypothermia and hemodilution on the ACT. In side-by-side comparisons between ACT and heparin concentration monitoring, the additional heparin administered seems to have little effect on blood loss or blood administration outcomes.

High dose thrombin time

The High dose thrombin time (HiTT) measures the conversion of fibrinogen to fibrin by thrombin. HiTT is not altered by hemodilution, hypothermia or aprotinin.

Standard blood tests of coagulation

After CPB and reversal of heparin with protamine, there are some patients that continue to bleed for unknown reasons. In these patients, standard tests of coagulation are indicated. These tests include a prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen and platelet count. The PT (normal 12–14 seconds) measures the extrinsic and common coagulation pathways. It is prolonged with factor VII deficiency, warfarin treatment, vitamin K deficiency and in the presence of large heparin doses. The aPTT measures the intrinsic and final common pathway of coagulation. It is extremely sensitive to heparin, deficiencies of factors XII, XI, IX and VIII, and kallikrein. Normal aPTT is 28–32 seconds. Fibrinogen and platelet levels measure the quantitative amount of these substances in the blood. Normal fibrinogen levels range from 180 to 220 mg/dL.

Cryoprecipitate (a source of concentrated fibrinogen) is indicated when the fibrinogen level is below 150 mg/dL. Thrombocytopenia is encountered when the platelet count falls below 100 000/μL. Platelet counts greater than 50 000/μL have no correlation with bleeding time or observed postoperative bleeding in cardiac surgical patients. Qualitative defects in platelet function are often more important than the platelet count.

Fibrin degradation

Evidence of normal or abnormal fibrinolysis is obtained by measuring the end products of fibrin degradation. When plasmin cleaves fibrin, dimeric units are released into the blood, and these "d-dimers" can be quantified. The presence of d-dimers in the blood signifies fibrin cross-link degradation and may represent a condition of abnormal fibrinolysis.

Bleeding time

The bleeding time is obtained by performing a precisely measured incision in the patient's forearm above which a cuff is inflated to 40 mmHg. The wound is dabbed with an absorbent tissue and the time until clot formation is measured. The bleeding time has no predictive value in cardiac surgical patients and has largely fallen out of favor.
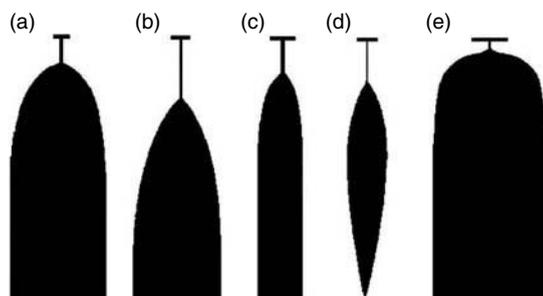
Fig. 3.39 Thromboelastograph tracings. (a) Normal. (b) Coagulation factor deficiency. (c) Platelet dysfunction or deficiency. (d) Fibrinolysis. (e) Hypercoagulability. (From Mallett SV, Cox DJ. *Br J Anaesth* 1992;**69**:307–13, with permission.)

Platelet aggregometry

Activated platelets aggregate. Aggregometry measures platelet responsiveness to various agonists and provides information on the quality of the circulating platelets to respond to various stimuli. Various agonists include epinephrine, adenosine diphosphate and collagen. Impaired aggregation is seen in patients taking aspirin and after exposure to CPB.

Thromboelastography

Thromboelastography (TEG) is a method of monitoring blood viscosity that can be used to evaluate various components of the coagulation system. The device usually contains two identical channels so that two blood samples can be run at once. Each channel consists of a disposable cylindrical plastic cup mounted in a base. The cup is filled with a blood and maintained at 37°C during testing. A piston is attached to a torsion wire that generates a signal as the blood clots. With this presentation, the real-time development of the TEG pattern can be assessed. A TEG sample trace is shown in Fig. 3.39. The test usually takes between 15–30 minutes to complete and allows diagnosis of a variety of pathologic conditions including coagulation factor deficiency, platelet and fibrinogen function and fibrinolysis. In clinical practice the TEG has been shown to function well as a predictor of abnormal bleeding. In some centers, TEG use is associated with a reduction in mediastinal exploration for bleeding and transfusion of blood products.

Suggested reading

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*. Available online at: http://www.asahq.org/publicationsAndServices/standards/02.pdf. Accessed June 28, 2006.

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CHAPTER 4

Anesthesia for Myocardial Revascularization

Coronary artery bypass graft (CABG) surgery accounts for approximately 500 000 operative procedures per year in the United States. Although there is great interest and development in alternatives to CABG, this operative procedure remains an appropriate, indicated therapy for a large number of patients. Patient outcome after percutaneous coronary intervention (i.e. stent placement, atherectomy, angioplasty, other) remains a moving target as new therapies and technologies are developed and employed. Similar to this, outcome after CABG is evolving. The indications for CABG are periodically reviewed by the American College of Cardiology (ACC) and the American Heart Association (AHA) (Tables 4.1 and 4.2). The reader is referred to the ACC's website (www.acc.org) for the latest update.

A firm understanding of the dynamics of coronary blood flow, the determinants of myocardial oxygen balance, and the consequences and treatment of ischemia are necessary to care for patients undergoing coronary revascularization. This chapter will review the physiology of coronary blood flow, the elements of myocardial oxygenation, the care and treatment of patients with active ischemia, and the anesthetic care of patients presenting for CABG.

Control of coronary blood flow

Coronary perfusion pressure

Coronary perfusion can only occur when aortic root pressure exceeds subepicardial and subendocardial pressure. Myocardial back-pressure, which is the summation of factors that tend to collapse microvessels, is important in determining coronary perfusion pressure (CPP). In clinical practice, myocardial back-pressure is equal to myocardial tissue pressure. The best estimate of myocardial tissue pressure is the ventricular pressure. In diastole, this will be the ventricular end-diastolic pressure. The best clinical estimate of left ventricular end-diastolic pressure (LVEDP) is the pulmonary capillary wedge pressure (PCWP); whereas the best estimate of right ventricular end-diastolic pressure (RVEDP) is the central venous or right atrial pressure (RAP).

In the absence of obstruction to flow within the coronary arterial system, left ventricular (LV) CPP is the driving force for blood going into the myocardium – the resistance to blood flow. Physiologically, in the left ventricle, this relationship translates as CPP = aortic root diastolic blood pressure – PCWP (Fig. 4.1). CPP will differ during systole and diastole. In the left ventricle, ventricular pressure during systole is equal to or, as in the case of aortic stenosis, greater than aortic root pressure. For this reason, most coronary blood flow to the left ventricle occurs during ventricular diastole. In the right ventricle, in which right ventricular (RV) systolic and diastolic pressures are both considerably less than aortic root pressure, coronary blood flow is distributed evenly between systole and diastole.

Autoregulation

Changes in coronary vascular resistance are necessary for the myocardium to regulate coronary

Table 4.1 The list of indications for coronary artery bypass graft surgery for patients with stable angina and unstable angina/Non-ST-segment elevation myocardial infarction (MI). The indications are assigned class and the level of evidence provided for the recommendation. (From Eagle KA, Guyton RA, Davidoff R *et al*. ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation* 2004;**110**:1168–76.)

Stable angina

Class I

1 CABG is recommended for patients with stable angina who have significant left main coronary artery stenosis *(Level of evidence: A)*

2 CABG is recommended for patients with stable angina who have left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery *(Level of evidence: A)*

3 CABG is recommended for patients with stable angina who have 3-vessel disease. (Survival benefit is greater when LVEF is <0.50) *(Level of evidence: A)*

4 CABG is recommended in patients with stable angina who have 2-vessel disease with significant proximal LAD stenosis and either EF < 0.50 or demonstrable ischemia on noninvasive testing *(Level of evidence: A)*

5 CABG is beneficial for patients with stable angina who have 1- or 2-vessel CAD without significant proximal LAD stenosis but with a large area of viable myocardium and high-risk criteria on noninvasive testing *(Level of evidence: B)*

6 CABG is beneficial for patients with stable angina who have developed disabling angina despite maximal noninvasive therapy, when surgery can be performed with acceptable risk. If the angina is not typical, objective evidence of ischemia should be obtained *(Level of evidence: B)*

Class IIa

1 CABG is reasonable in patients with stable angina who have proximal LAD stenosis with 1-vessel disease. (This recommendation becomes Class I if extensive ischemia is documented by noninvasive study and/or LVEF is <0.50) *(Level of evidence: A)*

2 CABG may be useful for patients with stable angina who have 1- or 2-vessel CAD without significant proximal LAD stenosis but who have a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing *(Level of evidence: B)*

Class III

1 CABG is not recommended for patients with stable angina who have 1- or 2-vessel disease not involving significant proximal LAD stenosis, patients who have mild symptoms that are unlikely due to myocardial ischemia, or patients who have not received an adequate trial therapy and the following:

a Have only a small area of viable myocardium *(Level of evidence: B)* or

b Have no demonstrable ischemia on noninvasive testing *(Level of evidence: B)*

2 CABG is not recommended for patients with stable angina who have borderline coronary stenoses (50–60% diameter in locations other than the left main coronary artery) and no demonstrable ischemia on noninvasive testing *(Level of evidence: B)*

3 CABG is not recommended for patients with stable angina who have insignificant coronary stenosis (<50% diameter reduction) *(Level of evidence: B)*

Unstable angina/non-ST-segment elevation MI

Class I

1 CABG should be performed for patients with unstable angina/non-ST-segment elevation MI with significant left main coronary artery stenosis *(Level of evidence: A)*

2 CABG should be performed for patients with unstable angina/non-ST-segment elevation MI who have left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery *(Level of evidence: A)*

Table 4.1   *(Continued).*

3 CABG is recommended for unstable angina/non-ST-segment elevation MI in patients in whom revascularization is not optimal or possible and who have ongoing ischemia not responsive to maximal nonsurgical therapy *(Level of evidence: B)*

Class IIa
1 CABG is probably indicated in patients with unstable angina/non-ST-segment elevation MI who have proximal LAD stenosis with 1- or 2-vessel disease *(Level of evidence: A)*

Class IIb
1 CABG may be considered for patients with unstable angina/non-ST-segment elevation MI who have 1- or 2-vessel disease not involving the proximal LAD when percutaneous revascularization is not optimal or possible. (If there is a large area of viable myocardium and high-risk criteria are met on noninvasive testing, this recommendation becomes Class I) *(Level of evidence: B)*

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful

Level of Evidence
Level of Evidence A: Data are derived from multiple randomized clinical trials or meta-analyses
Level of Evidence B: Data are derived from a single randomized trial, or nonrandomized studies
Level of Evidence C: Only consensus opinion of experts, case studies, or standard of care

Table 4.2 The classification of recommendations and level of evidence used by the American College of Cardiology and the American Heart Association Guidelines for Coronary Artery Bypass Graft Surgery. (From Eagle KA, Guyton RA, Davidoff R *et al*. ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation* 2004;**110**:1168–76.)

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blood flow in response to changes in myocardial oxygen consumption. Coronary autoregulation is the intrinsic ability of the myocardium to maintain coronary blood flow constant over a variety of perfusion pressures. As illustrated in Fig. 4.2, coronary autoregulation maintains coronary blood flow constant between perfusion pressures of 60 and 140 mmHg. Below and above these pressures, myocardial blood flow is pressure-dependent; that is, myocardial blood flow varies linearly with pressure and with the time available for perfusion

(diastole for the left ventricle, systole and diastole for the RV).

Autoregulation is dependent on changes in coronary vascular resistance. The arterioles are the primary source of resistance in the coronary arterial system. Autoregulation is tied to myocardial oxygen metabolism and coronary venous partial pressure of oxygen Po_2, although the exact mediators at the vascular level are unknown. During exercise, reductions in coronary vascular resistance result in increased coronary blood flow
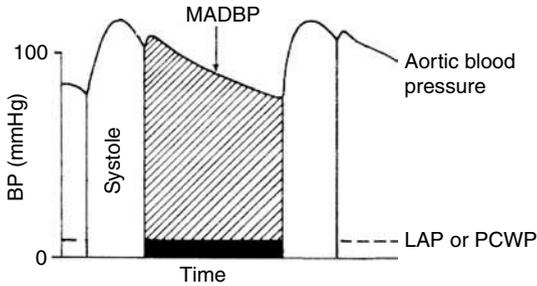
Fig. 4.1 Left ventricular coronary perfusion pressure (CPP) is the difference between aortic diastolic blood pressure and left ventricular end-diastolic pressure (LVEDP). Clinically, LVEDP is estimated by left atrial pressure (LAP) or pulmonary capillary wedge pressure (PCWP). Diastolic CPP is represented by cross-hatched area and can be seen to decrease as diastole progresses. Average diastolic CPP can be obtained by taking difference between mean aortic diastolic blood pressure (MADBP) and LAP or PCWP. Length of time available for perfusion of left ventricle is dependent on length of diastole. Shortening diastole by increasing length of systole per beat or by increasing heart rate will decrease the time available for left ventricular perfusion. (From DiNardo JA. Anesthesia for myocardial revascularization. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:81–108, with permission.)

(up to six-times normal). Likewise, as CPP falls, coronary vascular resistance decreases to maintain coronary blood flow. At pressures <60 mmHg, there is a progressive loss of autoregulation. At some point, the coronary arteries dilate maximally and coronary blood flow now decreases linearly with CPP. Autoregulation in the subendocardium is exhausted before that of the subpericardium.

Collateral blood flow

The development of collateral blood flow in humans is dependent on enlargement of pre-existing anastomoses between coronary arteries. These anastomoses may be either serial (pre-stenosis to post-stenosis in the same artery) or parallel (one artery to another). Collateral pathways enlarge in response to pressure gradients. After the collateral pathways have enlarged, the direction and magnitude of collateral blood flow remain pressure dependent. For this reason, collateral blood flow to a post-stenotic segment can be significantly reduced
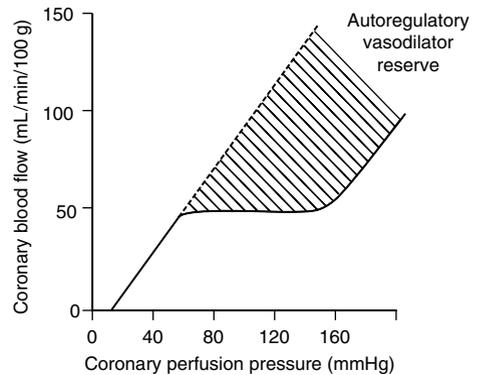
Fig. 4.2 Coronary blood flow is seen to be constant (autoregulated) over coronary perfusion pressures from 60–140 mmHg. When coronary perfusion pressure reaches 60 mmHg, there will be maximal autoregulatory vasodilation to maintain coronary blood flow. Further decreases in coronary perfusion pressure will result in decreases in coronary blood flow. At pressures higher than 60 mmHg, maximal autoregulatory vasodilation will provide autoregulatory vasodilator reserve. This reserve provides the increased coronary blood flow necessary to meet increases in myocardial oxygen consumption such as those induced by exercise. (From DiNardo JA. Anesthesia for myocardial revascularization. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:81–108, with permission.)

if perfusion pressure at the origin of the collateral is reduced.

There is evidence that coronary collateral flow improves the outcome in patients with an acute myocardial infarction (MI). This same relationship is also true after CABG surgery. In a review of 561 patients with a low-risk profile, the presence of collaterals protects against cardiac death and MI at 1 year after coronary revascularization (Fig. 4.3).

Causes of increased myocardial oxygen demand

Three factors are primarily responsible for determining myocardial oxygen consumption (MV_{O_2}): wall tension, contractility, and heart rate (HR).

Wall tension

Myocardial wall tension is determined by the relationship between ventricular radius (r), ventricular
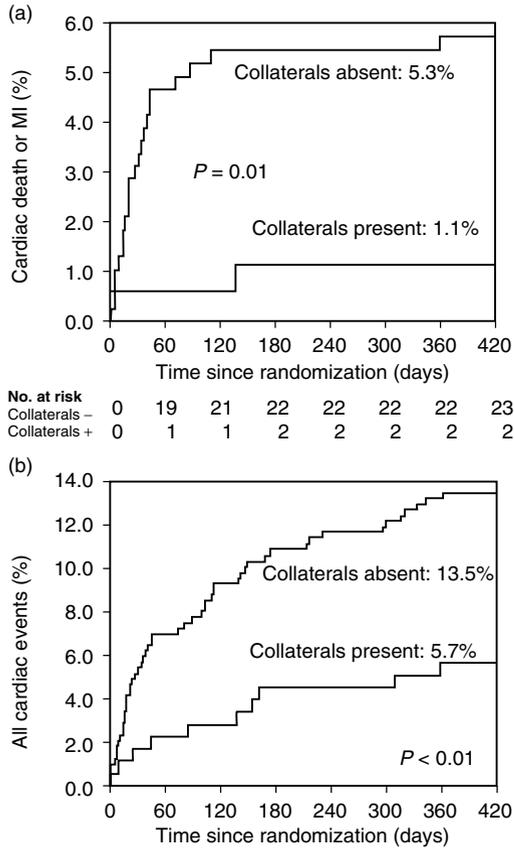
Fig. 4.3 Kaplan–Meier estimates of proportion of first clinical events at 1 year after coronary revascularization as stratified by collaterals. The *P*-values were calculated using the log–rank test. (a) Cardiac death or nonfatal myocardial infarction (MI). (b) All-cause death, nonfatal stroke, nonfatal MI, or repeat coronary revascularization. (From Nathoe HM, Koerselman J, Buskens E *et al.* Determinants and prognostic significance of collaterals in patients undergoing coronary revascularization. *Am J Cardiol* 2006;**98**:31–5, with permission.)

pressure (*P*), and ventricular wall thickness (*h*) according to Laplace's law: $T = Pr/h$. Ventricular wall tension constantly changes during the cardiac cycle. For example, during isovolumic contraction, ventricular pressure and wall thickness will be increasing while ventricular radius remains unchanged. During ventricular ejection, ventricular pressure will remain relatively constant while radius decreases and wall thickness increases. Inherent in the analysis of wall tension are the concepts of preload, afterload, and hypertrophy. Increases in end-diastolic volume (EDV) (preload) will increase ventricular radius and will reduce wall thickness if dilation is severe. These changes will increase wall tension. Increases in the impedance to ventricular ejection (afterload) will necessarily increase ventricular pressure and increase wall tension. Concentric ventricular hypertrophy will increase wall thickness and reduce wall tension.

There are important differences between the increase in MVO_2 induced by increases in preload and by those induced by increases in afterload. Work done in the isovolumic phase of ventricular contraction is very energy-consumptive. Increases in the impedance to ventricular ejection increase the pressure required to begin ventricular ejection, and thus increase the work done in the isovolumic contraction phase. The ejection phase of ventricular contraction, on the other hand, is a more energy-efficient process. Increases in preload induce ejection of a larger stroke volume (SV) and an increase in the work done in the ejection phase. For these reasons, when comparing equal work, the increase in MVO_2 induced by an increase in preload (volume work) is much less than that induced by an increase in afterload (pressure work).

Contractility
Contractility is the state of myocardial performance (inotropy) independent of preload and afterload. Increasing the contractile state of the heart will increase MVO_2. However, an increase in contractility may actually result in a reduced or unchanged MVO_2 under certain conditions. For example, if ventricular dilation (increased ventricular radius) exists to maintain cardiac output (CO), wall tension and MVO_2 will be high. Improving contractility through use of an inotropic agent can reduce ventricular radius while maintaining CO. The reduction in MVO_2 that accompanies the reduction in ventricular radius may more than offset the increase that accompanies an increase in contractility.

Heart rate
Heart rate directly affects myocardial oxygen balance. Tachycardia increases myocardial oxygen demand and reduces supply by diminishing the time

in diastole. Perhaps more importantly, one must consider the imbalance on a beat-to-beat basis. Myocardial ischemia does not occur with tachycardia simply because there are more beats per minute; rather, ischemia occurs with tachycardia because supply per beat is inadequate to meet demand per beat. Increases in HR increase MV_{O_2} per beat by increasing contractility via the Bowditch effect. Normally, increasing HR decreases EDV. This reduction in preload reduces wall tension and MV_{O_2} per beat. Thus, with tachycardia, the increase in MV_{O_2} per beat caused by enhanced contractility is offset by the reduction in MV_{O_2} per beat that accompanies reduced wall tension. On the other hand, oxygen delivery is sometimes compromised by tachycardia-induced reductions in the length of diastole per beat (discussed later).

Causes of reduced myocardial oxygen delivery

Adequate myocardial oxygen supply is dependent on delivery of the appropriate volume of oxygenated coronary blood flow. The following sections describe factors that may compromise myocardial oxygen delivery.

Reduction in CPP

LV CPP falls with either a reduction in diastolic blood pressure (DBP) or an increase in LV end-diastolic pressure. A commonly overlooked cause of reduced CPP is bradycardia. Bradycardia encourages diastolic runoff from the proximal aorta and may result in a wide pulse pressure and reduced DBP. Furthermore, maintenance of CO with bradycardia requires an increased SV. The increased SV occurs primarily by an increase in left ventricular end-diastolic volume (LVEDV) and pressure. This further reduces CPP.

Reduction in time available for coronary perfusion

The left ventricle receives most its perfusion during diastole; therefore, reductions in diastolic time are potentially detrimental. Figure 4.4 illustrates that as HR increases the length of time per beat spent in diastole falls while the length of systole
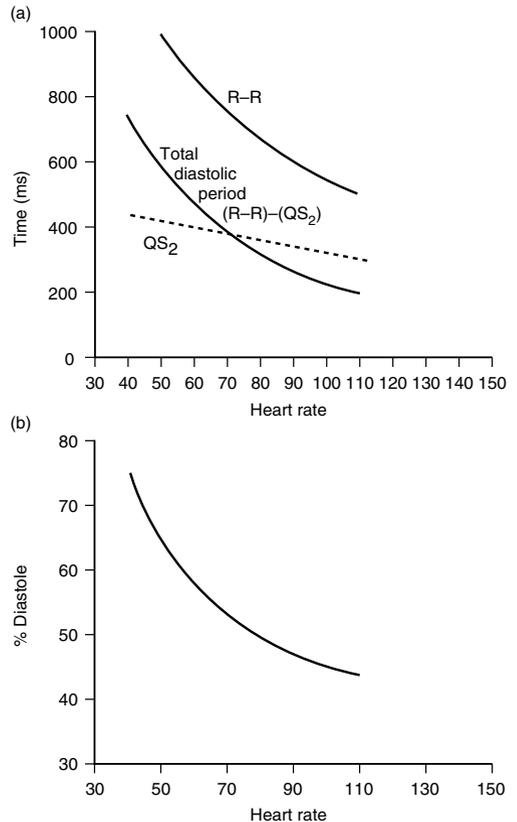
Fig. 4.4 (a) Increases in heart rate cause decreases in length of each cardiac cycle (R–R interval). Decreases in length of systole (OS_2) with increases in heart rate are far less dramatic than decreases in length of diastole (R–R–OS_2). (b) Percent of each cardiac cycle (R–R interval) spent in diastole at various heart rates. Small changes in heart rate are seen to cause large decreases in percent of time spent in diastole. (From Boudoulas H. Changes in diastolic time with various pharmacologic agents. *Circulation* 1979;**60**:165, with permission.)

remains constant. Because MV_{O_2} per beat is minimally affected by tachycardia, the primary disadvantage of tachycardia is a reduction in diastolic perfusion time per beat.

Obstruction to flow

Any obstruction to flow in a coronary artery results in a pressure drop across the obstruction. The high velocity of blood flow in the area of a stenosis (either stable, i.e. plaque disease; or

dynamic, i.e. coronary spasm) necessarily results in the conversion of pressure energy to kinetic energy. On the distal side of the obstruction, turbulent eddies form and dissipate. The transfer of kinetic energy to this turbulent energy and the subsequent dissipation of the turbulence reduce the quantity of kinetic energy available for conversion to pressure energy. This results in a pressure drop across the obstruction. The pressure drop will increase in direct proportion to any increase in flow across the obstruction as a greater proportion of kinetic energy dissipates as turbulence. For this reason, requirements for increased coronary blood flow, such as those that accompany exercise, will increase the hemodynamic significance of any obstructive lesion.

Arteriolar dilatation distal to the obstruction will help compensate for this pressure loss until the stenosis becomes critical. A stenosis is "critical" when the vasodilator reserve distal to the stenotic lesion is exhausted. This occurs with stenosis >90%. In the absence of autoregulation, coronary blood flow distal to a stenotic lesion will fall linearly with decreases in perfusion pressure. This places the distal subendocardium at risk for ischemia. It follows that in the presence of an obstructive coronary lesion, coronary perfusion is critically dependent on aortic DBP. The factors described in the following sections deserve attention.

Atherosclerotic disease

Atherosclerosis is a complex, heterogeneous disease often starting in the very young and evolving over several decades. There are both acute and chronic manifestations of the disease, the most significant of which, involves the development of coronary occlusive disease, unstable coronary syndromes, MI, and death. Other systemic manifestations include progressive neurologic dysfunction (dementia), renal impairment, claudication, mesenteric ischemia, hypertension, and stroke. The disease is progressive in nature with a defined pattern of morphologic evolution (Fig. 4.5).

The fate of atheromatous lesions is dependent on three additional factors:
- *Plaque disruption*. Atheromatous lesions are lipid rich, soft, and prone to disruption from mechanical forces. Plaque rupture may result in exposure of superficial vascular wall elements or of deep fibrillar collagen.
- *Thrombosis*. Exposure of vascular wall elements is a stimulus for thrombus formation. Platelet deposition occurs at the site of disruption. Superficial plaque disruption is a much milder thrombogenic stimulus than deep plaque disruption. Thrombus formation at the site of a superficial injury is likely to be labile and transient, whereas thrombus formation associated with deep plaque disruption is likely to be stable and permanent. This is often the cause of acute coronary syndromes.
- *Vasoconstriction*. Transient vasoconstriction accompanies plaque disruption and thrombus formation. Injury to the endothelium produces thrombin-mediated vasoconstriction; whereas, subsequent platelet deposition mediates vasoconstriction via release of thromboxane-A_2 and serotonin. In addition, endothelial injury may impair the release of nitric oxide (NO).

Using these concepts, one can understand the spectrum of coronary artery disease (CAD) from chronic stable angina to acute MI. Chronic stable stenotic lesions that cause angina develop as the result of progression of atherosclerotic lesions. Progression of early lesions is more rapid in patients with coronary risk factors. Progression is the result of mural thrombus formation and fibrotic organization, which follows minor plaque disruption. Initially, platelet thrombi form on the disruption. This is followed by migration of smooth muscle cells from the media into the intima. During the final phase, intimal thickening and progression of the lesion occur. Repetition of this process leads to gradual progression of the lesion. Ultimately, it may lead to a chronic vessel occlusion. The slow progression of the lesion allows time and provides stimulus for distal arteriolar collateral formation. This explains why thrombotic occlusion is frequent in patients with high-grade stenoses but does not lead to infarction.

In unstable angina, a small plaque disruption may change plaque morphology such that coronary blood flow is acutely reduced and angina intensifies. Alternatively, plaque disruption may be associated with labile thrombus, temporary vessel
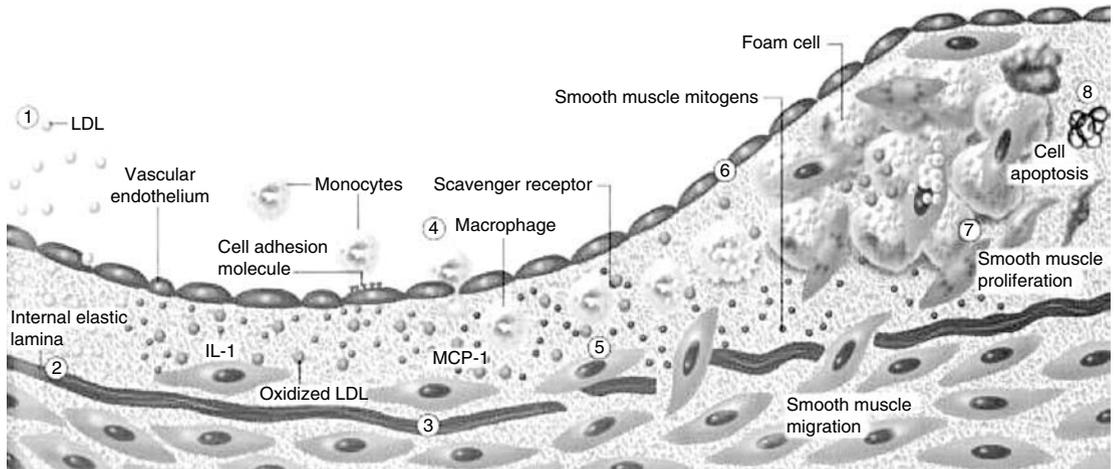
Fig. 4.5 Schematic of the evolution of the atherosclerotic plaque. **1**. Accumulation of lipoprotein particles in the intima. The modification of these lipoproteins is depicted by the darker color. Modifications include oxidation and glycation. **2**. Oxidative stress, including products found in modified lipoproteins, can induce local cytokine elaboration. **3**. The cytokines thus induced increase expression of adhesion molecules for leukocytes that cause their attachment and chemoattractant molecules that direct their migration into the intima. **4**. Blood monocytes, upon entering the artery wall in response to chemoattractant cytokines such as monocyte chemoattractant protein 1 (MCP-1), encounter stimuli such as macrophage colony stimulating factor (M-CSF) that can augment their expression of scavenger receptors. **5**. Scavenger receptors mediate the uptake of modified lipoprotein particles and promote the development of foam cells. Macrophage foam cells are a source of mediators such as further cytokines and effector molecules such as hypochlorous acid, superoxide anion (O_2^-), and matrix metalloproteinases. **6**. Smooth muscle cells in the intima divide other smooth muscle cells that migrate into the intima from the media. **7**. Smooth muscle cells can then divide and elaborate extracellular matrix, promoting extracellular matrix accumulation in the growing atherosclerotic plaque. In this manner, the fatty streak can evolve into a fibrofatty lesion. **8**. In later stages, calcification can occur (not depicted) and fibrosis continues, sometimes accompanied by smooth muscle cell death (including programmed cell death, or apoptosis) yielding a relatively acellular fibrous capsule surrounding a lipid-rich core that may also contain dying or dead cells and their detritus. IL-1, interleukin-1; LDL, low-density lipoprotein. (From Libby P. The vascular biology of atherosclerosis. In: Zipes DP, Libby P, Bonow RO, Braunwald E (eds). *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 7th edn. Philadelphia: Elsevier–Saunders, 2005:921–37, with permission.)

occlusion, and angina at rest. Coronary blood flow is further compromised by release of vasoconstrictor substances and impaired endothelial relaxation.

In non-Q-wave MI, the process is similar to that in unstable angina, except that the duration of vessel occlusion by labile thrombus is longer and there is resultant muscle injury and necrosis. Spontaneous thrombolysis or resolution of arterial spasm ultimately limits occlusion and prevents Q-wave MI (full thickness, or transmural MI). This process is responsible for 75% of non-Q-wave MIs. The other 25% occur when there is complete occlusion of the infarct-related vessel with distal collateralization.

In a Q-wave MI, plaque disruption is associated with formation of a fixed, persistent occlusion (usually by a thrombus, although this may occur with an embolized vegetation or other material). This leads to cessation of blood flow and myocardial necrosis. The coronary lesion involved usually is mild to moderate in severity with limited distal collateralization. Thus, it is the intensity of plaque disruption and subsequent thrombus formation rather than the severity of the lesion that is the determining factor.

Further discussion is necessary to explain the spectrum of anginal symptoms that can accompany

a chronic, stable, stenotic coronary lesion. The main coronary artery epicardial branches have lumens that are 2–4 mm in diameter. In the absence of collaterals, exertional angina occurs when lumen area is reduced to 1.0 mm^2 (50–60% reduction in lumen diameter or 75% reduction in cross-sectional area) and angina at rest occurs when lumen area is reduced to 0.65 mm^2 (75% reduction in lumen diameter or 90% in cross-sectional area).

Figure 4.6 illustrates how changes in coronary vascular tone can alter the clinical characteristics of a chronic, stable stenotic lesion. Atheromatous lesions may be localized to one area of the arterial wall. As these eccentrically located lesions enlarge, they encroach upon the arterial lumen. Because the remainder of the arterial wall is free of plaque, it remains responsive to vasoactive stimuli and is capable of contraction. Such contraction will cause the fixed atheromatous lesion to occupy a greater portion of the arterial lumen and will result in a larger pressure drop across the lesion. Therefore, the severity of the stenosis is not static but is dynamic and dependent on the vasomotor activity of the free arterial wall. This phenomenon is known as dynamic coronary stenosis. As illustrated in Fig. 4.6, a normal change in coronary vasomotor tone resulting in a 10% circumferential shortening of the outer arterial wall can convert an insignificant 49% eccentric stenosis to a 76% stenosis, which will result in rest ischemia. Likewise, Fig. 4.6 illustrates that a normal increase in arterial tone can convert an eccentric stenosis, which causes ischemia on exertion (60% stenosis), to one that also causes ischemia at rest (76% stenosis).

Atheromatous lesions may be static if the atheromatous changes involve the entire circumference of the arterial wall. In this instance, the luminal area is fixed and is unaltered by changes in arterial vasomotor activity. Figure 4.6 illustrates that a lesion that occupies the entire circumference of the arterial wall and causes exertional ischemia (60% stenosis) will be unaffected by changes in arterial vasoconstriction.

Variations in coronary vasomotor tone

There is a large variation in the extent of coronary vasomotor activity across a population. At one end of the spectrum is the normal 10% reduction in outer arterial wall circumference that occurs with α-adrenergic stimulation. At the other end of
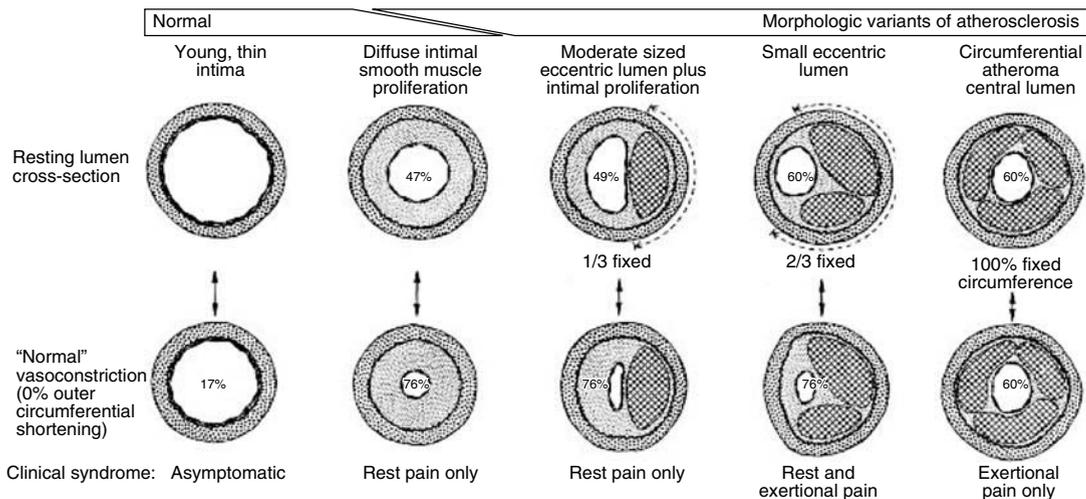
Fig. 4.6   Cross-sections of normal and diseased coronary arteries. Morphologic state of arteries is illustrated. Percent reduction in lumen diameter for each morphologic state at rest and following normal degree of vasoconstriction is also shown. Clinical syndromes associated with both resting and vasoconstricted state of normal and diseased arteries are summarized at bottom of diagram. (From Brown BG. Dynamic mechanisms in human coronary stenosis. *Circulation* 1985;**70**:921, with permission.)

the spectrum, is the intense vasoconstriction that occurs with variant or Prinzmetal's angina. The exaggerated coronary spasm seen in these patients results in total or near total occlusion in response to stimuli that cause only minimal constriction in individuals who do not have variant angina. For patients with coronary spasm, myocardial ischemia may develop in the absence of coronary stenosis. For patients with normal coronary vasoconstriction, myocardial ischemia will occur only if coronary stenoses also exist.

Coronary steal

Coronary steal refers the physiologic condition whereby blood flow is directed away from ischemic prone areas of the myocardial dependant upon upstream coronary artery anatomy (Fig. 4.7). Coronary steal occurs in some patients with specific coronary artery lesions upon the exposure of coronary vasodilators. Approximately one-fourth of patients with CAD meet these anatomical criteria. In these patients, the administration of an arteriolar dilator, such as dipyridamole or adenosine, may produce a steal.

In the mid-1980s a series of reports suggested that isoflurane induced coronary steal by abnormally redistributing flow away from ischemic areas of the myocardium. Subsequent work and clinical experience, however, have refuted this proposition. Although isoflurane-induced hypotension may

reduce myocardial perfusion, true coronary steal does not occur when CPP is maintained. Further studies demonstrate that the volatile agents do not abnormally reduce or redistribute coronary collateral flow.

In contrast to these initial concerns regarding isoflurane, recent evidence suggests a myocardial protective benefit with volatile agent use (Fig. 4.8). These protective benefits extend beyond a favorable alteration in the oxygen supply and demand balance. The benefits may be related to physiologic alterations in response to ischemia and reperfusion. Many of these actions are similar to those found with ischemic preconditioning, and are in fact, termed, anesthetic-induced preconditioning (discussed later).

Anemia

Myocardial oxygen delivery is the product of coronary blood flow and the oxygen content of the transported blood. Anemia reduces myocardial oxygen delivery by reducing the oxygen-carrying capacity of blood. The degree of anemia that an area of myocardium can tolerate without developing ischemia is dependent on the relationship between regional MV_{O_2} and regional coronary blood flow. In the absence of coronary stenoses, hematocrit levels <15% result in subendocardial ischemia in anesthetized canines. In the presence of the increased MV_{O_2} that accompanies large increases
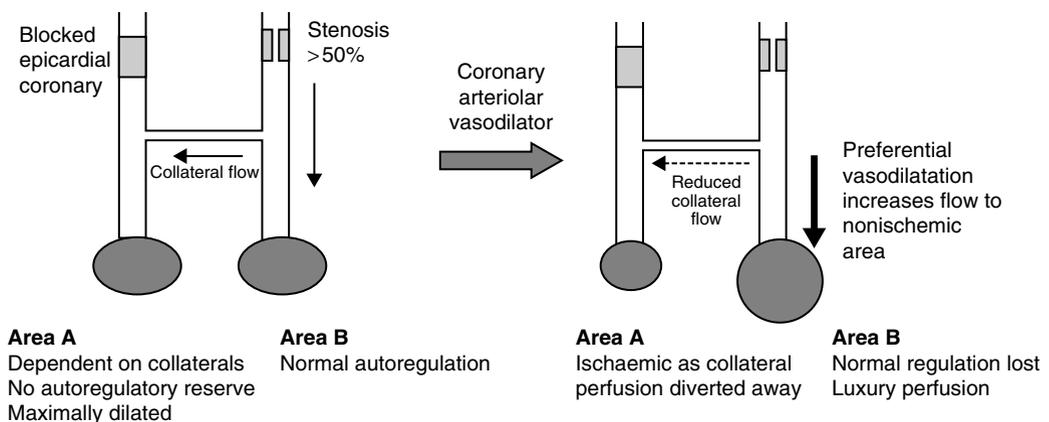
Fig. 4.7 Schematic diagram illustrating coronary steal. Arrows represent coronary blood flow. (From Agnew NM, Pennefather SH, Russell GN. Isofurane and coronary heart disease. *Anaesthesia* 2002;**57**:338–47, with permission.)
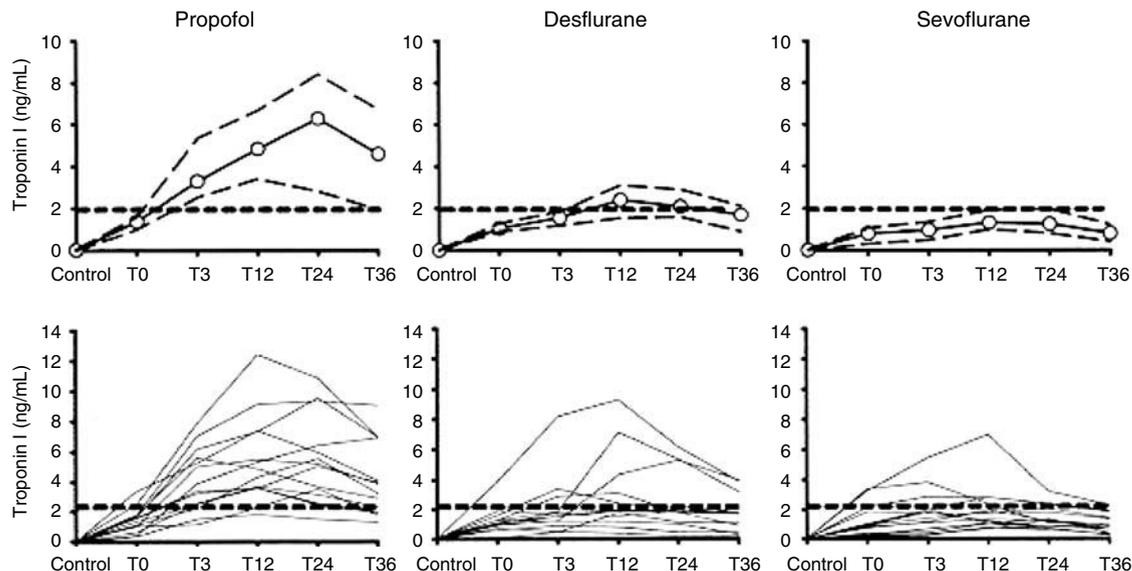
Fig. 4.8   Coronary artery patients ($n = 45$) were randomly assigned to receive either target controlled infusion of propofol or inhalational anesthesia with desflurane or sevoflurane. After coronary artery bypass (CPB), the cardiac index was lower in the propofol group. Cardiac troponin I concentrations in the three groups before surgery (control), at arrival in the intensive care unit (T0), and after 3 (T3), 12 (T12), 24 (T24), and 36 (T36) hours. The upper panel show the median values with 95% confidence intervals. The lower panels show the evolution of the individual values. Concentrations were significantly higher with propofol anesthesia. (From De Hert SG, Cromheecke S, ten Broecke PW *et al*. Effects of propofol, desflurane, and sevoflurane on recovery of myocardial function after coronary surgery in the elderly high-risk patients. *Anesthesiology* 2003;**99**:314–23, with permission.)

in afterload, hematocrit levels <30% produce subendocardial ischemia in the same canine model.

There is great debate about the ideal hematocrit in any patient and especially in the patient with known CAD. Recent investigation in a medical population after MI reveals that a hematocrit of at least 33% is associated with improved outcome. Hematocrit levels must be individualized for each patient; however, low hematocrit levels (<30%) are potentially dangerous in awake patients with CAD for the following reasons:

- Increased CO necessarily accompanies normovolemic anemia to maintain systemic oxygen transport; this CO increase results in an increased MV_{O_2}.
- Increases in coronary blood flow to maintain coronary oxygen delivery result in increased pressure drops across stenoses and potential for subendocardial hypoperfusion.

Myocardial ischemia

Regional or global imbalances in myocardial oxygen supply and demand result in myocardial ischemia. The metabolic consequences of ischemia are discussed in detail in Chapter 12. The clinical manifestations of myocardial ischemia are varied. Angina pectoris, with or without signs of ventricular failure or dysrhythmias, is the classic manifestation of myocardial ischemia. However, it is important to remember that angina is not a universal manifestation of ischemia. In fact, myocardial ischemia may present as ventricular failure or dysrhythmias without angina. In some individuals, especially diabetics, ischemia may remain clinically silent. Furthermore, patients have varying thresholds for the development of ischemia during the course of a day. The dynamic nature of coronary stenoses accounts for the changes in the caliber of a stenosis that

may produce rest pain at one time and angina with varying degrees of exercise at other times.

Despite these varied clinical presentations, the progression of hemodynamic and electrocardiographic changes with ischemia tends to follow a consistent pattern in a given patient. Myocardial ischemia is heralded by a decrease in regional ventricular diastolic distensibility (see Chapter 2), which usually results in an elevation in LVEDP or RVEDP, and central venous pressure (CVP). This is followed by systolic dysfunction, electrocardiogram (ECG) changes, and finally by angina during symptomatic episodes. Patients manifesting elevations in PCWP with symptomatic episodes are likely to do so with asymptomatic episodes as well. Some patients will not manifest wedge pressure changes with either symptomatic or asymptomatic episodes.

Symptomatic versus asymptomatic myocardial ischemia

Ambulatory Holter monitoring of patients with chronic stable angina demonstrates that 83% of ischemic episodes with ST-segment depression of 1–2 mm are asymptomatic, and 63% of ischemic episodes with ST-segment depression of 3 mm or more are asymptomatic. Of the ischemic ECG changes seen in elective CABG surgery patients monitored for 48 hours in the preoperative period, up to 80% are asymptomatic. The reasons why some episodes of ischemia are symptomatic while others are not remain unclear. There is some evidence that asymptomatic episodes are of shorter duration and lesser severity than symptomatic episodes, but this is not consistently true. There is also evidence to suggest that patients with asymptomatic episodes have a higher pain tolerance, but this is not uniformly true. Diabetic patients with autonomic dysfunction are at higher risk for asymptomatic ischemia.

Incidence of perioperative ischemia

Efforts to prevent myocardial ischemia usually target control of the readily obtainable hemodynamic determinants of myocardial oxygen demand such as HR and blood pressure (BP). Contrary to this practice, however, most ischemic episodes are not preceded by increases in HR or rate-pressure product (RPP) (the product of HR and systolic BP). In fact, most episodes are clinically silent. The same is true in cardiac surgical patients in the preoperative period. Approximately 40% of cardiac surgical patients will experience ST-segment evidence of ischemia sometime in the 48 hours prior to elective cardiac surgery. Less than one-fourth of these episodes are preceded by a HR increase of 20% or more. In addition, most of these episodes are clinically silent.

As with preoperative ischemic events, approximately half of intraoperative ischemic events are unrelated to changes in HR and BP. This unprovoked ischemia suggests that decreases in myocardial oxygen supply may be important in the genesis of intraoperative ischemia. In the cardiac surgical patient, ischemia consists of a background of hemodynamically unrelated silent ischemia, upon which is superimposed episodes of hemodynamically related ischemia. Rigorous intraoperative hemodynamic control will not worsen the preoperative ischemic pattern and may actually improve it.

In the noncardiac surgical population, the postoperative period is the most common time for ST-segment myocardial ischemia. In addition to the underlying propensity towards silent ischemia (as described above), the postoperative period is subject to increasing metabolic demands, increased MVO_2, and a hypercoagulable state. There may be plaque fissure and subsequent thrombus formation. In the patient recovering from CABG, one anticipates a reduction in the incidence of ischemia. After all, the coronary artery stenoses are bypassed, and myocardial blood flow normalized. In reality, however, CABG patients may suffer postoperative ischemia for a number of reasons including acute graft occlusion, coronary air or debris embolism, technical anastomoses failure or disruption, tamponade with graft obstruction, or myocardial oxygen supply–demand mismatch. CABG patients require close monitoring for ischemia in the hours after surgery.

Outcome after myocardial ischemia

The most significant consequence of pre- and intraoperative ischemia is postoperative myocardial

infarction (PMI). The risk of PMI is approximately 7% in CABG patients who had preoperative ischemia, intraoperative ischemia, or both, and 2.5% in patients who did not have ischemia. The risk of PMI correlates with the severity of ischemia. In patients with ST-segment depressions >2 mV, the PMI incidence is 9%; whereas those with ST-segment depressions between 1.0–1.9 mV, the incidence is 6%.

There are many factors well beyond the control of the anesthesiologist that are responsible for increasing the incidence of PMI. An aortic cross-clamp time in excess of 40 minutes increases the incidence of PMI from 2.6 to 10.9%. PMI occurs in 14.3% of patients in whom the distal anastomoses were rated by the surgeon as poor as compared with 3.4% of patients in whom the anastomoses were considered of good quality.

Diagnosing myocardial ischemia

ECG changes
The gold standard for diagnosis of myocardial ischemia is the presence of ECG changes. Unfortunately, ECG changes occur relatively late in the temporal sequence of myocardial ischemia after deterioration of ventricular diastolic and systolic function. Lead selection greatly enhances ischemic detection. Simultaneous monitoring of leads II and V5 is commonly used because of the high sensitivity of this combination in detecting myocardial ischemia.

PCWP trace
The PCWP trace of the pulmonary artery catheter (PAC) can assist in the early diagnosis of LV ischemia. Reduction in LV compliance occurs in the early stages of LV ischemia because of diastolic dysfunction. In particular, LVEDP is elevated. Under these circumstances, left atrial pressure (LAP) will be elevated to maintain LV diastolic filling. Movement of the left atrium (LA) to a steeper potion of its pressure–volume relationship will result in magnification of the normal LAP waveforms. In addition, dilation of the LA may result in a more forceful atrial contraction and production of an enlarged A wave. The peak of this A wave

will reflect LVEDP. LV ischemia, which produces LV dilation or papillary muscle dysfunction, may cause mitral regurgitation with generation of a prominent V wave. If there is inferior ischemia with RV dysfunction, some of these same observations may be seen on the CVP waveform.

The PCWP trace is a reflection of LAP. However, because the PCWP waveform is transmitted through the compliant pulmonary venous system, it is a damped version of the LAP. In particular, the left atrial A wave may be poorly seen. As a result, it has been demonstrated that mean PCWP reflects mean LV diastolic pressure and may underestimate LVEDP by 10–15 mmHg during ischemia.

Changes in PCWP and the PCWP waveform have poor sensitivity and specificity in detecting episodes of myocardial ischemia. This is true for a number of reasons:
- PCWP does not necessarily reflect LVEDP as previously described.
- When only a small region of LV wall develops diminished compliance with an ischemic episode, overall LV function may be only minimally affected. This will reduce the observed changes in LVEDP as reflected by the PCWP.
- The quantitative change in PCWP and the qualitative change in the PCWP waveform necessary to define an ischemic event have not been systematically defined.
- Acute elevations in afterload in the absence of ischemia can produce elevations in PCWP. This may lead to a false positive interpretation of the PCWP tracing.

Myocardial ischemia does not result in PCWP chances in all patients, and therefore, PCWP cannot be relied upon as the sole indicator of ischemia. For this reason, it is important to emphasize that suspicious ECG or transesophageal echocardiography (TEE) changes cannot be ignored simply because there is no change in the PCWP or the PCWP waveform.

Transesophageal echocardiography
Regional wall motion abnormalities (RWMA) during systole (diminished inward excursion and thickening) occur with ischemia. These RWMA precede ECG changes. The development of severe

hypokinesis, akinesis, or dyskinesis is more specific for ischemia than mild hypokinesis. Changes in wall thickening are more sensitive for detecting ischemia than changes in wall excursion. Typically, wall motion abnormalities and ECG changes occur within 60 seconds of each other. However, in a situation in which ischemia is less severe, RWMA may precede ECG changes by several minutes. In fact, numerous studies have shown intraoperative TEE qualitative analysis of regional wall excursion and thickening to be a more sensitive detector of myocardial ischemia than ECG changes and to be capable of detecting ischemia before ECG changes.

As with all monitors, there are occasional discrepancies between ischemia detected by ECG and that detected by TEE. There are both TEE-detected ischemic episodes not detected by ECG and ECG-detected ischemic episodes not detected by TEE. This may be due to several factors:

• Normally, the TEE probe is placed at the mid-LV level (level of the papillary muscles), at which wall segments in the distribution of all three coronary arteries can be monitored. Because a short-axis view of the left ventricle can only be obtained at one level at a time, ischemic changes occurring in the basal or apical ventricular levels will be missed. Obtaining multiple TEE windows, allowing visualization of all 17 segments of the heart will reduce or eliminate this as a source of error.

• Ischemic episodes may be missed because qualitative wall motion analysis is difficult for patients with preexisting wall motion abnormalities.

• Some RWMA (particularly in areas tethered to scar) may not be ischemic in origin. Changes in afterload may unmask areas of previous scarring.

• Ventricular pacing or a bundle-branch block may make detection of RWMA more difficult because of asynchronous contraction.

• Stunned myocardium may exhibit continued RWMA despite adequate perfusion.

• The ECG may detect ischemia with small areas of subendocardial ischemia undetectable by TEE.

Predicting myocardial ischemia

The ability to predict hemodynamic alterations that are likely to result in myocardial ischemia in individual patients would allow prompt treatment and avoidance of events initiating ischemia. Unfortunately, the diverse nature of myocardial oxygen imbalance in patients leaves the anesthesiologist with no predictor of myocardial ischemia that is reliable in all circumstances. The indices described in the next sections all have limited usefulness.

Rate-pressure product and triple index

The RPP is the product of HR and systolic BP, whereas the triple index (TI) is the product of HR, systolic BP, and PCWP. The RPP provides a useful assessment of MVO_2 and predicts ischemia in patients undergoing stress testing. Most patients experience the onset of ischemia at an RPP of 20 000. However, its usefulness in assessing MVO_2 and predicting ischemia in anesthetized patients is not reliable. In fact, it is common for a patient under anesthesia to have a low RPP and yet be at high risk for ischemia (tachycardia and hypotension with acute blood loss).

The TI is subject to the same criticisms as the RPP. The addition of PCWP to the product adds the variable of wall radius to the assessment of MVO_2. However, the TI still fails to account for large reductions in myocardial oxygen delivery in the genesis of ischemia.

Myocardial supply–demand ratio (DPTI:SPTI)

Efforts to account for beat-to-beat variations in both myocardial supply and demand in the genesis of ischemia led to development of the supply–demand ratio. In this evaluation, supply is defined by the diastolic pressure time index (DPTI): DPTI = (mean diastolic pressure – LVEDP) × duration of diastole. Demand is defined as the systolic pressure time index (SPTI): SPTI = (mean arterial pressure) × duration of systole. Ratios below 0.5 may result in subendocardial ischemia. Unfortunately, use of this ratio is also unreliable for several reasons:

• Increases in MVO_2 due to increased contractility are not reflected in BP and HR changes and therefore are not accounted for by SPTI.

• A higher ratio is required in the presence of anemia to compensate for the reduced oxygen carrying capacity of blood.

• The presence of pressure drops across coronary stenoses makes the DPTI an unreliable index of distal coronary perfusion.

• Changes in coronary vascular resistance make DPTI an unreliable index of distal coronary perfusion.

• Use of the ratio is cumbersome because it requires calculation of the areas under the diastolic and systolic pressure curves, respectively.

Mean arterial blood pressure–heart rate (BP–HR) quotient

Animal work demonstrates that ischemia occurs in the distribution of a critical coronary stenosis and in collateral-dependent myocardium when the pressure rate quotient (PRQ), defined as mean arterial pressure (MAP)/HR, is <1. This relationship is valid over a wide range of pressures and HRs. An increase in HR can cause or worsen ischemic dysfunction at any mean arterial BP; however, the absolute HR at which ischemia occurs is dependent on the pre-existing MAP. In other words, higher HRs are tolerated without ischemia at higher MAPs. For patients undergoing coronary revascularization, PRQ < 1.0 has poor sensitivity and specificity in predicting myocardial ischemia as detected by both ECG and TEE.

In summary:

• The combination of hypertension and tachycardia may result in myocardial ischemia by increasing myocardial oxygen demand.

• The combination of hypotension and tachycardia is particularly detrimental to myocardial oxygen balance because it reduces both the time and the pressure gradient available for myocardial perfusion.

• Tachycardia, in and of itself, is detrimental to myocardial oxygen balance. Experimentally, tachycardia causes or worsens ischemic dysfunction at any given mean arterial BP. Clinically, tachycardia is associated with the development of ischemia in patients undergoing coronary revascularization whereas hypertension per se is not a risk factor. In particular, HRs > 110 b/min are associated with a dramatically increased incidence of intraoperative ischemia in patients undergoing coronary revascularization.

Treatment of ischemia

The most effective ischemic therapy involves identification of the cause of ischemia and targeted treatment of this causative factor or factors. In some cases, the specific cause for new ischemia is unclear.

Tachycardia

No single value of HR is uniformly detrimental to myocardial oxygen balance in a given patient. As already discussed, the HR at which ischemia is likely to occur will vary with mean arterial BP and the other determinants of myocardial oxygen balance. When an increase in HR results in ischemia or is likely to result in ischemia, immediate therapy is necessary.

Eliminating inadequate anesthetic depth as a cause is among the first and immediate steps in the patient undergoing surgery. Preload must be adequate. This is particularly important for patients with diminished ventricular compliance. In these patients, a higher-than-normal end-diastolic pressure is necessary to ensure an adequate ventricular EDV. Once anesthetic depth and volume status are eliminated as a cause of the tachycardia, treatment with a beta-blocker may be necessary. Many patients taking beta-blockers preoperatively may have plasma concentrations that are too low to blunt the hemodynamic responses to surgery and will require supplemental medication. Propranolol in incremental doses of 0.5–1.0 mg IV to a total of 0.1 mg/kg may be used for patients without severe ventricular systolic dysfunction. For patients with a history of bronchospasm or reactive airway disease, a β_1 selective agent such as metoprolol is useful. Incremental doses of 2.5–5.0 mg IV to a total of 0.5 mg/kg can be used. Because elevations in PCWP will reduce CPP, concomitant intravenous (IV) therapy with nitroglycerin 0.5–1.0 µg/kg/min is indicated in the presence of an elevated PCWP. The clinician must titrate drug use against anticipated or observed hypotension.

In some instances, the ultra-short-acting beta-blocker esmolol may be useful. Esmolol has an elimination half-life of 9 minutes due to metabolism by red-cell esterases and is β_1 selective. Esmolol is started with a bolus of 0.5 mg/kg given over

several minutes followed by an infusion of 50 μg/kg/min and titrated up to 300 μg/kg/min as necessary. In a patient under general anesthesia, however, the initial dose should be significantly reduced (10–50 μg). Esmolol is useful in patients with poor ventricular function or bronchospastic disease. A striking advantage to this medication is the short half-life. If the drug is poorly tolerated, therapy can be quickly terminated. Furthermore, unlike longer-acting beta-blockers, esmolol can be used aggressively in the pre-cardiopulmonary bypass (CPB) period without fear that it will compromise termination of CPB.

Hypotension

Many patients with coronary disease will tolerate brief episodes of hypotension without ischemic sequelae, but others will not. The extent of hypotension that can be tolerated before ischemia develops is dependent on several variables. For example, a reduction in arterial BP may reduce MVO_2 by reducing afterload (decreasing demand); however, at the same time, aortic perfusion pressure may fall to a critical level (decreasing supply). Furthermore, as discussed previously, at higher HRs, hypotension adversely effects perfusion. In any case, the source of hypotension must be quickly and accurately determined. Determination of CO and systemic vascular resistance (SVR) will help direct therapy.

When hypotension is due to a reduction in CO, HR and preload should be optimized. If these measures fail to correct the fall in CO, one should consider starting an inotrope and eliminating or reducing any inhalational anesthetic agents (eliminating their negative inotropic properties). A fall in SVR can be treated with an α-adrenergic agonist such as phenylephrine in incremental doses of 40–100 μg IV. It should be kept in mind that α-adrenergic agonists may constrict coronary arteries with dynamic stenoses and should therefore be titrated carefully. Because elevations in PCWP will reduce CPP (increasing ventricular wall tension), concomitant therapy with nitroglycerin 0.5–1.0 μg/kg/min is indicated in the presence of an elevated PCWP.

Hypertension

Hypertension is classically associated with tachycardia in the genesis of myocardial ischemia. Treatment, in this instance, is directed toward deepening of anesthesia. If hypertension is persistent despite adequate anesthetic depth, vasodilator therapy is warranted. Many agents reduce systemic BP. Sodium nitroprusside is an easily titrated, potent arteriolar dilator that effectively treats hypertension. An infusion can be started at 0.25 μg/kg/min and titrated upward. However, because sodium nitroprusside is a potent arteriolar dilator, it has the potential to induce a coronary steal in the presence of the appropriate anatomy. Another concern is over treating the patient and inducing acute, severe hypotension.

Nitroglycerin preferentially dilates large coronary vessels and is not implicated in the steal phenomenon. Nitroglycerin has its greatest dilating effect on the venous beds and arterial dilatation occurs only at higher doses. Despite this, when used in appropriate doses, nitroglycerin and nitroprusside have been shown to be equally effective in treatment of hypertension associated with coronary artery bypass surgery. Both agents have comparable effects on HR, CO, and PCWP. With comparable reductions in systolic BP, nitroglycerin causes less reduction in diastolic BP than does nitroprusside. Therefore, CPP may be better preserved with nitroglycerin than with nitroprusside. For these reasons, nitroglycerin may be the preferred agent for treatment of hypertension associated with myocardial ischemia. For treatment of hypertension, start nitroglycerin at 0.5 μg/kg/min and titrate to effect.

Dynamic stenosis

Evidence of myocardial ischemia may occur with little or no initial change in HR or BP. In these instances, acute reductions in coronary blood flow may occur due to vasoconstriction in the area of a coronary stenosis or due to true coronary spasm in an area free of a stenosis. The mainstays of therapy are nitroglycerin and calcium channel blockers to reduce coronary vasomotor tone. Nitroglycerin can be started at 0.5 μg/kg/min and titrated upward. When an elevated PCWP accompanies the ischemic

episode, nitroglycerin effectively reduces PCWP through both vasodilation (reducing preload) and treatment of the underlying ischemia. Nifedipine is a calcium channel blocker and systemic vasodilator that can be administered sublingually in a 10-mg dose to reduce coronary vasomotor tone.

Systemic hypotension may occur with administration of these agents. CPP improves when the pressure drop across the stenosis diminishes with vasodilation in the area of the stenosis and when vasodilation reduces PCWP. However, extreme diastolic hypotension offsets any potential improvement of CPP. For this reason, administration of phenylephrine in addition to nitroglycerin acts to preserves diastolic BP and CPP.

Anesthetic management for CABG surgery

Goals

- Avoid increases in myocardial oxygen consumption.
- Avoid tachycardia; it compromises oxygen delivery at any MAP.
- Appreciate that the patient's baseline ischemic pattern will continue into the preoperative and intraoperative periods; these episodes must be treated when recognized.

Preoperative cardiac assessment

Preoperative evaluation is discussed in detail in Chapter 1. Careful review of the cardiac catheterization data is also an essential part of the preoperative visit. The important features of the catheterization report are reviewed here and discussed in detail in Chapter 2.

Diastolic function

To varying degrees, many patients with CAD manifest diminished ventricular compliance. In many patients with diastolic dysfunction, an elevated LVEDP is necessary for adequate LVEDV. The measurement of LVEDP at the time of cardiac catheterization will provide some index of the degree of diastolic impairment. In addition to diminished distensibility, patients with long-standing systemic hypertension may have concentric hypertrophy and diminished ventricular compliance. Patients functioning on the steep portion of their diastolic pressure–volume curve will be dependent on a well-timed atrial systole (the A wave in the atrial pressure trace) to adequately fill the ventricle at end diastole.

Echocardiography offers another avenue for evaluation of diastolic dysfunction. This noninvasive modality allows precise quantification of diastolic parameters. The function can be characterized as normal, delayed relaxation, pseudo-normal and restrictive. These quantifications represent a continuum of disease (Figs 4.9 and 4.10).

For patients undergoing repeat coronary revascularization procedures, elevated right heart pressures increase the risk of inadvertent right atriotomies and ventriculotomies during sternotomy. Similarly, if the pericardium was left open after the original surgical procedure, the anterior surface of the RV is more likely to be adherent to the sternum (Fig. 4.11). The hemorrhage induced by these traumatic atriotomies, and ventriculotomies can be life threatening. A femoral vein and artery are often exposed before sternotomy in redo patients so that partial bypass can be initiated emergently if hemorrhage occurs with sternotomy. Partial bypass provides the circulatory support and the decompression of the right heart that may be necessary for surgical repair.

Systolic function

Ejection fraction (EF) and assessment of wall motion are the most commonly obtained assessments of systolic function (Fig. 4.12). Because EF is an ejection-phase index, it is dependent on loading conditions. For this reason, the presence of a low-impedance outflow tract, such as that which exists via the mitral valve in mitral insufficiency, will cause the EF to overestimate systolic function. EF is an assessment of global systolic function and will not be depressed until a relatively large portion of ventricle exhibits compromised systolic function. An EF lower than 40% is abnormal. Wall motion abnormalities are seen with ventriculography, advanced magnetic resonance imaging (MRI) or computed tomography (CT) imaging, or commonly, with echocardiography. When large areas of

Transmitral flow velocity			
Normal	Delayed Relaxation	Pseudonormal	Restrictive
$E \geq A$	$E < A$	$E < A$	$E \gg A$
DT 140–220	DT > 220	DT 140–220	DT < 140
IVRT 60–100	IVRT > 100	LAP increased	IVRT < 60

Pulmonary vein flow velocity			
Normal	Delayed relaxation	Pseudonormal	Restrictive
$S \geq D$	$S > D$	$S < D$	$S < D$
Ar < 25 cm/s	Ar < 25 cm/s	Ar > 25 cm/s	Ar > 25 cm/s
		LAP increased	LAP increased

Mitral annular velocity (lateral wall)			
Normal	Mild Dysfunction (Delayed relaxation)	Moderate Dysfunction (Pseudonormal)	Severe Dysfunction (restrictive)
$E_M/A_M > 1$			
$E_M > 8$ cm/s	$E_M \leq 8$ cm/s	$E_M < 8$ cm/s	$E_M \ll 8$ cm/s

Fig. 4.9 Transmitral Doppler imaging, pulmonary view Doppler imaging and tissue Doppler imaging (TDI) profiles corresponding to normal, delayed relaxation, pseudonormal, and restrictive filling patterns. (From Groban L, Dolinski SY. Transechocardiographic evaluation of diastolic function. *Chest* 2005;**128**:3652–63, with permission.)

akinesis and dyskinesis exist, systolic function will be severely compromised.

RV EF and wall motion analysis generally are not obtained at the time of catheterization. For patients with suspected RV systolic dysfunction, either first-pass or equilibrium noninvasive radionuclear imaging can be used to determine EF.

Coronary anatomy and coronary lesions

The surgeon and anesthesiologist must know the extent of coronary disease and the presence or absence of collateral flow. This will allow intelligent assessment of the areas most at risk for developing ischemia. This knowledge will help guide monitoring decisions (i.e. ECG monitoring selection and TEE window).

The coronary angiograms guide the surgeon in target vessel location. Distal disease in small vessels makes the technical success of the operative procedure less likely. Furthermore, bypassing a vessel supplying a dyskinetic or aneurysmal area of ventricle may yield little in terms of improved systolic function postoperatively because such areas have little salvageable myocardium. There are strong data to suggest that bypassing areas of hibernating myocardium result in improved LV function at 1 year after surgery. In some patients, the EF% may dramatically improve from 20 to 40% or better.

The term "left main equivalent" is commonly used and deserves clarification. A high-grade left main coronary artery lesion potentially jeopardizes

EF ≥ 45%

= To do

= Diagnosis

Doppler
mitral inflow

E < A
DT > 140 ms

TDI
E_M ≤ 8 cm/s

E/E$_M$ ≤ 8   8 ≤ *E/E*$_M$ ≤ 15   *E/E*$_M$ > 15

Impaired relaxation normal filling pressures

Impaired relaxation increased filling pressures

Doppler pulmonary vein

Ar wave < 25 cm/s

Ar wave ≥ 25 cm/s

Impaired relaxation normal filling pressures

Impaired relaxation increased filling pressures

E > A
DT > 140 ms

TDI
E_M > 8 cm/s E_M ≤ 8 cm/s

E/E$_M$ ≤ 8   8 ≤ *E/E*$_M$ ≤ 15   *E/E*$_M$ > 15

Normal diastolic function

Pseudonormal

Valsalva and mitral inflow

E > A

E < A

Normal diastolic function

Pseudonormal

And/or

Doppler pulmonary vein

Ar wave < 25

Ar wave ≥ 25

Normal

Pseudonormal

E ≫ A
DT < 140 ms

TDI
E_M > 8 cm/s E_M ≤ 8 cm/s

E/E$_M$ < 8   *E/E*$_M$ > 15

High suspicion of pericardial disease

Restrictive myocardial disease

Valsalva and mitral inflow

E > A

E ≫ A
(unchanged)

Reversible, restrictive

Fixed, restrictive

Fig. 4.10 Algorithm for the assessment of diastolic function in the patient with a normal or near-normal ejection fraction (EF) (i.e. ≥ 45%). A, atrial peak velocity; Ar, retrograde velocity; E, early filling peak velocity; E_M, early filling; TDI, tissue Doppler imaging. (From Groban L, Dolinski SY. Transechocardiographic evaluation of diastolic function. *Chest* 2005;**128**:3652–63, with permission.)

Fig. 4.11 Lateral and posterior/anterior chest radiographs of a woman presenting for a re-do sternotomy. Note the sternal wires and the heart adherent to the sternum. This woman has a thoracoabdominal aortic aneurysm.
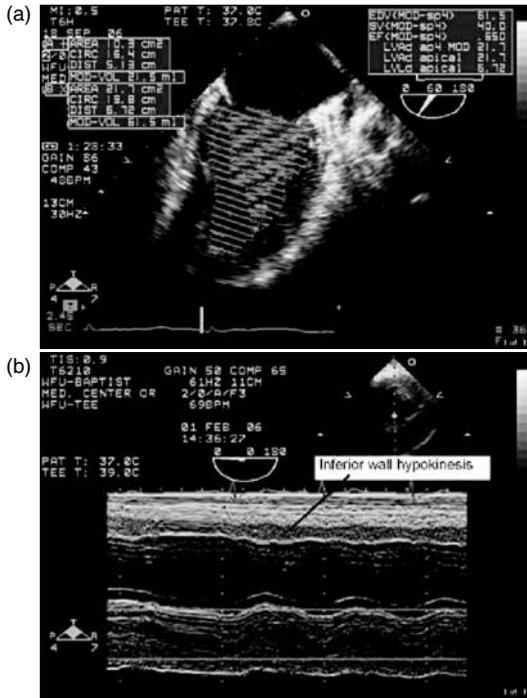
Fig. 4.12 Systolic function is easily assessed with transesophageal echocardiography (TEE). (a) Ejection fraction (EF) is determined by the modified method of disk. Capturing the image in both end systole and end diastole allows the echocardiographer to trace the endocardial border and determine ejection fraction. The EF in this patient is normal (65%). (b) M-mode Doppler allows determination of wall motion and fractional shortening. In this patient, there is significant inferior wall hypokinesis as evidenced by a lack of thickening and movement during systole. Compare the thickening and movement of the anterior wall (far field) to that of the inferior wall.

most of the LV muscle mass. Likewise, high-grade stenoses of both the left anterior descending (LAD) and circumflex arteries jeopardize the same territory. As a result, this combination of lesions is functionally the same as a left main lesion; hence, the designation left main equivalent. The difference is that with the true left main lesion, only one vessel (the left main) must become completely occluded to compromise LV blood flow. In the case of the LAD and circumflex lesions, both vessels would have to be occluded simultaneously to produce the same effect. Another high-risk combination

of lesions occurs when collaterals from a vessel with a high-grade stenosis supply myocardium distal to an occluded vessel. An example would be myocardium distal to an occluded LAD supplied by collaterals from a right coronary artery (RCA) with a high-grade proximal stenosis. In this setting, complete occlusion of the remaining vessel (RCA) compromises most of the LV.

For patients undergoing redo procedures, evaluation of the extracardiac conduits (internal mammary arteries and reverse saphenous veins) is required. These grafts may now have varying degrees of stenosis. Inadvertent compromise (i.e. transection, laceration, kinking) of these conduits during the difficult dissection that often accompanies a redo procedure may severely compromise myocardial perfusion. Likewise, surgical manipulation of these conduits may result in embolization of atherosclerotic plaques into the distal coronary vascular bed with subsequent transmural myocardial ischemia.

Premedication

Reassurance and allowing time to address the patient's concerns are perhaps the best anxiolytic. This is especially import when one considers the relative risk CABG surgery involves. In the very best of hands, the risk of mortality is approximately 1–3%, and there is a further risk of neurocognitive deficit, stroke, renal failure and respiratory failure. Our patients are facing a major risk which induces significant anxiety. It is our obligation to treat them with care, compassion and patience.

There are a number of safe premedication prescriptions than a clinician may chose. Patients with preserved ventricular function can be premedicated with morphine 0.10–0.15 mg/kg intramuscularly (IM), scopolamine 0.005 mg/kg IM, and diazepam 0.15 mg/kg or lorazepam 0.04 mg/kg orally (PO) approximately 1.5 hours before scheduled induction time. Alternatively, morphine 0.10–0.15 mg/kg IM and midazolam 0.03–0.05 mg/kg IM may be used. The dysphoric effects of scopolamine may be troublesome for elderly patients. For elderly patients or patients with poor ventricular function, the doses can be reduced and supplemental premedication can be given in the operating room holding area

under direct observation. Supplemental oxygen with a face mask should be started at the time of premedication. Most prudently, premedication can be held until the patient arrives in the preoperative holding area. At this time, the physician or nurse anesthetist can administer either fentanyl or midazolam under direct supervision and observation.

All cardiac medications should be continued on schedule until the time of surgery. Preoperative beta-blocker therapy has been shown to blunt the hemodynamic responses to surgical stimulation during coronary revascularization and to reduce the incidence of HR-related intraoperative ischemic events. Continuation of preoperative beta-blockade therapy does not compromise myocardial performance during the post-CPB period. Furthermore, abrupt withdrawal of beta-blockade therapy has been associated with myocardial ischemia, hypertension, and tachydysrhythmias secondary to a beta-blockade induced increase in β-receptor density. In fact, continuation of beta-blockers in patients undergoing surgery who are receiving the medication for angina, symptomatic arrhythmias, hypertension or other ACC/AHA class I indications carries a class I level recommendation.

Some preoperative medications require additional comment. Patients treated with diltiazem and nifedipine preoperatively demonstrate a diminished response to phenylephrine. Thus, treatment of intraoperative hypotension may require higher than usual doses of phenylephrine for patients continued on preoperative calcium channel blockers. The incidence of perioperative ischemia during coronary revascularization is greater in patients receiving just calcium channel blockers (nifedipine, diltiazem, or verapamil) preoperatively than in patients receiving beta-blockers or a combination of calcium channel and beta-blockers. This is probably due to better attenuation of tachycardia-induced ischemia in patients receiving beta-blockers. The angiotensin converting enzyme inhibiting drugs are associated with refractory hypotension after CPB in some patients. These medications should be held on the morning of surgery. If hypotension is encountered, treatment is most effective using IV vasopressin (2 units IV bolus titrated to effect or

an infusion of 2–6 units/h). The antiplatelet medications pose an unusual management problem. Patients on clopidogrel should have the medication held for 3–5 days before elective surgery. Surgery in patients on clopidogrel is associated with excessive bleeding and transfusion of blood and blood products.

Preinduction

After arrival in the operating room, all patients should be attached to an ECG system capable of monitoring leads I, II, III, aV_R, aV_L, AV_F, and V_5. Baseline recording of all seven leads should be obtained for comparative purposes. Normally, two leads (II and V_5) are monitored simultaneously intraoperatively. However, if the areas of myocardium at risk are better assessed in other leads, then those leads should be monitored.

All patients should have a radial arterial catheter and adequate peripheral IV access (14- or 16-gauge). Alternatively, if peripheral IV access is poor, a peripheral IV suitable for induction can be started and a large-bore multilumen (16- or 14-gauge) central venous line can be placed at the same time as the PAC. For patients who are to have an internal mammary artery (IMA) harvested, the arterial waveform obtained in the ipsilateral radial or brachial artery may be compromised during IMA dissection. This occurs when the patient's arm is tucked at the side and is compressed between the body and the retractor used for IMA dissection. This results in compression of the brachial artery against the humerus and is particularly common in large patients. The arterial line may be placed in the contralateral arm or the ipsilateral arm can be abducted to avoid this problem. When the arm is tucked at the side, care should be taken to provide ample padding between the arm and the retractor. Many surgeons harvest the radial artery for additional arterial conduit. In these cases, the nonsurgical arm is only site available for radial artery cannulation. If cannulation is impossible, a femoral artery catheter is required.

The use of PACs for all patients undergoing coronary revascularization is controversial. PACs allow measurement of thermodilution CO; pulmonary artery, right atrial, and PCWPs; systemic and

pulmonary vascular resistances (PVRs); and LV and RV stroke work. Some PACs monitor continuous CO, mixed venous oxygen saturation, right heart EF, and RV diastolic volume. Analysis of the PCWP and RAP traces may be helpful in the early diagnosis of ischemia. There are several reviews of outcome and pulmonary artery catheterization. It is extremely difficult to demonstrate a benefit in placing a PAC, and in many studies, the PAC is associated with worse outcome. Nonetheless, PAC use is common during cardiac surgery.

The PAC may be safely placed either before or after the induction of anesthesia. If placed before, the information can be used during the induction sequence. However, some patients may experience undue anxiety, or if sedated, potential respiratory compromise during line placement. If placed after induction, the patient will be under general anesthesia and paralyzed thereby facilitating rapid and safe placement. As with any central line placement, certain precautions are required. All of the equipment and medications for treatment of dysrhythmias should be on hand before placement of the catheter is attempted. In particular, a defibrillator with demonstrated consistent synchronization to the patient's ECG signal must be in the room in case cardioversion is necessary. In addition, strict sterile technique is required to reduce the incidence of perioperative line colonization and sepsis.

The information obtained at cardiac catheterization about LV diastolic function and LV end-diastolic pressure can be used in conjunction with the PCWP to optimize LV preload. Patients with reduced compliance may require a PCWP in the range of 12–15 mmHg to ensure an adequate preload (LVEDV). When preload is inadequate, SV and CO will be reduced and systemic BP and CPP will be maintained by increases in SVR. Subsequent reductions in SVR (as with induction) may lead to hypotension and potentially to tachycardia. In this setting, any advantage of a low PCWP in terms of CPP is offset by systemic hypotension.

For patients with poor systolic function, preload reserve will be limited or exhausted to meet baseline CO demands. Any increase in afterload will produce afterload mismatch and result in progressive reductions in SV and CO. Because poor systolic function associated with ischemic heart disease is accompanied by reduced diastolic distensibility, maintenance of an adequate preload will require a PCWP in the range of 12–18 mmHg.

All episodes of ischemia in the preinduction period require aggressive therapy. Therapy should be directed toward the specific cause of the ischemic episode. A high proportion of ischemic episodes are likely to be asymptomatic and to occur in the absence of hemodynamic changes, the ECG, RAP, and PCWP traces are important in diagnosing ischemia in these patients.

Induction and maintenance

No one anesthetic technique is superior to another for patients presenting for coronary artery bypass grafting. Two types of techniques are discussed: a traditional high-dose narcotic technique and a "fast-track" technique geared toward shorter postoperative ventilation and earlier discharge from the intensive care unit (ICU).

High-dose narcotic technique

Fentanyl and sufentanil generally provide the stable hemodynamics essential in preventing imbalance in myocardial oxygen supply and demand. These agents have no effect on myocardial contractility and cause a reduction in peripheral vascular resistance only through a diminution in central sympathetic tone. In a high-dose narcotic technique, 50–75 μg/kg of fentanyl, or 10–15 μg/kg of sufentanil serve as the primary anesthetic for induction and maintenance before CPB. A benzodiazepine must be included to avoid awareness.

Sufentanil is associated with greater decreases in arterial BP and SVR on induction than fentanyl. However, sufentanil is more effective than fentanyl in blunting the hypertensive responses to skin incision, sternotomy, sternal spread, and aortic manipulation. To avoid hypotension on induction with either narcotic, adequate preload is essential.

The choice of muscle relaxant influences the hemodynamic stability of a high-dose narcotic anesthetic. Pancuronium has a vagolytic effect as well as the capacity to enhance sympathetic outflow by

blockade of sympathetic postganglionic muscarinic receptors, inhibition of catecholamine reuptake, and stimulation of release of catecholamine from nerve terminals. Vecuronium and cisatracurium are devoid of these effects. Induction with fentanyl–pancuronium provides stable induction hemodynamics without ischemia. In some patients, induction with fentanyl–vecuronium or sufentanil–vecuronium results in bradycardia and hypotension. Induction with sufentanil–pancuronium provides stable induction hemodynamics and HR. Caution is urged in any case in a patient receiving beta-blocking agents preoperatively. In these patients, a high-dose narcotic is more likely to be associated with significant bradycardia.

Preoxygenation is important in cardiac surgical patients. The induction sequence must be tailored to the individual patient. A system of graded stimulation is used to individualize the narcotic dose for each patient. After loss of consciousness, the hemodynamic response to insertion of an oral airway, followed by insertion of a urinary catheter, can gauge the need for additional narcotic to blunt the anticipated hemodynamic response to tracheal intubation. If an upward trend in HR or BP is noted during laryngoscopy, additional narcotic should be administered. If there is poor visualization of the trachea, laryngoscopy should be terminated and intubating conditions should be improved by changing head position, using a stylet, or changing blades. This approach will help prevent long, stimulating laryngoscopies that compromise hemodynamics. After the airway is secure, the stomach should be evacuated with an oral-gastric tube, after which, a TEE probe can be placed.

It is sometimes helpful to administer a priming dose of muscle relaxant prior to the narcotic administration. Vecuronium or pancuronium 0.02 mg/kg or cisatracurium 0.04 mg/kg are appropriate approximately 1–2 minutes before starting the narcotic infusion. As the patient loses consciousness, the remainder of the total dose of 0.1 mg/kg of vecuronium or pancuronium or 0.2 mg/kg of cisatracurium is administered and controlled ventilation with 100% oxygen is initiated. This technique minimizes the risk of narcotic-induced rigidity without undue stress to the patient.

Bradycardia with hypotension requires prompt treatment. A small dose of pancuronium (1–3 mg) is often effective if vecuronium or cisatracurium has been used. Glycopyrrolate, ephedrine, or atropine may be appropriate alternatives. Atropine should be used cautiously. Atropine administration may initiate tachycardia. Atropine, unlike β_1-adrenergic agents, increases HR without any reduction in the duration of systole. Thus, for equal increases in HR, atropine will cause a greater reduction in the duration of diastole and will compromise subendocardial perfusion to a greater degree than will a β_1-adrenergic agent. Ephedrine (a direct- and indirect-acting β- and α-agonist), 5 mg, is a reliable agent to increase HR without compromising diastole. In addition, the augmentation in diastolic BP obtained is beneficial when hypotension accompanies bradycardia.

Tachycardia requires aggressive treatment to avoid subendocardial ischemia and hemodynamic compromise. The first strategy should be to terminate any noxious stimuli, assure proper intravascular volume and increase the depth of anesthesia when necessary. Failing this, a short- or long-acting beta-blocker is usually appropriate therapy.

Should hypotension due to reduced SVR occur, small doses of phenylephrine (40–120 μg) and volume infusion to increase preload to preinduction levels usually will correct the problem. A dose of phenylephrine reliably causes an increase in SVR with a concomitant increase in wall stress and a reduction in ejection phase indices of contractility in CABG patients. The peak effect of a phenylephrine dose occurs 30–40 seconds after injection.

If surgical stimulation (skin incision, sternotomy, sternal spreading, and aortic manipulation) produces hypertension, additional doses of sufentanil (1–5 μg/kg) or fentanyl (5–25 μg/kg) may be necessary. If this fails to control the hypertension, the use of additional agents will be necessary. As discussed previously, treatment of hypertension with vasodilator therapy must take into account the effect of these agents on regional myocardial blood flow and on their ability to improve concomitant ischemia.

As mentioned, this technique requires the administration of benzodiazepines and possibly

inhalational anesthetics to reduce the incidence of operative recall. Diazepam, midazolam, and lorazepam administered in conjunction with fentanyl or sufentanil may decrease peripheral vascular resistance resulting in subsequent hypotension. Therefore, they must be titrated with caution. Midazolam in increments of 1–2 mg or lorazepam in increments of 0.5–1.0 mg are reasonable.

Nitrous oxide (N_2O), in association with high-dose opiates, causes systolic dysfunction in patients with CAD, particularly those with an LVEDP >15 mmHg. N_2O combined with high-dose opiates also elevates PVR, particularly in the presence of pre-existing pulmonary hypertension. The potent inhalational agents, isoflurane, sevoflurane and desflurane are safe in patients undergoing coronary revascularization. The role of anesthetic preconditioning with inhalational agents is discussed later in this chapter.

Fast-track technique

The "fast track" is a comprehensive program designed to improve perioperative outcome and reduce costs by reducing hospital stay for patients undergoing coronary revascularization. Early extubation (<8 hours) is the hallmark of this program. A number of anesthetic techniques allow early extubation without increasing the risk of adverse cardiac and noncardiac outcomes. Generally, patients selected for inclusion in the protocol are low-risk coronary revascularization patients, but more centers are including all cardiac surgical patients. Risk factors contributing to prolonged postoperative ventilation in coronary revascularization patients are female sex, advanced age, congestive heart failure (CHF) requiring preoperative diuretic therapy, and unstable angina. Both the anesthetic technique and the maintenance of normothermia are important with this technique; however; the most important element for success in a hospital system is the adoption of a "fast-track extubation protocol." Using such a protocol identifies appropriate patients, alerts the care team of the clinical pathway, and facilitates a scheduled weaning process.

The following is an example of a fast-track protocol. There are many approaches, however, and

the clinician will soon master a technique suitable for his or her practice.

- Premedication with midazolam 1–2 mg IV in the preoperative holding area.
- Fentanyl 15–20 μg/kg and etomidate 0.20–0.30 mg/kg for induction in combination with cisatracurium or vecuronium. The considerations used in choosing a relaxant are the same used in the high-dose narcotic technique.
- Maintenance of anesthesia with isoflurane 0.5–1.0%.
- Either Propofol 75–100 μg/kg/min, or isoflurane is administered while on CPB.
- Intermediate-acting neuromuscular blocking agent (Fig. 4.13).
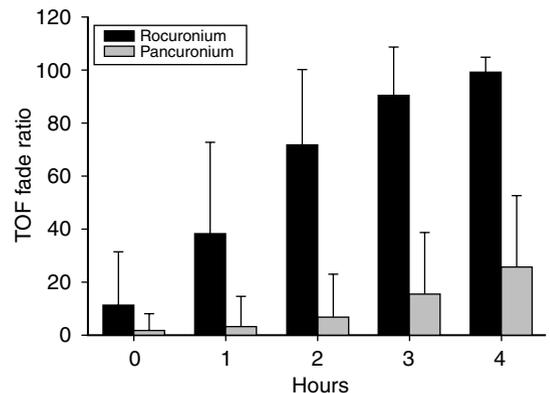
Postoperative recovery

Variable	Rocuronium	Pancuronium	P value
Duration of ventilatory weaning (min)	90 (40–315)	180 (50–180)	<0.05
ICU arrival until extubation (min)	335 (185–1290)	460 (225–1350)	<0.05
TOF ratio at initiation of ventilatory weaning	0.99 (0.87–1.21)	0.14 (0.00–1.11)	<0.05

Data are median (range).
ICU, intensive care unit; TOF, train-of-four.

Fig. 4.13 The use of pancuronium (0.08–0.10 mg/kg) or rocuronium (0.6–0.8 mg/kg) was evaluated in 82 patients undergoing coronary artery bypass grafting surgery. The bar graph shows the train-of-four ratios were measured upon arrival to the intensive care unit and then each hour for the next 4 hours. Significant differences were noted between groups at all time intervals ($P < 0.05$). The postoperative recovery profiles are shown below in the figure. Data are median (range). ICU, intensive care unit; TOF, train-of-four. (From Murphy GS, Szokol JW, Marymont JH *et al*. Recovery of neuromuscular function after cardiac surgery: pancuronium versus rocuronium. *Anesth Analg* 2003;**96**:1301–7, with permission.)

• Post-CPB, the isoflurane is maintained and no additional narcotic is administered. Either propofol, 20–50 μg/kg/min or dexmedetomidine 0.1–0.7 mg/kg/min is started prior to transport to the ICU.

Off-pump coronary artery bypass grafting

Off-pump coronary artery bypass (OPCAB) graft surgery offers an alternate technique to traditional on-pump CABG. Advantages of this technique include potentially decreased postoperative morbidity in some patients and reduced resource utilization and total cost. CPB is avoided in this technique, and therefore, so are all of the potential problems with myocardial preservation. Various investigators have demonstrated better myocardial energy preservation, less oxidative stress, and minimal myocardial damage with this technique. New advances in myocardial stabilizing devices allow a still operative field and excellent surgical conditions (the main advantage of CABG with cardioplegia and a flaccid heart). There are several reports in the literature comparing outcome between on-pump CABG and OPCAB. As expected, the results vary; however, it appears that there is no difference in outcome in low risk patients with either technique (Fig. 4.14). There is a consistent cost savings with OPCAB. The anesthetic management of these patients is strikingly different from traditional on-pump CABG. These differences are reviewed below.

In contrast to on-pump CABG, brief periods of ischemia are necessary during the operative procedure. These ischemic periods may be reduced in some patients with the placement of a temporary coronary stent, however, there remains some time of interrupted blood flow. The ischemic burden is usually of such short duration, that there is little risk of significant long-term damage; however, there may be some element of stunning and immediate myocardial dysfunction. In addition, there may be a cumulative global dysfunction after several sequential occlusions in multiple graft procedures. In fact, it is common for a patient to tolerate a one-or-two vessel OPCAB bypass, but a three-or-four-vessel procedure often results in significant support required to complete the procedure. Because ischemia is anticipated, monitoring for
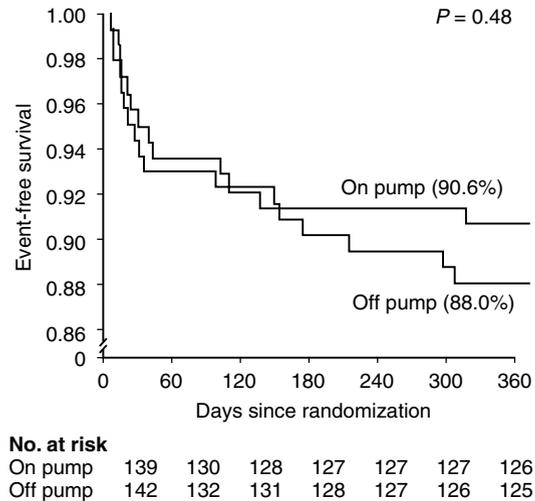
Fig. 4.14 Kaplan–Meier estimates of survival free from stroke, myocardial infarction, and repeated coronary revascularization. $P = 0.48$ by log-rank test. Results from a multicenter, randomized evaluating off pump coronary artery bypass grafting to traditional on-pump coronary artery bypass grafting. In this investigation, 139 patients with single or double vessel coronary disease were randomly assigned to on-pump surgery and 142 patients to off-pump surgery. At 1 year, the rate of freedom from death, stroke, myocardial infarction and coronary reintervention was 90.6% after on-pump surgery and 88.0% after off-pump surgery (absolute difference, 2.6%; 95% confidence interval, $-4.6 - 9.8$). The graft patency was similar between groups. On-pump surgery was associated with $1839 in additional direct costs per patient compared to off-pump surgery. (From Nathoe HM, van Dijk D, Jansen EW *et al*. A comparison of on-pump and off-pump coronary bypass surgery in low risk patients. *N Engl J Med* 2003;**348**:394–402, with permission.)

significant ischemia is essential. During the occlusion and anastomoses, the anesthesiologist should monitor the appropriate ECG leads highlighting the target area, the TEE for new RWMA, continuous CO, and mixed venous oxygen saturation. It is important to note that OPCAB procedures require extensive positioning of the heart, and this positioning changes the observed monitoring (especially TEE windows); nonetheless, following trends will allow the clinician opportunity to intervene when appropriate in these complex procedures.

OPCAB procedures are associated with hemodynamic instability. These hemodynamic changes

may be secondary to the ischemic episodes as well as the positioning requirements of the heart and resultant preload alterations. In general, maintaining systemic BP (and, hence, CPP) is essential. Techniques to maintain BP include adequate volume loading prior to ischemia, Trendelenburg position, norepinephrine or phenylephrine infusions, and atrial pacing if bradycardia occurs. Placement of a coronary stent allows blood flow during much of the anastomoses and is helpful in reducing ischemic time. Occasionally, the patient may require inotropic support during the OPCAB procedure. In some patients, ischemic mitral regurgitation develops of worsens with heart manipulation, positioning and ischemia. In addition to the steps outlined above to support the systemic BP, milrinone may be effective in this circumstance. Obviously, the quicker the operative procedure and the less time the heart is ischemic, the better the patient will tolerate the procedure. One last caution involves the occurrence of sudden, significant dysrhythmias during OPCAB. Occasionally, upon reperfusion, the heart may respond with multifocal premature contractions, ventricular tachycardia, or even ventricular fibrillation. Awareness of this potential and prompt intervention for fibrillation is essential. In most cases, the ventricular dysrhythmias are self-limiting.

There are many potential methods to reduce the impact of the obligate ischemic insult. Maintaining a normal acid-base balance and electrolyte profile are important. In addition, pharmacologic interventions may include nitroglycerin infusion, magnesium supplementation, use of calcium antagonists (with the anticipated ischemic-reperfusion injury and possible calcium overload), tight glucose control, and choice of anesthetic and ischemic preconditioning.

Ischemic preconditioning and anesthetic preconditioning

Ischemic preconditioning is process whereby short, transient periods of tissue ischemia render the tissue resistant to subsequent usually lethal periods of ischemia. This process exists in many organ systems in the body including the heart, kidneys, lungs, brain and spinal cord. In the myocardium, ischemia results in an immediate reduction in contractile effort, with cellular death ensuing after approximately 15 minutes. If the ischemic episode is preceded by one or more sub-lethal ischemic episodes, the myocardium is altered in such a way as to limit tissue injury and prolong the interval of ischemic tolerance. In experimental models, infarct size is measured with and without ischemic preconditioning. With ischemic preconditioning, the infarct size is approximately 25% smaller. This protective benefit is seen immediately after the preconditioning event, and again at 24 hours (a "second window" of protection). There are several proposed mechanisms for both acute and late preconditioning. In the acute phase, the preconditioning involves an alteration of the K_{atp} channel. Late protection involves heat shock protein synthesis.

Several pharmacologic agents can induce ischemic preconditioning like effects. Recent work suggests that some anesthetic agents may possess pharmacologic ischemic preconditioning properties. Anesthetic preconditioning (APC) is defined as the administration of a volatile anesthetic before the period of myocardial ischemia. In animal studies, contractility is preserved and infarct size is reduced approximately 40%. The mechanism of the APC effect is likely multifactorial and includes preservation of adenosine triphosphate (ATP) and high energy phosphates, decreased polymorphonuclear neutrophil (PMN) adhesion during reperfusion, reduced calcium loading and alteration of the K_{atp} channel (Fig. 4.15).

There are compelling animal data in multiple studies affirming the anesthetic preconditioning effects of the volatile anesthetics. In clinical practice, the data remains indirect and there is currently no clear translated therapeutic approach utilizing APC. Anesthetic preconditioning is difficult to demonstrate clinically because of the complicated patient scenario, the hemodynamic alterations during surgery, and the uncontrolled mix of anesthetic, analgesics and vasoactive medications used during surgery. *In vitro*, isoflurane, sevoflurane, and desflurane all enhance muscle recovery in atrial tissue after an ischemic-reperfusion event. Isoflurane immediately before aortic cross-clamping in patients undergoing CABG decreases the troponin I and creatine kinase-MB release postoperatively. There is reduced ST segment
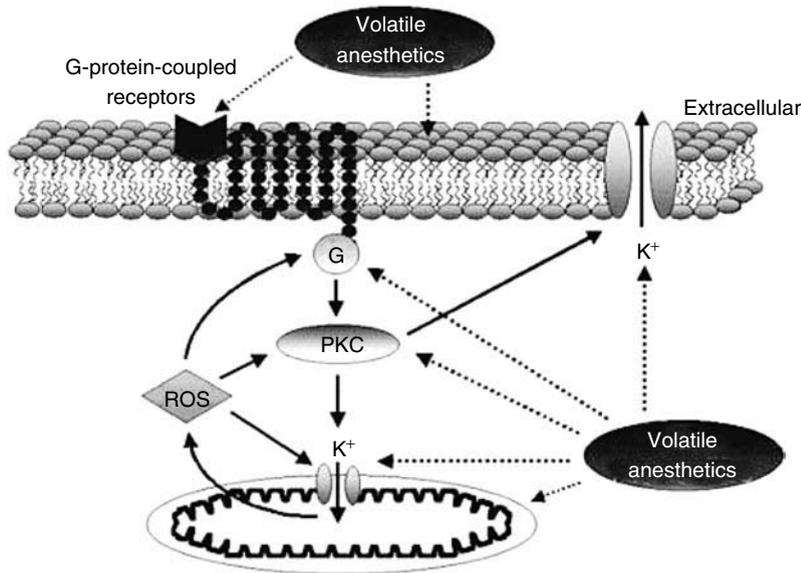
Fig. 4.15 Multiple endogenous signaling pathways mediate volatile anesthetic-induced myocardial protection. A trigger initiates a cascade of signal transduction events, resulting in the activation of an end-effector that promotes resistance against ischemic injury. Mitochondrial adenosine triphosphate-sensitive potassium (K_{ATP}) channels have been implicated as the end-effector in this protective scheme, but sarcolemmal K_{ATP} channels may also play a role. Volatile anesthetics signal through adenosine and opioid receptors, modulate G proteins, stimulate protein kinase C (PKC) and other intracellular kinases, or have direct effects on mitochondria to generate reactive oxygen species (ROS) that ultimately enhance K_{ATP} channel activity. Volatile anesthetics may also directly facilitate K_{ATP} channel opening. *Dashed arrows* delineate the intracellular targets that may be regulated by volatile anesthetics; *solid arrows* represent potential signaling cascades. (From Tanaka K, Ludwig LM, Kersten JR *et al*. Mechanisms of cardioprotection by volatile anesthetics. *Anesthesiology* 2004;**100**:707–21, with permission.)

changes and preservation of cardiac index compared to inpatients who did not receive pretreatment with a volatile anesthetic. In off-pump CABG, patients randomized to sevoflurane had less troponin I release compared to those randomized to propofol.

In summary, ischemic preconditioning and anesthetic preconditioning are new and exciting areas of investigation. The full clinical impact of these physiologic and pharmacologic mechanisms remains to be determined.

Intrathecal and epidural anesthesia and analgesia for cardiac surgery

Pain after cardiac surgery may be severe and limit patient recovery. Traditionally, pain treatment is with IV opioids; however, there is recent interest in advanced techniques of pain control including intrathecal and epidural analgesia. In the acute setting, pain is largely surgical in origin; persistent pain may be due to tissue destruction, intercostal nerve trauma, rib fractures, wound infection, the sternal wires, or nonunion of the sternum. The techniques for postoperative analgesia are many including local anesthetic infiltration, nerve blocks, opioids, nonsteroidal anti-inflammatory agents, α-adrenergic drugs, and intrathecal and epidural techniques. Each technique has unique advantages and disadvantages.

Intrathecal analgesia has been widely investigated since the 1980s. Intrathecal opioids (morphine, fentanyl, sufentanil) reliably extend the duration of analgesia without significant impact on extubation times. The addition of clonidine to the opioid further

enhances the opioid effect. Some authors have administered hyperbaric bupivacaine (20–30 mg), hyperbaric lidocaine (150 mg), or both with morphine to induce a "total spinal" and complete thoracic cardiac sympathectomy. This technique reduces β-receptor dysfunction and lowers the stress response (as measured by circulating epinephrine, norepinephrine and cortisol levels) during CABG surgery. As predicted, the fall in HR and BP in the majority of these patients required pharmacologic intervention. The role of total spinal anesthesia for CABG is controversial and remains undefined at this time. In summary, although safe, intrathecal administration of analgesics reliably produces analgesia, however, there is no additional clinical benefit.

The same is true of epidural analgesia. Multiple clinical reports demonstrate that thoracic epidural analgesia is associated with good pain control, but there is limited benefit beyond this single measure. For both intrathecal and epidural techniques, there is no evidence of improved outcome in mortality or MI.

Both techniques carry risk. Hypotension is common and can be significant. Administration of local anesthetics always carries the risk of IV absorption and myocardial depression. Dense analgesia may mask postoperative myocardial ischemia. Neuroaxial opioids are associated with pruritus, nausea and vomiting, urinary retention, and respiratory depression. Finally, and perhaps most concerning, is the risk of spinal hematoma formation. The incidence of hematoma formation is approximately 1:220 000 for intrathecal instrumentation and 1:150 000 for epidural instrumentation. This risk increases in the cardiac surgical patient because of the systemic heparinization; however, it is difficult to quantify this risk.

In summary, intrathecal and epidural techniques are practiced in some hospitals with good results. The data affirm reliable analgesia, but there is no improvement in mortality or MI. Other parameters, such as dysrhythmias, respiratory failure and early extubation may be improved with regional techniques (Table 4.3). There remains significant controversy regarding the role of these techniques in adult cardiac surgical practice.

Glucose management during coronary artery bypass surgery

Recent data suggest that tight perioperative control of blood glucose in diabetic patients improves outcome after cardiac surgery (Fig. 4.16). Hyperglycemia has several adverse effects on the heart after an ischemic-reperfusion injury. In animal models, blood glucose correlates with infarct size and the beneficial effects of ischemic preconditioning are abolished with hyperglycemia. Further, hyperglycemia reduces coronary collateral blood flow through a nitric-oxide-mediated mechanism. Effective treatment with insulin during the perioperative period is enhanced with a continuous infusion of insulin as compared to intermittent bolus insulin. Most agree that maintaining a glucose level < 200 mg/dL is appropriate. Some evidence suggests that insulin therapy should be initiated when the glucose level is > 110–150 mg/dL.

Emergency coronary artery bypass surgery

Anesthesia for emergency coronary artery bypass surgery provides some unique challenges. These patients typically are those suffering from complications of cardiac catheterization or of catheter-based interventional techniques to treat coronary stenosis. Patients presenting with failed coronary angioplasty procedures fall into three categories:

1 Hemodynamically stable, nonischemic patients. Some of these patients will have sustained no endothelial damage and can be managed as elective coronary revascularization patients. Some patients will have sustained endothelial damage and are at risk for subsequent thrombus formation and vessel closure. These patients may require surgical revascularization but can afford to wait several hours. This is time enough to complete a comprehensive anesthetic evaluation and to allow further gastric emptying if necessary.

2 Hemodynamically stable, ischemic patients. These patients require urgent revascularization. The ischemic interval should be limited to < 3 hours to avoid infarction. An intra-aortic balloon pump may be in place to temporize this condition. Anesthetic evaluation should be concise and focused. Communication with the cardiologist is essential to

Table 4.3 Outcomes for thoracic epidural analgesia (TEA) and intrathecal analgesia (IT) versus general anesthesia (GA) for cardiac surgery. A meta-analysis of 15 trials enrolling 1178 patients having neuroaxial analgesia after cardiac surgery demonstrates no differences in the rates of mortality or myocardial infarction after coronary artery bypass grafting with central neuroaxial analgesia. There were associated improvements in faster time until tracheal extubation, decreased pulmonary complications and cardiac dysrhythmias in reduced pain scores. The majority of these benefits, however, may be reduced or eliminated with changing cardiac practice using fast track techniques, use of beta-blocking agents, amiodarone, or nonsteroidal anti-inflammatory drugs for postoperative analgesia. (From Liu SS, Block BM, Wu CL. Effects of perioperative central neuraxial analgesia on outcome after coronary artery bypass surgery. *Anesthesiology* 2004;**101**:155–61.)

Outcome	No.	TEA	GA	OR or WMD (95% confidence interval)	*P*-value
Death	1178	0.7%	0.3%	1.56 (0.35–6.91)	0.56
Myocardial infarction	1026	2.3%	3.4%	0.74 (0.34–1.59)	0.44
Dysryhthmias	913	17.8%	30%	0.52 (0.29–0.93)	0.03
Pulmonary complications	644	17.2%	30.3%	0.41 (0.27–0.60)	<0.00001
Time to tracheal extubation (h)	905	6.9*	10.4*	−4.5 (−7 to −2)	0.0005
VAS pain score at rest (mm)	392	12.4*	19.6*	−7.8 (−15 to −0.6)	0.03
VAS pain score with activity (mm)	222	14*	27.6*	−11.6 (−19.7 to −3.5)	0.005
Death	668	0.3%	0.6%	0.88 (0.13–5.72)	0.89
Myocardial infarction	290	3.9%	5.7%	0.75 (0.24–2.31)	0.61
Dysryhthmias	204	24.8%	29.1%	0.81 (0.42–1.53)	0.51
Time to tracheal extubation (h)	588	10.4*	10.9*	−0.85 (−1.83 to 0.12)	0.09
Time to tracheal extubation for small-dose IT (h)	189	7.1*	9.3*	−1.2 (−1.8 to −0.7)	<0.0001
Morphine use per day (mg)	816	14*	22*	−11 (−15 to −7)	<0.00001
VAS pain score (mm)	315	13.4*	23.4*	−16 (−27 to −4.9)	0.005
Pruritus	506	10.1%	2.5%	2.9 (1.2–6.7)	0.01
Nausea/vomiting	490	31.3%	28.5%	1.27 (0.81–2.0)	0.3

Random effects model used for all analyses.

∗Weighted by number of subjects.

GA, general anesthesia; IT, intrathecal analgesia; OR, odds ratio; TEA, thoracic epidural analgesia; VAS, visual analog scale; WMD, weighted mean difference (inverse variance method).

determine the extent of jeopardized myocardium, current vasoactive agents, anticoagulation methods (heparin, streptokinase, tissue plasminogen activator (tPA), clopidogrel, and abciximab), NPO status, current laboratory values, and vascular access. The arterial access used for the catheterization procedure (femoral artery) should be left in place and used for monitoring in the operating room. Femoral vein sheaths can be used for venous access. A PAC is commonly placed via the femoral vein and can be used as well. Induction can be accomplished easily and safely using the high-dose narcotic technique described previously. For patients deemed at high risk for aspiration, a nonparticulate antacid and metoclopramide 10–20 mg IV can be administered. A rapid sequence induction can be accomplished with etomidate 0.15–0.30 mg/kg and succinylcholine 1.0–1.5 mg/kg, in conjunction with fentanyl (10 μg/kg) or sufentanil (1 μg/kg). Etomidate produces minimal cardiovascular effects at this dosage when administered in conjunction with narcotics. Alternatively, sufentanil 5 μg/kg and succinylcholine 1.0–1.5 mg/kg can be used in a rapid-sequence technique. Hypotension and ischemia must be aggressively treated. After induction, placement of additional intravascular catheters can be
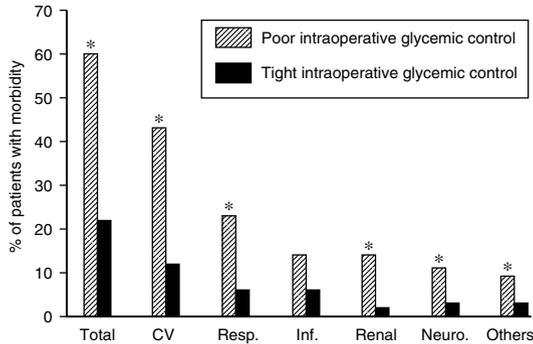
Fig. 4.16 Incidence of severe in-hospital morbidity between patients in whom intraoperative glycemic control was poor or tight. Two hundred consecutive diabetic patients undergoing on-pump heart surgery were enrolled. A standard insulin protocol based on subcutaneous intermediary insulin was given the morning of the surgery. Intravenous insulin therapy was initiated intraoperatively from blood glucose concentrations of 180 mg/dL or greater and titrated according to a predefined protocol. Poor intraoperative glycemic control was defined as four consecutive blood glucose concentrations >200 mg/dL without any decrease in despite insulin therapy. Postoperative blood glucose concentrations were maintained below 140 mg/dL by using aggressive insulin therapy. The main endpoints were severe cardiovascular, respiratory, infectious, neurologic, and renal in-hospital morbidity. Insulin therapy was required intraoperatively in 36% of patients, and poor intraoperative glycemic control was observed in 18% of patients. Poor intraoperative glycemic control was significantly more frequent in patients with severe postoperative morbidity (37 vs. 10%; $P < 0.001$). The adjusted odds ratio for severe postoperative morbidity among patients with a poor intraoperative glycemic control as compared with patients without was 7.2 (95% confidence interval, 2.7–19.0). CV, cardiovascular morbidity; Inf., infectious morbidity; Neuro., neurologic morbidity; Resp., respiratory morbidity (see text for definitions of different morbidities). *$P < 0.05$ vs. tight control. (From Ouattara A, Lecomte P, Le Manach Y et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology* 2005;**103**:677–94, with permission.)

accomplished in parallel with the surgical preparation. In particular, a PAC can be placed via the right internal jugular vein. This substantially improves the ability to manipulate and position the PAC and to infuse vasoactive agents at a proximal site.

The femoral vein PAC often is not in a sterile sheath and is distant from the head of the bed. If peripheral venous access is poor, a large-bore double lumen (16- or 14-gauge) central venous line can be placed at the same time as the PAC. Because these patients usually are anticoagulated with at least heparin, placement of these catheters using ultrasonic guidance should be considered.

3 Hemodynamically unstable, ischemic patients. These patients require emergent revascularization. Evaluation must often be performed in the hallway on the way to the operating room. Communication with the cardiac catheterization team is essential. Some of these patients are mildly hypotensive, requiring minimal cardiovascular pharmacologic support; whereas, others may be intubated and receiving cardiopulmonary resuscitation (CPR). The goal is to establish CPB as expeditiously as possible. Vascular access for monitoring and volume infusion can be obtained on the surgical field if necessary. All existing intravascular access should be used. For more stable patients, the induction techniques described above are applicable. For patients receiving CPR, scopolamine 0.005 mg/kg or midazolam 0.05–0.1 mg/kg in conjunction with a nondepolarizing muscle relaxant may be all that is necessary. Although the in-hospital mortality is high (approximately 50%), there are good data demonstrating a benefit to emergency surgical intervention (surgery or angioplasty) versus initial medical stabilization in patients presenting in cardiogenic shock after a MI (Fig. 4.17).

Post-CPB management

The assumption that coronary revascularization will produce a patient with normal myocardial function after CPB is erroneous. Immediate improvements in LV systolic and diastolic function may occur within the first 10 minutes after termination of CPB; however, many patients require inotropic and vasoactive support. There may be depression of both RV and LV systolic function (reduced EF, LV stroke work index (SWI), cardiac index (CI)) with the nadir occurring approximately 4 hours after termination of CPB.

Coronary revascularization may be less than complete for technical reasons, such as occurs with
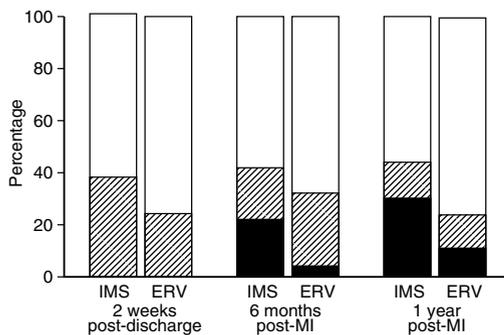
Fig. 4.17 Outcome of 126 SHOCK trial hospital survivors with at least one interview, 69 assigned to the emergency revascularization (ERV) group and 57 assigned to the initial medical stabilization (IMS) group. There were significant differences between treatment groups at 6 months ($P = 0.035$) and 1 year ($P = 0.014$). *White bars* = New York Heart Association (NYHA) functional class I/II; *ruled bars* = NYHA functional class III/IV; *black bars* = deceased. MI, myocardial infarction. (From Sleeper LA, Ramanathan K, Picard MH *et al*. Functional status and quality of life after emergency revascularization for cardiogenic shock complicating acute myocardial infarction. *J Am Coll Cardiol* 2005;**46**:266–73, with permission.)

small distal vessels. Communication with the surgeon is necessary to determine the success of the operative procedure. The sense of security that accompanies a "successful" operative procedure must be tempered with the knowledge that a significant number of patients (35–50%) continue to have evidence of myocardial ischemia in the post-bypass period after apparently successful revascularization. Most episodes occur in the immediate (0–8 hours) postoperative period. The development of post-CPB RWMA and the development of ECG-detected ischemia in the immediate postoperative period are both associated with adverse clinical outcome.

There may be alterations in the vascular tone of the native coronary circulation during the post-CPB period. Coronary vasospasm may occur distal to bypass grafts or in segments of artery that have not been bypassed. This usually is heralded by the presence of elevated ST segments in the absence of a precipitating hemodynamic event. Spasm is effectively treated with IV nitroglycerin.

Vasoactive substances used during the post-CPB period may affect flow through the IMA and saphenous vein grafts. In humans, infusion of epinephrine to increase systemic BP during the post-CPB period increases IMA graft flow, norepinephrine infusion does not change IMA graft flow, and phenylephrine infusion reduces IMA graft flow. Some animal models suggest that such changes are due to the effects of vasoactive substances on IMA vascular tone, whereas others implicate changes in systemic BP. In humans, vasopressor associated increases in systemic BP are accompanied by increases in saphenous vein graft flows. Additional work is required to determine more precisely how changes in graft vascular resistance, systemic BP, and myocardial oxygen consumption contribute to these flow variations. Nonetheless, it should be kept in mind that the choice of vasopressor may affect flow through engrafted arteries and veins.

Inadequate myocardial protection during the procedure will adversely affect LV systolic function. This is particularly likely if the patient has suffered a preoperative ischemic event or has poor preoperative ventricular function. In these patients, optimization of preload and HR are necessary first steps in obtaining hemodynamic stability. Patients with compromised systolic function are often dependent on HR for increases in CO. In addition, patients with reduced ventricular compliance and distensibility will be dependent on atrial systole to provide an adequate LVEDV without a high mean PCWP. For these reasons, pacing of the atrium (with intrinsic conduction via the atrioventricular (AV node) or of the atrium and ventricle (when AV nodal dysfunction exists) may be necessary.

Attention to the metabolic condition of the patient is required in the postoperative period. These patients often require electrolyte supplementation (potassium and magnesium), as well as strict ventilatory management to control acid-base balance in the immediate hours after CABG. There are significant issues regarding continued thermal regulation, coagulation and glycemic control. There is a growing body of research in the area of strict glycemic control. Several authors have published data suggesting that tight control of glucose (110–150 mg/dL) is associated with superior outcome in both critically ill patients and those

after CABG. A regular insulin infusion (2–8 units/h) is indicated when the glucose is >150 mg/dL.

Optimization of preload after termination of CPB requires careful attention and is facilitated by use of TEE and the PCWP and CVP. Preload reserve (preload recruitable stroke work) can be assessed by infusion of blood from the CPB circuit in increments of 10–15 mL/kg ("give a hundred"). One of three distinct hemodynamic responses will be observed:

• *Intact preload reserve*. Infusion of volume produces an increase in MAP with little or no change in PCWP or CVP. TEE demonstrates normal LV and RV chamber volume. CO increases. For this subset of patients, further infusion of volume to improve hemodynamics is warranted.

• *Optimized preload*. Infusion of volume produces little or no change in MAP with no change or a small increase in PCWP or CVP. TEE demonstrates a LV or RV at the upper limits of size for the particular patient. Obviously, pre-CPB assessment of LV and RV dimensions is necessary to take full advantage of this modality. CO may increase slightly or remain unchanged. For this subset of patients, no further infusion of volume to improve hemodynamics is warranted.

• *Exhausted preload reserve*. Infusion of volume will produce no change or a fall in MAP with a substantial increase in PCWP or CVP. TEE will demonstrate a distended LV or RV. CO may decrease slightly or should remain unchanged. For this subset of patients, no further infusion of volume to improve hemodynamics is warranted. Initiation of inotropic support will improve hemodynamics and reduce ventricular dimensions.

Several risk factors are associated with an increased incidence of inotropic agent use after CPB. Factors related to inotrope use include low EF <55%, older age, cardiac enlargement, female sex, and higher baseline and post-contrast LVEDP. For patients with an EF >55%, the presence of preoperative wall motion abnormalities and an increase of >10 mmHg in LVEDP with contrast injection is associated with the need for inotropes. In addition, for patients with an EF > 45%, prolonged duration of CPB is associated with the need for inotropes.

The most commonly used inotropic agents are described below. Use of inotropic agents post-CPB should be used with the knowledge that both adults and children exhibit uncoupling of β-adrenoceptors from the G_S-protein-adenylate cyclase complex after CPB. This desensitization may contribute to a relative catecholamine resistance in the post-CPB period.

Dopamine

Dopamine possesses β_1-adrenergic, α_1-adrenergic, and dopaminergic activities. Some of the α activity is due to release of endogenous norepinephrine. At doses of 2–3 μg/kg/min, the dopaminergic activity is maximal, resulting in preferential dilation of renal, mesenteric, and coronary vasculature. Alpha-agonists do not antagonize this dopaminergic activity. This makes dopamine a useful agent for preservation of renal blood flow in the presence of α-agonists. β_1-Induced enhanced inotropy occurs at doses between 1 and 10 μg/kg/min; however, at doses above 4–6 μg/kg/min dopamine's α-adrenergic activity increases such that SVR, PVR, and PCWP increase with little concomitant increase in CO. This combination of increased ventricular wall radius and afterload may cause detrimental increases in myocardial oxygen consumption. At doses >10 μg/kg/min, the α-adrenergic effects of dopamine predominate, producing vasoconstriction. Dopamine's chronotropic and dysrhythmic effects increase as the dose increases.

Dobutamine

Dobutamine possesses β_1-, β_2-, and α_1-adrenergic activities. The predominant effect is enhanced inotropy through β_1 stimulation. The β_2 and α_1 activities are balanced such that mild vasodilation occurs at the commonly used doses from 5–20 μg/kg/min. Dobutamine decreases PVR, blunts hypoxic pulmonary vasoconstriction, and increases coronary blood flow. Dobutamine may actually reduce myocardial oxygen consumption in the failing heart. Although dobutamine increases contractility, it reduces LV radius and end-diastolic pressure while increasing arterial pressure and maintaining HR. Dobutamine is less likely to cause tachycardia than dopamine.

Epinephrine

Epinephrine possesses β_1-, β_2-, and α_1-adrenergic activities. At doses of 1–$3\,\mu g/min$, epinephrine has a potent inotropic effect mediated through β_1 stimulation, with little effect on vasomotor tone due to the balance of β_2 and α_1 stimulation. As the dose increases above $3\,\mu g/min$, progressively more α_1 activity occurs, with resultant mixed inotropic and vasoconstrictive effects. Doses above $3\,\mu g/min$ also cause progressive decreases in renal blood flow. Above $10\,\mu g/min$, epinephrine is primarily a vasoconstrictor. Epinephrine's vasoconstrictive effects also reduce venous capacitance. Although coronary blood flow is maintained, epinephrine may not be favorable to myocardial oxygen balance, because in addition to increasing contractility, it increases systolic BP, increases LVEDV and pressure, and reduces diastolic BP while increasing HR.

Epinephrine is often the agent of choice to terminate CPB. The potent inotropic and balanced peripheral vascular effects allow prompt, reliable termination of CPB while avoiding the ventricular distension and systemic hypotension that compromise subendocardial perfusion. Critics point out that the potent inotropic effects of epinephrine may not be necessary in every instance, and thus, epinephrine's potentially deleterious effects on the myocardial and renal blood flow can be avoided if another agent is selected.

Norepinephrine

Norepinephrine possesses β_1- and α_1-adrenergic activity. The α_1 effects of norepinephrine are manifest at low doses (1–$2\,\mu g/min$) and predominate as the dose increases. Norepinephrine reduces renal blood flow, elevates both systolic and diastolic BP, reduces venous capacitance, and generally causes a reflex decrease in HR. Although coronary blood flow is maintained, norepinephrine may not be favorable to myocardial oxygen consumption, because there is increased contractility and afterload.

Milrinone

Milrinone is a potent inotropic agent that acts by inhibiting phosphodiesterase III (PDE III) to increase intracellular cyclic adenosine monophosphate (cAMP). In addition, milrinone possesses vasodilator activity by virtue of PDE III inhibition in vascular smooth musc1e. Milrinone increases cardiac index, reduces LVEDP and LVEDV, reduces systolic BP, and has little effect on HR. Like dobutamine in the failing heart, this increase in cardiac index may be associated with a decrease in myocardial oxygen consumption due to the concomitant reduction in wall stress. Milrinone reduces PVR.

Milrinone does not act via β_1-receptors, and is synergistic with β_1-agents in augmenting inotropy. Evidence demonstrates that PDE III inhibitors are at least as effective as epinephrine in improving post-CPB function and that the combination of the two agents produces effects at least as large as the sum of the two agents individually. The benefit of the two agents together is particularly marked for the RV.

Milrinone requires a $50\,\mu g/kg$ loading dose followed by an infusion of 0.375–$0.500\,\mu g/kg/min$. Loading milrinone while on CPB just before termination attenuates the effects of the acute vasodilation.

Levosimendan

The catecholamines and PDE III inhibiting drugs act through different pathways to increase inotropy by ultimately increasing intracellular calcium concentration (Fig. 4.18). Levosimendan is a new inotropic agent that acts without increasing intracellular calcium concentration. There is increased inotropy without impairment of diastolic function. Levosimendan is a myofilament calcium sensitizer that increases myocardial contractility by stabilizing the calcium bound conformation of troponin C. The systolic interaction of actin and myosin is prolonged. The enhanced calcium binding is dependent on the intracellular calcium concentration, with augmentation occurring in the presence of higher systolic calcium concentrations; however, the augmentation is unaffected by the lower calcium concentrations during diastole. This selective action preserves diastolic relaxation and diastolic function. In addition to the inotropic effects, levosimendan inhibits PDE III in higher concentrations. The drug causes vasodilation and an increase in HR. Finally, levosimendan stimulates ATP-sensitive potassium
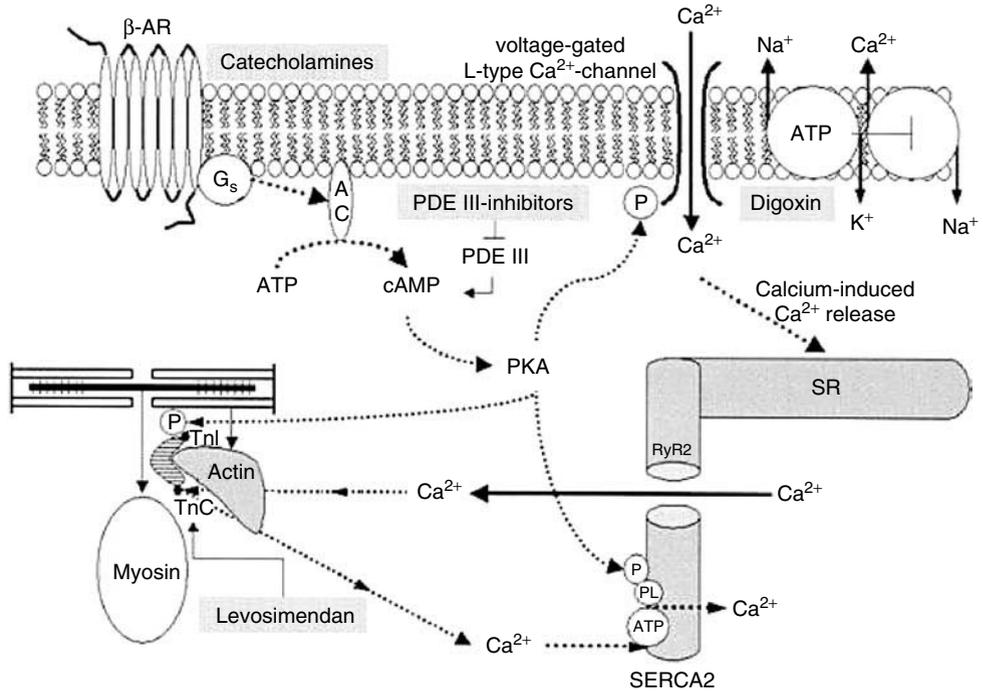
Fig. 4.18 Schematic illustration mechanism of action of positive inotropic drugs. β-adrenergic stimulation (catecholamines) and phosphodiesterase (PDE) III inhibition increase cyclic adenosine monophosphate (cAMP), which acts *via* protein kinase A (PKA) to phosphorylate calcium channel protein, phospholamban (PL), and troponin I (TnI). Phosphorylation (P) of calcium channel protein enhances sarcolemmal inward movement of Ca^{2+}, which subsequently increases Ca^{2+} movement from the sarcoplasmic reticulum (SR) through the calcium release channel (ryanodine receptor type 2, RyR2) to the cytosol (calcium-induced Ca^{2+} release). Digoxin increases cytosolic Ca^{2+} by inhibition of sarcolemmal Na^+–K^+–adenosine triphosphatase and Na^+–Ca^{2+} exchange. Cytosolic Ca^{2+} binds to troponin C (TnC) and initiates contraction (inotropic effect). Phosphorylation of PL enhances relaxation by increased reuptake of Ca^{2+} back into the SR by the SR Ca^{2+} adenosine triphosphatase isoform 2 (SERCA2) (lusitropic effect). Phosphorylation of TnI enhances the rate of relaxation by decreasing the sensitivity of myofilaments to Ca^{2+}. Levosimendan binds to TnC during systole and thereby increases the sensitivity of myofilaments to Ca^{2+} without alteration of Ca^{2+} levels. AC, adenylate cyclase; ATP, adenosine triphosphate; β-AR, β-adrenoceptor; G_s, stimulatory guanine nucleotide binding proteins. (From Toller WG, Stranz C. Levosimendan, a new inotropic and vasodilator agent. *Anesthesiology* 2006;**104**:556–69, with permission.)

channels, which improves coronary blood flow, reduces preload and afterload, and may have relevant anti-ischemic actions.

At the time of this writing, levosimendan is approved for use in over 30 countries world-wide, and there are ongoing trials in the United States and Europe. Indications for the drug include treatment for the acute decompensation of CHF, inotropic support during myocardial ischemia, cardiogenic shock, and use in the perioperative period in cardiac surgical patients. Currently the drug is approved for 24-hour administration due to its metabolism yielding biologically active metabolites (OR-1896, a weak calcium sensitizing agent and PDE III inhibitor with an elimination half life of 96 hours). In placebo-controlled trials of cardiac surgical patients, levosimendan effectively increased HR, MAP, and CO. There were decreases in SVR, SV, and PVR.

Levosimendan was administered in either an 18 or 36 μg/kg bolus and 0.2–0.3 μg/kg/h infusion.

Calcium

Calcium chloride 5–10 mg/kg is a commonly used adjuvant during termination of CPB. Recent evidence, however, suggests that calcium administration may be no better than placebo in augmenting LV function, RV function, and CI after emergence from CPB. Calcium administration does increase MAP, however.

The higher doses of calcium (10 mg/kg) can attenuate the effects of inotropic agents that are β-adrenergic receptor agonists, such as dobutamine and epinephrine. No such effects are seen with milrinone. A recent investigation suggests that entry of calcium ions through calcium channels attenuates adenylyl cyclase, which may explain the observation.

Ionized calcium levels decrease during CPB but approach normal before separation from CPB. Hypocalcemia is rarely present as an indication for calcium administration, except perhaps in neonates and infants, who are more prone to hypocalcemia. In addition, because loss of calcium homeostasis is one of the hallmarks of ischemia, the administration of calcium in the vulnerable reperfusion interval after aortic cross-clamp removal may exacerbate cell injury and death.

For routine termination of CPB in which SVR is in the normal range and inotropic support is needed, epinephrine, 0.015–0.05 μg/kg/min, dopamine, 1–5 μg/kg/min, or dobutamine, 5–10 μg/kg/min, are reasonable choices because they provide inotropic support with little concomitant vasoconstriction and afterload increase. For situations in which cardiac index is low and SVR is elevated, therapy with a vasodilator such as nitroprusside may be all that is necessary to relieve afterload mismatch. If an inotrope is necessary in this situation, dobutamine is a good choice because it possesses some vasodilatory activity.

When the CI remains low (<2.0 L/min/m^2), it is appropriate to increase the inotrope dose or add a second agent. Dobutamine may be increased to 15–20 μg/kg/min; however, the progressive decrease in SVR may require the addition of a small dose (0.5–1.0 μg/min) of norepinephrine to normalize SVR. As the doses of epinephrine and dopamine are increased, SVR may increase, and the addition of nitroprusside to the inotropic may be necessary to reduce afterload and improve systolic performance. Epinephrine in combination with nitroprusside is a reliable approach to severe ventricular failure. Elevations of PCWP above 15–18 mmHg should be treated with nitroglycerin to prevent ventricular dilatation and pulmonary congestion and to improve subendocardial blood flow.

The addition of milrinone is useful when these measures fail to produce acceptable hemodynamics (CI > 2 L/min/m^2, PCWP < 18 mmHg, CVP < 15 mmHg, systolic BP > 90 mmHg, or MAP > 50 mmHg). More specific guidelines for treatment of RV dysfunction are addressed in Chapter 7. Continued LV and RV dysfunction in the setting of aggressive inotropic and vasodilator support is an indication for placement of a mechanical circulatory assist device, as discussed in Chapter 11.

Long-term outcome after CABG

More than 800 000 patients undergo CABG surgery each year around the world. The patient population is changing (older patients with more significant morbidities), and the pharmacologic and surgical interventions are ever evolving. Nonetheless, CABG remains a mainstay therapy. The long-term adverse events after CABG are many and reflect the morbidities and insult seen in this population. In a recent review of 176 studies (205 717 patients) the in-hospital adverse events were death (1.7%); nonfatal MI (2.4%); nonfatal stroke (1.3%); gastrointestinal bleeding (1.5%); and renal failure (0.8%). The 30-day mortality was 2.1%. Meta-analyses show that age greater than 70 years, female sex, low EF, history of stroke, MI, or heart surgery, and the presence of diabetes or hypertension are all associated with increased 30-day mortality after CABG (Table 4.4).

Longer-term outcome is also a subject of great interest. Recent work in patients with multivessel disease demonstrates that there is no difference in mortality between stenting and surgery (Fig. 4.19). There is no difference in stroke or MI between these

Table 4.4 Post-coronary artery bypass graft surgery (CABG) adverse event incidence and mortality in 205 717 patients.

	In-hospital adverse event incidence							
	MI	Non-fatal MI	Stroke	Non-fatal stroke	GI bleeding	Renal failure	Mortality	30-day mortality
All CABG								
Mean % (SE)	3.89 (0.66)	2.44 (0.28)	2.24 (0.27)	1.32 (0.15)	1.46 (0.29)	0.79 (0.15)	1.65 (0.14)	2.06 (0.16)
Median %	2.94	2.44	1.8	1.29	1.23	0.67	1.54	1.99
n (k)	69 487 (52)	11 973 (52)	26 750 (21)	31 132 (52)	12 897 (8)	22 798 (23)	75 933 (105)	81 136 (70)
North America								
Mean % (SE)	3.56 (0.59)	2.82 (0.58)	2.29 (0.39)	1.25 (0.19)	1.11 (0.14)	0.88 (0.16)	1.96 (0.20)	2.00 (0.19)
Median %	3.30	2.83	1.71	1.06	1.01	0.86	2.00	1.98
n (k)	49 969 (32)	2454 (18)	13 777 (12)	25 555 (28)	7332 (3)	21 410 (14)	59 014 (49)	47 158 (39)
Europe								
Mean % (SE)	2.59 (0.33)	2.55 (0.36)	2.42 (1.18)	1.30 (0.27)	1.33 (0.91)	0.99 (0.74)	1.30 (0.22)	2.21 (0.40)
Median %	2.53	2.52	1.66	0.67	1.66	0.49	1.00	2.08
n (k)	13 418 (15)	8389 (24)	6515 (4)	4256 (13)	220 (2)	625 (5)	12 893 (33)	21 156 (21)
Multinational/other								
Mean % (SE)	9.81 (5.54)	1.94 (0.51)	2.43 (0.22)	1.27 (0.31)	1.93 (0.62)	0.06 (0.16)	1.38 (0.33)	1.72 (0.38)
Median %	3.92	1.66	2.18	1.96	1.32	0.00	1.52	1.61
n (k)	6100 (5)	1130 (10)	6458 (5)	1321 (11)	5345 (3)	763 (4)	4026 (23)	13 240 (10)
Elective CABG								
Mean % (SE)	2.84 (0.81)	2.32 (0.40)	2.35 (0.60)	1.01 (0.21)	1.18 (0.48)	0.45 (0.18)	1.48 (0.19)*	1.50 (0.29)*
Median %	2.17	2.00	1.59	0.64	1.23	0.22	1.00	1.23
n (k)	3313 (17)	3371 (32)	1680 (7)	9170 (24)	510 (2)	1333 (6)	7912 (47)	7764 (21)
Mixed CABG								
Mean % (SE)	4.32 (0.89)	2.64 (0.36)	2.21 (0.31)	1.51 (0.20)	1.50 (0.35)	0.89 (0.18)	1.81 (0.18)*	2.23 (0.19)*
Median %	3.22	2.59	1.86	1.56	1.24	0.89	1.89	2.07
n (k)	66 174 (35)	8602 (20)	25 070 (14)	21 962 (28)	12 387 (6)	21 465 (17)	68 021 (58)	73 372 (49)
RCTs								
Mean % (SE)	6.26 (1.66)*	2.64 (0.42)	2.73 (0.98)	1.00 (0.16)**	1.23 (0.41)	0.39 (0.23)*	1.51 (0.21)*	1.57 (0.28)
Median %	4.21	2.94	1.86	1.78	1.23	0.05	0.98	1.69
n (k)	3449 (22)	2604 (34)	1111 (5)	3790 (19)	730 (4)	2189 (10)	4949 (48)	4913 (23)
Cohort studies								
Mean % (SE)	2.70 (0.22)*	2.21 (0.38)	2.15 (0.27)	1.52 (0.18)**	1.53 (0.40)	0.98 (0.14)*	1.80 (0.18)*	2.21 (0.19)
Median %	2.51	1.75	1.67	0.61	1.24	0.89	1.83	2.03
n (k)	66 038 (30)	9369 (18)	25 639 (16)	27 342 (33)	12 167 (4)	20 609 (13)	70 984 (57)	76 223 (47)

Table 4.4 (*Continued*).

	In-hospital adverse event incidence							
	MI	Non-fatal MI	Stroke	Non-fatal stroke	GI bleeding	Renal failure	Mortality	30-day mortality
Single centre								
Mean % (SE)	2.77 (0.26)**	2.34 (0.28)	2.17 (0.37)	1.29 (0.16)	1.06 (0.23)	0.97 (0.19)	1.47 (0.15)*	1.87 (0.16)*
Median %	2.55	2.37	1.60	1.40	1.16	0.84	1.30	1.83
n (k)	48 655 (40)	11 742 (49)	11 728 (16)	26 977 (47)	1977 (4)	6472 (15)	45 572 (93)	54 218 (54)
Multicentre								
Mean % (SE)	7.87 (2.66)**	6.10 (3.50)	2.43 (0.30)	1.43 (0.41)	1.60 (0.40)	0.62 (0.22)	2.52 (0.26)*	2.68 (0.38)*
Median %	4.04	6.45	2.59	1.18	1.31	0.51	2.63	2.65
n (k)	20 832 (12)	231 (3)	15 022 (5)	4155 (5)	10 920 (4)	16 326 (8)	30 361 (12)	26 918 (16)
Mean EF < 50%								
Mean % (SE)	2.79 (0.92)	1.82 (0.58)	3.81 (3.02)	0.82 (0.48)	1.47 (0.29)	1.09 (0.41)	1.45 (0.38)	1.56 (0.42)
Median %	2.20	1.82	4.03	0.00	1.42	0.89	2.00	1.92
n (k)	4722 (8)	698 (5)	256 (2)	2824 (7)	1697 (1)	2758 (5)	7622 (15)	5338 (9)
Mean EF > 50%								
Mean % (SE)	5.99 (1.85)	2.37 (0.46)	1.69 (0.26)	1.21 (0.24)	1.02 (0.24)	0.48 (0.17)	1.68 (0.25)	1.61 (0.35)
Median %	3.07	2.41	1.67	1.18	1.16	0.49	1.51	1.23
n (k)	22 213 (18)	8100 (18)	10 186 (9)	7973 (15)	1757 (2)	6567 (7)	29 121 (40)	8535 (17)
Mean age ≤ 60yrs								
Mean % (SE)	3.19 (0.94)	2.49 (0.54)	2.75 (0.82)	1.41 (0.42)	N/A	0.00 (2.80)	1.21 (0.27)	1.15 (0.44)**
Median %	2.37	2.68	2.33	0.80	N/A	0.00	1.00	0.78
n (k)	4303 (12)	2540 (13)	1613 (5)	1273 (6)	N/A	25 (1)	5885 (25)	3260 (12)
Mean age > 60 yrs								
Mean % (SE)	4.14 (0.84)	2.44 (0.36)	1.94 (0.23)	1.28 (0.16)	1.46 (0.29)	0.75 (0.16)	1.77 (0.16)	2.26 (0.17)**
Median %	3.18	2.51	1.67	1.45	1.23	0.6	1.59	2.07
n (k)	63 035 (39)	9219 (37)	24 681 (15)	26 524 (44)	12 897 (8)	13 926 (20)	45 921 (76)	74 288 (54)
No prior CABG								
Mean % (SE)	2.73 (0.72)	1.99 (0.46)	1.82 (0.40)	0.99 (0.31)	2.63 (1.84)	1.23 (1.10)	1.18 (0.28)	1.66 (0.35)
Median %	3.33	1.83	1.27	0.66	2.63	1.00	1.00	1.81
n (k)	2606 (11)	2115 (18)	1097 (4)	3240 (10)	76 (1)	270 (4)	27 625 (25)	8390 (14)
Some patients with prior CABG								
Mean % (SE)	6.47 (1.83)	2.57 (0.88)	2.19 (0.34)	1.80 (0.15)	1.53 (0.40)	0.86 (0.22)	1.92 (0.25)	2.27 (0.23)
Median %	3.32	1.86	1.8	1.74	1.24	0.9	2.01	2.52
n (k)	45 306 (18)	6986 (6)	19 252 (12)	17 619 (15)	12 167 (4)	16 263 (9)	32 177 (30)	48 599 (28)

* $P < 0.05$. ** $P < 0.01$.

CABG, coronary artery bypass graft surgery; EF, ejection fraction; GI, gastrointestinal; MI, myocardial infarction; N/A, not available; RCT, randomized controlled trial; SE, standard error. (From Nalysnyk L, Fahrbach K, Reynolds MW *et al.* Adverse events in coronary artery bypass graft (CABG) trials: a systematic review and analysis. *Heart* 2003;**89**:767–72.)
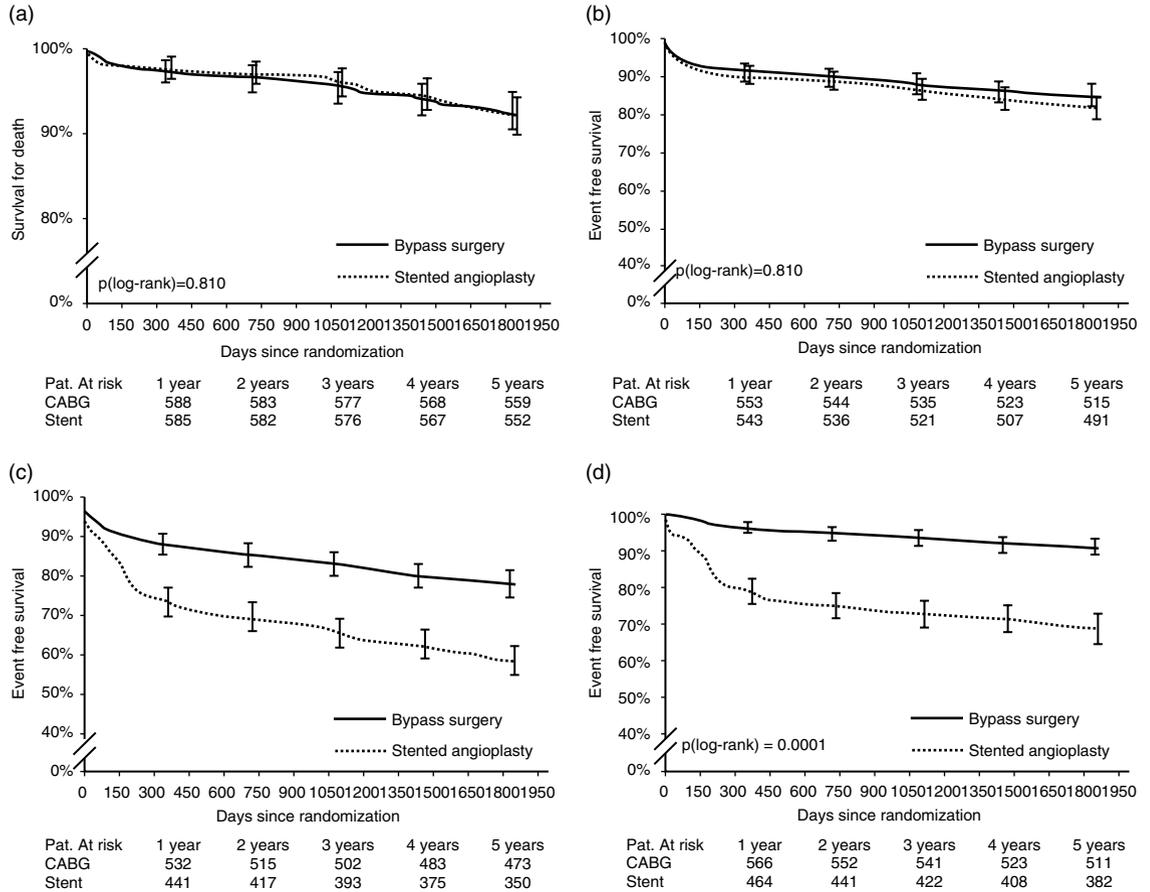
Fig. 4.19 (a) Kaplan–Meier curves showing freedom from death. (b) Kaplan–Meier curves showing freedom from death/cerebrovascular accident/myocardial infarction or revascularization. (c) Kaplan–Meier curves showing freedom from death/cerebrovascular accident/myocardial infarction or revascularization. (d) Kaplan–Meier curves showing freedom from revascularization. A total of 1205 patients with the potential for equivalent revascularization were randomly assigned to coronary artery bypass graft (CABG) surgery ($n = 605$) or stent implantation ($n = 600$). The primary clinical end point was freedom from major adverse cardiac and cerebrovascular events (MACCE) at 1 year; MACCE at 5-year follow-up constituted the final secondary end point. At 5 years, there were 48 and 46 deaths in the stent and CABG groups, respectively (8.0 vs. 7.6%; $P = 0.83$; relative risk (RR), 1.05; 95% confidence interval (CI), 0.71–1.55). Among 208 diabetic

patients, mortality was 13.4% in the stent group and 8.3% in the CABG group ($P = 0.27$; RR, 1.61; 95% CI, 0.71–3.63). Overall freedom from death, stroke, or myocardial infarction was not significantly different between groups (18.2% in the stent group vs. 14.9% in the surgical group; $P = 0.14$; RR, 1.22; 95% CI, 0.95–1.58). The incidence of repeat revascularization was significantly higher in the stent group (30.3%) than in the CABG group (8.8%; $P < 0.001$; RR, 3.46; 95% CI, 2.61–4.60). The composite event-free survival rate was 58.3% in the stent group and 78.2% in the CABG group ($P < 0.0001$; RR, 1.91; 95% CI, 1.60–2.28). (From Serruys PW, Ong AT, van Herwerden LA *et al*. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. *J Am Coll Cardiol* 2005;**46**:575–81, with permission.)

two groups. The stenting group had a significantly higher incidence of repeat revascularization.

Suggested reading

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Groban L, Dolinski SY. Transesophageal echocardiographic evaluation of diastolic function. *Chest* 2005;**128**: 3652–63.

Lan Kwak Y. Reduction of ischemia during off-pump coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2005;**19**:667–77.

Nalysnyk L, Fahrbach K, Reynolds MW *et al.* Adverse events in coronary artery bypass graft (CABG) trials: a systematic review and analysis. *Heart* 2003;**89**:767–72.

Tanaka K, Ludwig LM, Kersten JR *et al.* Mechanisms of cardioprotection by volatile anesthetics. *Anesthesiology* 2004;**100**:707–21.

Van Mastrigt GA, Maessen JG, Heijmans J *et al.* Does fast track treatment lead to a decrease of intensive care unit and hospital length of stay in coronary artery bypass patients? A meta-regression of randomized clinical trials. *Crit Care Med* 2006;**34**:1624–34.

CHAPTER 5

Anesthesia for Valvular Heart Disease

While the number of cardiac procedures for coronary artery bypass grafting (CABG) is falling in the USA, the number operations for heart valve disease is increasing. Over 5 million persons have moderate to severe valvular regurgitation in the USA alone. The aging population, expanding indications for surgery, improvements in valve construction, and improvements in patient morbidity and mortality after surgical intervention all suggest that valve surgery is likely to increase in coming years. This chapter will review anesthesia for patients with a variety of valvular heart conditions. There will be special emphasis on the more common lesions of the aortic and mitral valves.

General considerations

Preoperative evaluation

In valvular heart disease, there are a number of history and physical findings that directly influence anesthetic management. Posting a case as "aortic valve replacement" or "mitral valve replacement" provides no information on whether this is for aortic stenosis (AS), aortic regurgitation (AR), or both; mitral stenosis (MS), mitral regurgitation (MR), or both. The anesthesiologist must dig further and find out the specific valvular pathology. This knowledge is essential in preparing hemodynamic goals for the induction, maintenance, and postoperative care of these patients.

Additional information is required unrelated to the valve pathology. For example, will there be other procedures during this repair (i.e. carotid endarterectomy, CABG, septal myomectomy, a Maze procedure (a series of surgical incisions in the atrium intended to interrupt the circular pattern of electrical activity associated with atrial fibrillation), or other intervention)? What is the clinical condition of the patient? Is the patient in a compensated or uncompensated state? With AS the timing of surgery will have a great impact on outcome depending on the patient's condition. For example, a patient in the early to mid-stages of AS will have a hyperdynamic, hypertrophied heart that will likely perform well after cardiopulmonary bypass (CPB). In contrast, a patient in the late stages of AS will be in congestive heart failure (CHF), have a reduced ejection fraction (EF), and will likely require extensive inotropic support after CPB.

Review of imaging and laboratory studies is essential prior to moving the patient to the operating room. Imaging of the heart will give the diagnosis and degree of the structural abnormality. Preoperative echocardiography will establish the type of lesion (stenotic versus regurgitant), the heart function, and the valve gradients. The valve area is of critical importance in assessing any stenosis. In patients with normal left ventricular (LV) function, aortic valve gradients in severely stenotic lesions may be very high (Fig. 5.1). In patients with poor ventricular performance, there may be anatomically critical lesions (aortic valve area $<0.7\,cm^2$) and a low gradient. These patients are especially prone to
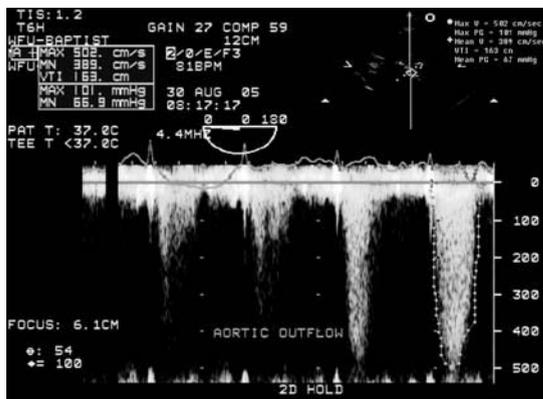
Fig. 5.1 Deep transgastric long-axis transesophageal echocardiographic image in a patient with severe aortic stenosis. The velocity of flow is very high at 5 m/s with a peak gradient of 101 mmHg and a mean gradient of 67 mmHg. This is clearly severe aortic stenosis.

intraoperative instability with the induction of general anesthesia and may require significant inotropic support post-CPB. Other important imaging studies include coronary angiography to rule out concurrent coronary artery disease, a chest radiograph, and perhaps, thoracic computed tomography (CT) or magnetic resonance imaging (MRI) to evaluate thoracic anatomy. A chest X-ray is essential in "redo" operations involving the heart and mediastinum. The heart may be adhered to the posterior margin of the sternum rendering sternotomy quite hazardous. All precautions including adequate venous access, immediate availability of blood products, and intraoperative awareness and vigilance are required in these situations.

Atrial natriuretic peptides are useful markers when following patients with heart failure due to valvular pathology. In severe AS, natriuretic peptides increase with increasing New York Heart Association (NYHA) functional classes and decreasing LV EF. Natriuretic peptide levels fall after successful aortic valve surgery.

Monitoring

Monitoring during valvular surgery varies little from monitoring required during other types of heart surgery. In addition to the American Society of Anesthesiologists (ASA) standard monitors, a urinary Foley catheter, and arterial and central lines are essential. Many institutions routinely use pulmonary artery catheters to monitor cardiac output (CO), mixed venous oxygenation, pulmonary artery pressures, and pulmonary capillary wedge pressures (PCWPs). Although this is standard practice by many clinicians, outcome data supporting pulmonary artery catheterization are lacking.

Intraoperative transesophageal echocardiography (TEE) is rapidly becoming an essential component of anesthesia for all heart valve procedures. Extensive preoperative evaluation by TEE often reveals previously unknown structural or functional defects. In addition, TEE can provide instant assessment of the status of a valve repair procedure. TEE may also diagnose perivalvular leaks after valvular replacement requiring prompt intervention. The assessment of air in the left side of the heart is important after an open-heart procedure. TEE may assist in locating the air thereby facilitating direct venting procedures. TEE is helpful in guiding post-CPB hemodynamic intervention and treatment. In recognition of this tool's utility in cardiac surgical procedures, the American Society of Echocardiography and the American Heart Association provide a class 1 recommendation for TEE use in all heart valve surgical procedures (Table 5.1).

Other special monitoring devices in heart valve surgery may include processed electroencephalogram (EEG) monitoring for either patient awareness or for EEG activity during procedures in which it is desirable that all electrical activity stop (i.e. deep hypothermic circulatory arrest). Cerebral oximetry has no special application in surgery for heart valve disease.

Premedication

Great caution is advised when prescribing premedication in patients with valvular heart disease. In patients with preserved LV function, morphine sulfate 0.1 mg/kg intramuscularly (IM) and oral lorazepam 1.5 hours before scheduled incision time are appropriate. Supplemental oxygen should be instituted at the time of premedication. Reducing dosing, or no premedication at all, is indicated for

Table 5.1 Recommendations for intraoperative echocardiography. (Reprinted from Cheitlin MD, Armstrong WF, Aurigemma GP *et al*. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography–summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *J Am Coll Cardiol* 2003;**42**:954–70.)

Class I

1 Evaluation of acute, persistent, and life-threatening hemodynamic disturbances in which ventricular function and its determinants are uncertain and have not responded to treatment

2 Surgical repair of valvular lesions, hypertrophic obstructive cardiomyopathy, and aortic dissection with possible aortic valve involvement

3 Evaluation of complex valve replacements requiring homografts or coronary re-implantation, such as the Ross procedure

4 Surgical repair of most congenital heart lesions that require cardiopulmonary bypass

5 Surgical intervention for endocarditis when preoperative testing was inadequate or extension to perivalvular tissue is suspected

6 Placement of intracardiac devices and monitoring of their position during port-access and other cardiac surgical interventions

7 Evaluation of pericardial window procedures in patients with posterior or loculated pericardial effusions

Class IIa

1 Surgical procedures in patients at increased risk of myocardial ischemia, myocardial infarction, or hemodynamic disturbances

2 Evaluation of valve replacement, aortic atheromatous disease, the Maze procedure, cardiac aneurysm repair, removal of cardiac tumors, intracardiac thrombectomy, and pulmonary embolectomy

3 Detection of air emboli during cardiotomy, heart-transplant operations, and upright neurosurgical procedures

Class IIb

1 Evaluation of suspected cardiac trauma, repair of acute thoracic aortic dissection without valvular involvement, and anastomotic sites during heart and/or lung transplantation

2 Evaluation of regional myocardial function during and after off-pump coronary artery bypass graft procedures

3 Evaluation of pericardiectomy, pericardial effusions, and pericardial surgery

4 Evaluation of myocardial perfusion, coronary anatomy, or graft patency

5 Dobutamine stress testing to detect inducible demand ischemia or to predict functional changes after myocardial revascularization

6 Assessment of residual duct flow after interruption of patent ductus arteriosus

Class III

1 Surgical repair of uncomplicated secundum atrial septal defect

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elderly or debilitated patients, patients with poor ventricular function, or patients with poor pulmonary function. Most prudently, premedication can wait until the patient arrives in the preoperative holding area. At this time, the anesthesiologist may administer intravenous (IV) midazolam and/or fentanyl while directly observing and monitoring the patient.

All cardiac medications may be continued until the time of surgery. There is debate on holding angiotensin converting enzyme inhibitors (ACE-I) prior to surgery. These medications are associated with significant hypotension during and after CPB in some patients. Data on the harmful effects of withholding ACE-I medications are undetermined. Consultation with the cardiologist and surgeon is required before stopping any antiplatelet agents prior to surgery. In many centers, patients with stable symptoms will wait 3–5 days after stopping clopidogrel. It is common for patients with valvular heart disease to present with atrial fibrillation or a mechanical valve, and thus require anticoagulation.

Coordination regarding the administration of these medications during the perioperative period is essential.

Induction and maintenance of anesthesia

No specific agents or techniques are indicated for either induction or maintenance of anesthesia in any specific valvular condition. Rather, adherence to preset hemodynamic goals will provide appropriate guidance when choosing anesthetic agents. There are a number of ways to achieve these goals safely in the patient presenting for valve surgery.

Patient awareness during cardiac surgical procedures requires special attention. Awareness occurs in approximately 0.13% of surgical patients. Multivariate logistic regression identified increasing ASA status, and type of procedure as risk factors for recall. For cardiac surgical procedures, the odds ratio for recall is 3.58 with a 95% confidence interval of 0.72–17.9. As with any procedure, attention to hemodynamic signs, depth of anesthesia, the use of benzodiazepines, and inhalational agents will likely reduce the risk of operative recall.

There are good data to support the concept of "fast-track" or early extubation protocols in the care of patients presenting for CABG surgery. These benefits include reduced hospital stay, intensive care unit stay, and reduced cost of care. Data on early extubation protocols in valve surgery are less common, although one might expect similar benefit as observed in CABG surgery. One should be aware, however, that many valvular procedures are complex in nature, requiring extended CPB time, potential deep hypothermic circulatory arrest, and increased requirements for blood and blood product transfusion. All of these factors may limit the opportunity for early extubation.

There are limited reports of regional anesthesia for valvular heart surgery. Most reports provide data on combined general anesthesia and thoracic epidural anesthesia. When applied, upwards of 65% of these patients may be extubated in the operating room. Typically, an epidural catheter is placed at T1–3 on the day of surgery. A rigid anticoagulation protocol must be followed both before and after surgery. There are case reports of aortic valve replacement in conscious patients under regional anesthesia without intubation. Given the significant issues with anticoagulation, it is unlikely that regional anesthesia will replace traditional general anesthesia for valvular surgery.

Weaning from bypass and the post-bypass period

Repairing or replacing the valve may fundamentally change the hemodynamic goals of the patient from the pre-bypass period. A normal valvular profile may be observed immediately after CPB (Fig. 5.2). The anticipation is that the heart will now perform normally; however, that does not necessarily follow. The heart suffers an acute insult with the surgical intervention, aortic cross-clamping, and the myocardial depressant effects of the various anesthetic agents. As with any cardiac surgical procedure, there may be evidence of new regional wall motion abnormalities, global cardiac dysfunction, and peripheral vascular dysfunction. In valvular heart surgery, the heart requires time to remodel before significant improvement is observed.

In some patients, however, hemodynamics may be greatly improved post-bypass. In simple, compensated AS, the patient may be hyperdynamic
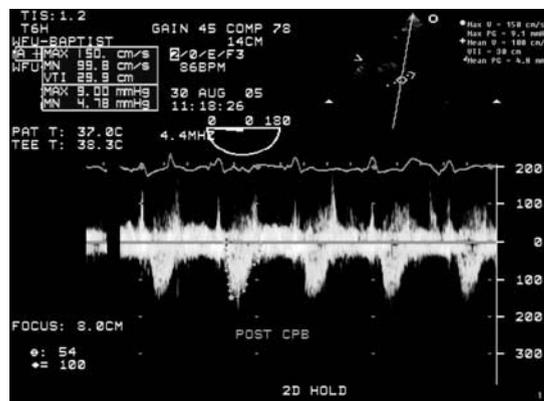
Fig. 5.2 This is the same patient as seen in Fig. 5.1 after aortic valve replacement with a stentless freestyle aortic valve. The deep transgastric long axis view through the aortic valve now shows a peak gradient of 9 mmHg and a mean gradient of 4 mmHg. Both of these gradients are now normal.

and hypertensive after weaning from bypass. It may also be possible, however, that due to the LV hypertrophy, cardioplegia may have been incomplete for total myocardial protection, and the patient may emerge from bypass with transient myocardial dysfunction. In complex repairs, or multiple valve surgery, an extended bypass run may be required, thereby increasing the risk of immediate postoperative cardiac dysfunction and the requirement of inotropic support. EF and LV function may decline after surgery to repair MR; this is commonly thought to be due to the new loading conditions of the heart after removal of the "pop-off" mitral regurgitant outflow. This is likely untrue, as emerging data on mitral valve repair procedures, in which there is sparing of the mitral valve apparatus, show little alteration in EF. This preservation of mitral annular integrity stabilizes LV shape and contractility, thereby preserving function. The diminished performance is likely secondary to other factors including extended cross-clamp time, inadequate myocardial protection, and myocardial stunning. Combined CABG and valvular heart surgery is associated with inotrope use during separation from CPB.

TEE is especially useful in the immediate post-bypass period. TEE will facilitate the assessment of myocardial function and filling parameters, rendering important information affecting decisions about inotropes and volume management. TEE can also assess the condition of the valve repair or replacement. On every case in which TEE is used, a complete evaluation of valve structure and function is required. In a valve repair, the degree of residual regurgitation must be documented. Determination of the Doppler gradient across the repaired valve is required, and images of the valve movement are necessary. In a valve replacement, all of the above are essential, and a further evaluation for a perivalvular leak is required. After mitral valve repair, an assessment for systolic anterior motion (SAM) of the mitral valve is required. These images must be stored as a part of the patient record and a note made in the patient's chart or anesthetic record.

The post-bypass period may be a time of unstable hemodynamics. The heart is adjusting to a new conditions of preload, afterload, and inotropy. There is usually ongoing bleeding, which in many patients, and especially in "re-do" procedures, may be severe. Constant vigilance regarding hemodynamics, blood volume, blood gas chemistry, and metabolic state (i.e. ionized calcium, glucose concentrations, and urine output) is required. There may be new rhythm disturbances. Patients with preoperative atrial fibrillation may now be in sinus rhythm after mitral valve repair and a Maze procedure. These patients may be dramatically improved. Other patients, however, may suffer from third-degree heart block, bradycardia, tachycardia, or other rate and rhythm abnormalities making management difficult.

In the intensive care unit, these patients will likely remain intubated for some hours. The usual considerations of temperature management, metabolic and hemodynamic management, vigilance for excessive chest tube bleeding and evidence of cardiac tamponade must be performed. Elderly patients and those with additional risk factors may require additional support.

Special considerations and long-term prognosis

Cardiac anesthesia for valvular heart surgery carries numerous special considerations not found in other aspects of cardiothoracic anesthesiology. Among these considerations is familiarity with the type of valve used in the operative repair. There are a number of valve types including allografts, autografts, xenografts, mechanical, and bioprosthetic valves. The choice of valve is up to the surgeon; however, the anesthesiologist is frequently consulted to provide TEE measurements that may guide the surgeon in valve choice. For example, the measurement of the aortic valve annulus size is important when determining the size of a prosthetic valve. In the assessment for a possible Ross procedure (pulmonary valve moved to the aortic position and pulmonary allograft placement), the pulmonary annulus size and the degree of pulmonary insufficiency are important factors before committing to the procedure. After the repair, it is important to assess the new valve function. Bioprosthetic valves all come with a complete hemodynamic profile in

their packaging and this information is important when rendering a decision on the function of a new valve. The expected gradients are sometimes higher, and the calculated valve area may be less than one might expect. The impact of valve prosthesis-patient mismatch (VP-PM) on mortality is as high as 25% in those patients with a severe VP-PM mismatch. Reference to the packaging insert will guide the clinician as to whether intraoperative gradients and calculated valve areas are acceptable. In valve repair procedures, one must not only look for the cessation of regurgitation, but one must ensure that there is no new stenosis. Measurement of valve gradients and orifice areas will help in this regard.

Valve repair for patients with endocarditis present all of the aforementioned hemodynamic considerations in addition to the frequently septic condition of the patient. Patients with endocarditis usually have acute regurgitant lesions and present in heart failure. The in-hospital mortality for acute endocarditis is 20%. The early predictors of in-hospital mortality include embolic events, diabetes mellitus, *Staphylococcus aureus*, and APACHE II score. The use of intraoperative TEE is especially helpful in the diagnosis of endocarditis and quantification of the valve defect. Valve surgery reduces 6-month mortality.

There are solid data to support valve repair and replacement in patients with heart valve disease over medical management. After surgery for AS there is initial remodeling of the heart, with subsequent LV mass reduction. In MR, there is symptomatic relief, and improvement in LV EF. Although there is a known early mortality with heart valve surgery, the long-term benefit remains superior to medical management. As the population extends longevity, more patients will present for valve procedures. Although advancing age is associated with worse outcome, there is no upper limit of age contraindicating valvular surgery.

It is unknown what impact percutaneous valves and other nonsurgical valve repair procedures will have on the volume of valvular surgery. It is likely, that anesthesiologists will provide sedation and/or general anesthesia in patients presenting for percutaneous valve procedures. In such cases, all of the hemodynamic principles described below apply. In addition, TEE will be required for percutaneous mitral annular reduction for MR, and endovascular mitral valve repair (Alfieri procedure).

The aortic valve

Aortic valve anatomy

The aortic valve consists of three semilunar valves named according to their relationship with the appropriate coronary arteries: the right coronary cusp, the left coronary cusp, and the noncoronary cusp. At the center of the free-edge of each cusp is a tiny, elevated nodule commonly referred to as the nodule of Arantius. All three nodules coapt at the center of a normal, closed aortic valve (Fig. 5.3). The lunulas are the free-edges of the cusps and span from the nodule of Arantius to the wall of the aorta. When the lunulas of the cusps are apposed and the nodules of Arantius are coapted in a normal aortic valve, the valve is completely closed.

Figure 5.4 demonstrates normal subvalvular, valvular, and ascending aortic anatomy in the mid-esophageal aortic valve long-axis view. In this image, the left ventricular outflow tract (LVOT), aortic valve annulus, sinuses of Valsalva, sinotubular junction, and proximal ascending aorta are well visualized. Measurements of these structures are
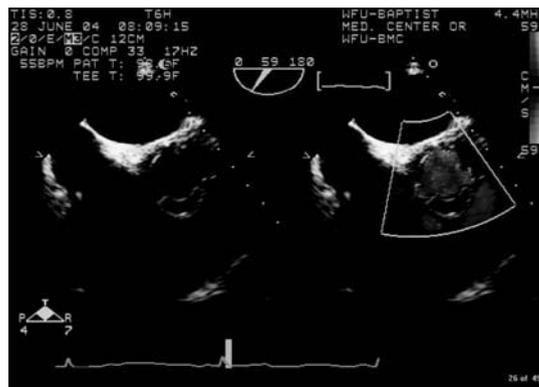
Fig. 5.3 This is a mid-esophageal short axis transesophageal echocardiographic image of a normal aortic valve in the color compare mode. To the left the trileaflet valve is seen during systole. To the right, color Doppler demonstrates a normal flow pattern.

Fig. 5.4 This is the same patient as in Fig. 5.3. This is a mid-esophageal long axis view of the aortic valve in the color compare mode. To the left one can clearly identify the left ventricular outflow tract, aortic valve, sinus of Valsalva, sinotubular ridge, and the aortic root. To the right, color Doppler demonstrates a normal flow pattern with aliasing as the blood accelerates through the aortic valve.

part of a complete examination and are integral in determining annular dilatation and aortic aneurysm pathology. AR can be quantified in this view. The aortic valve complex, including the junction of the aortic valve with the ventricular septum and the anterior mitral valve leaflet, is easily visualized in this imaging plane.

Aortic stenosis (AS)

AS is the most common valvular lesion in the USA. The incidence is increasing due to the aging population and the presence of calcific degenerative changes in the aortic valve with time. This process was once viewed as simply a byproduct of the ageing process; however, new data suggest that calcific AS is the result of an inflammatory process. Isolated AS in adults is more common in males than females and is usually nonrheumatic in origin. Most commonly, AS is degenerative with calcification of the valve leaflets. Congenital bicuspid valves develop the same degenerative changes seen in normal tricuspid aortic valves.

In rheumatic AS, the valve commissures are fused and aortic valve leaflet excursion is limited. The result is a stenotic valve orifice. This stenosis is usually accompanied by regurgitation. In rheumatic heart disease, the mitral valve is usually involved in addition to the aortic valve.

Pathophysiology and adaptation in AS

AS is a chronic LV pressure overload lesion. The natural history of the lesion involves a gradual reduction in the aortic valve area from the normal 2.6–3.5 cm^2 to <1.0 cm^2 occurring over several years. Replacement is generally considered before the aortic valve area is <0.7 cm^2 or the peak systolic pressure gradient is >50 mmHg. The relationship of valvular gradient to orifice area is given by the Gorlin formula: gradient $=$ $(CO)^2$/(aortic valve area)^2. Using this relationship, one can immediately appreciate that reducing the aortic valve area while maintaining CO has a huge impact on the valvular gradient. In a valve with a gradient of 60 mmHg, the LV must generate a systolic pressure of 180 mmHg in order to maintain a normal aortic systolic pressure of 120 mmHg.

As the disease progresses, there is an increasing pressure load on the left ventricle. This pressure load is compensated by ventricular hypertrophy. Under these circumstances, left LV stress (afterload) is greatly elevated. The law of LaPlace provides the relationship between wall stress and pressure: Load or stress in the myocardium $=$ (ventricular pressure) (radius)/2 (wall thickness), or $T = Pr/2h$ where $P =$ peak ventricular pressure, $r =$ ventricular radius, and $h =$ wall thickness). Therefore, as the afterload increases (the pressure in the numerator), the myocardial tension is compensated by increasing wall thickness (in the denominator). The increased wall stress results in concentric ventricular hypertrophy. The degree of thickening parallels the increased ventricular pressure demands. The result is normalization of ventricular wall stress despite greatly elevated peak ventricular pressure (Fig. 5.5a,b). This normalization of wall stress allows maintenance of EF despite the high impedance to ejection found in AS. Eventually, the valve orifice narrows to the point at which stroke volume (SV) and EF fall (Fig. 5.6).

Concentric hypertrophy has several hemodynamic implications. There is reduced ventricular compliance which results in diastolic dysfunction with reduced early diastolic filling of the ventricle.

(a)

(b)
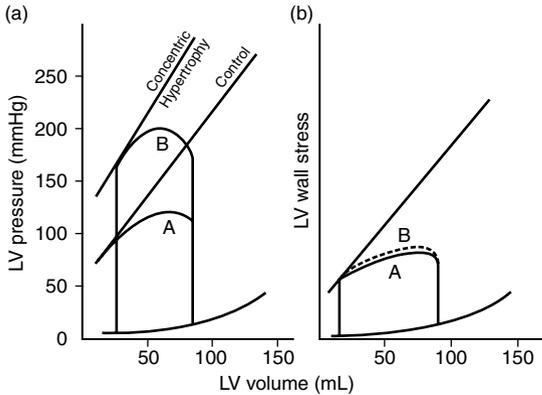
Fig. 5.5 (a) Left ventricular pressure–volume loops demonstrating adaptation to chronic pressure overload. Loop A represents a normal ventricle before the development of aortic stenosis. Loop B represents the same ventricle after prolonged exposure to elevated afterload and development of concentric hypertrophy. End-systolic and end-diastolic volumes in loop B are unchanged from those in loop A, but left ventricular systolic pressure is greatly elevated. (b) The same loops illustrated in (a) are shown again here, except that wall stress is plotted against volume. It is obvious that elevated ventricular systolic pressure seen in loop A does not result in elevated wall stress compared with loop B. Development of concentric hypertrophy allows normalization of wall stress in the face of chronically elevated left ventricular systolic pressure. LV, left ventricular. (From Ross J Jr. Afterload mismatch in aortic and mitral valve disease: implications for surgical therapy. *J Am Coll Cardiol* 1985;**5**:811–26, with permission.)

Normal end-diastolic volumes are maintained with normal sinus rhythm. In patients with severe AS, atrial systole contributes nearly 30% of the left ventricular end-diastolic volume (LVEDV), whereas in patients without AS, atrial systole contributes 20%. This late diastolic filling occurs on the steep portion of the diastolic pressure–volume curve. The well-timed atrial systole allows late diastolic filling to occur with minimal elevation in mean left atrial pressure (LAP). With loss of atrial systole (atrial fibrillation), normal end-diastolic volume is maintained by increasing mean LAP to equal or exceed left ventricular end-diastolic pressure (LVEDP). When compliance is poor, a normal LVEDV may occur at a LVEDP in excess of 25 mmHg. Acute increases in mean LAP may result in pulmonary
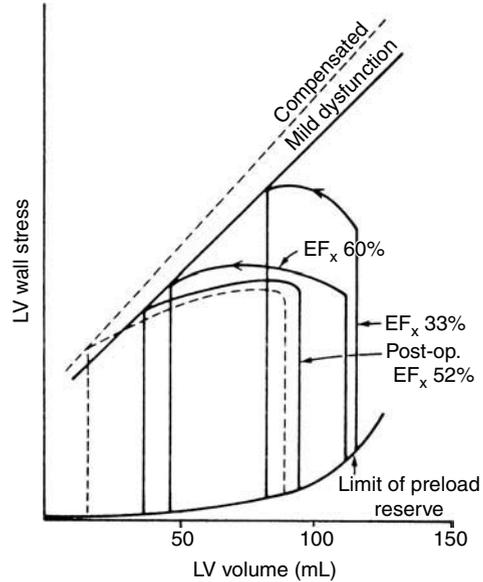
Fig. 5.6 Left ventricular wall stress–volume loops in progressive aortic stenosis (AS). The dotted loop represents a ventricle with concentric hypertrophy and preserved systolic function. As systolic dysfunction develops, stroke volume (SV) and ejection fraction (EF) can be maintained by making use of the preload reserve (EF = 60%). Further progression of systolic dysfunction results in exhaustion of preload reserve. At this point, further progression of AS results in afterload mismatch and reduction in SV and EF (EF = 33%). Surgical therapy for replacement of the stenotic aortic valve results in a reduction in afterload, the abolition of afterload mismatch, and the ability of the ventricle to deliver nearly normal SV and EF despite the presence of systolic dysfunction (EF = 52%). Post-op., postoperative. (From Ross J Jr. Afterload mismatch in aortic and mitral valve disease: implications for surgical therapy. *J Am Coll Cardiol* 1985;**5**:811–26, with permission.)

congestion. Unfortunately, in AS with atrial fibrillation, low mean LAP results in diminished LVEDV and, therefore, SV and CO.

Diminished ventricular compliance also limits the use of preload reserve. With the ventricle operating on the steep portion of its diastolic pressure–volume curve, incremental increases in end-diastolic volume result in prohibitive increases in end-diastolic pressure. Hence, even with preserved atrial systole, it may be impossible to augment preload unless mean LAP is above 20–25 mmHg. Again, at these

Table 5.2 Myocardial oxygen supply and demand in aortic stenosis.

Myocardial oxygen consumption is increased by:
- The increased mass of myocardium
- The demands of LV pressure work, which is much more energy-consumptive than volume work. A large portion of the total myocardial workload is devoted to the isovolumic contraction phase because of the high intraventricular pressures necessary to commence the ejection phase (see Fig. 5.5). Recall that the isovolumic contraction phase is a very energy consumptive process
- The prolonged ejection phase

Myocardial oxygen delivery is compromised by:
- Elevated LVEDP secondary to diminished ventricular compliance
- An aortic diastolic pressure that is low relative to the elevated LVEDP
- Diminished diastolic coronary perfusion time secondary to the prolonged ejection phase
- Compression of subendocardial vessels by hypertrophied myocardium
- Absence of any systolic coronary perfusion because LV systolic pressure greatly exceeds aortic systolic pressure

LV, left ventricle; LVEDP, left ventricular end-diastolic pressure.

pressures the patient is a risk for pulmonary congestion. In this end-stage disease, increases in preload only minimally increase SV. Thus, for a given contractile state, SV is nearly fixed.

Patients with AS are especially susceptible to ischemia. Several factors are responsible for the myocardial oxygen supply–demand imbalance seen in AS (Table 5.2). This combination of factors explains why 30% of patients with AS experience angina in the absence of significant coronary artery disease.

In general, global ventricular function (EF%) is normal in AS. The mechanism for depressed EF in patients with severe AS is not entirely clear. Concentric hypertrophy, inadequate to normalize wall stress, will result in excessive afterload and reduced EF. Subendocardial ischemia may also play a role. In patients without myocardial infarction, irreversible myocardial damage is relatively uncommon, and there is remarkable improvement in EF after uncomplicated aortic valve replacement. Many patients with depressed function preoperatively will exhibit a normal EF postoperatively. The patient with a low gradient, low CO and low EF is at highest risk for surgery. These patients have lost their ability to compensate for the disease process. Survival in these patients depends on medical versus surgical treatment and the presence of inotropic reserve (Fig. 5.7).
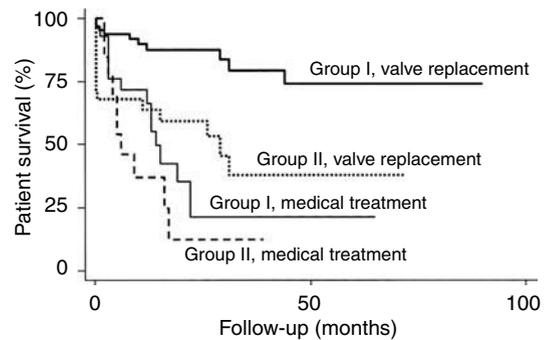
Fig. 5.7 Survival for aortic stenosis patients with low gradient and low ejection fraction. Group I patients demonstrated inotropic reserve and had a better outcome with aortic valve replacement (AVR) than did similar patients treated medically, and better than group II patients who lacked inotropic reserve. (From Monin JL, Quere JP, Monchi M *et al*. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome. A multicenter study using dobutamine stress hemodynamics. *Circulation* 2003;**108**:319–24, with permission.)

In patients with systolic dysfunction, there is a progressive increase in LVEDV so that SV and EF are maintained through use of preload reserve (see Fig. 5.6). Reduced ventricular compliance limits the increase in end-diastolic volume and the pressure tolerated without pulmonary congestion. With severe systolic dysfunction, the maximal wall stress

that the ventricle can generate is severely limited. In this situation, afterload mismatch may limit maintenance of SV and EF despite use of preload reserve. In these patients, the aortic valve gradient may be low secondary to the reduced flow across the stenotic valve. The calculated valve area will give a much better indication of the severity of the stenosis.

Severe AS does not directly affect right ventricular (RV) function until the occurrence of pulmonary artery hypertension. In patients with severe AS and an EF <50%, a reduced SV and CO is maintained at the expense of elevated left atrial and pulmonary artery pressures. Pulmonary artery pressures begin to rise through passive pulmonary venous congestion when LAPs exceed 18 mmHg. Ultimately, pulmonary artery fibrosis develops and pulmonary arterial hypertension follows. As the mean pulmonary artery pressure gradually rises to exceed 50 mmHg, the right ventricle, which normally functions with low impedance to ejection, fails. Patients with AS and an EF < 40% have CO maintained by a gradual increases in mean LAP to 25–30 mmHg, with mean pulmonary artery pressure in excess of 50 mmHg. These patients may have clinical evidence of RV failure with peripheral edema and liver congestion.

Increases in heart rate normally result in a marked decrease in the time of diastole, whereas the length of systole remains largely unchanged (Fig. 5.8a,b). Over the heart rate range of 50–110 b/min, the length of systole decreases from 441 to 315 ms; whereas, the time of diastole decreases from 759 to 230 ms. Hence, tachycardia in patients with AS is detrimental because, although there is adequate time in systole to allow ejection across the stenotic valve, diastolic time and subendocardial perfusion are drastically reduced.

Bradycardia in these patients is also detrimental. Recall that the valve gradient increases as the square of the flow across the valve. Maintaining CO at a reduced heart rate requires increased SV (CO = HR × SV). Because SV is flow, the gradient must increase. Figure 5.9(a–c) demonstrates that for a given CO, progressive decreases in heart rate result in large increases in the transvalvular gradient. With aortic valve areas <0.5 cm^2, gradients in excess of 150 mmHg are possible, even
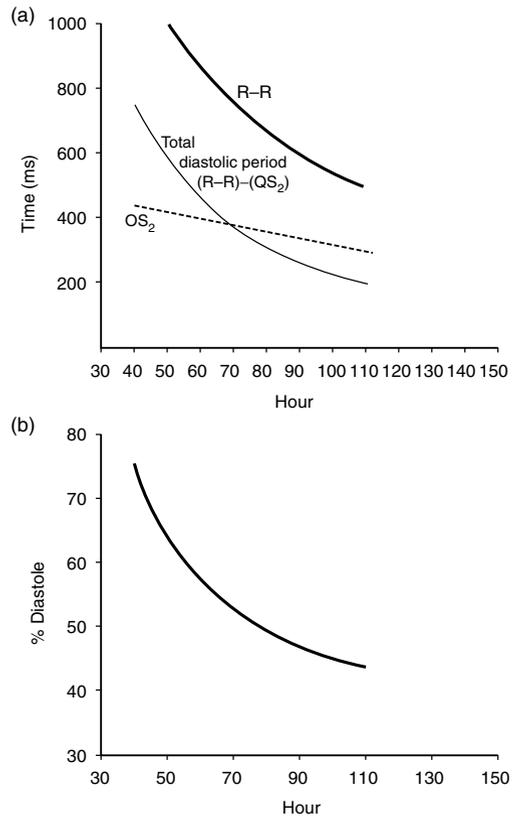
Fig. 5.8 (a) Increases in heart rate cause decreases in length of each cardiac cycle (R–R interval). Decreases in length of systole (OS$_2$) with increases in heart rate are far less dramatic than decreases in the length of diastole (R–R–QS$_2$). (b) Percent of each cardiac cycle (R–R interval) spent in diastole at various heart rates. Small changes in heart rate cause large decreases in percent of time spent in diastole. (From Boudoulas H, Rittgers SE, Lewis RP *et al*. Changes in diastolic time with various pharmacologic agents: implication for myocardial perfusion. *Circulation* 1979;**60**:164–9, with permission.)

with low normal SVs. Because the left ventricle is capable of generating peak pressures in the range of 250–300 mmHg, maximal ventricular pressures are needed to maintain a systolic blood pressure >100 mmHg. In this setting, bradycardia with an increase in the gradient will result in systemic hypotension. The result is poor subendocardial perfusion and ischemia. In addition, diminished diastolic compliance may prohibit the increase in end-diastolic volume necessary to augment SV in
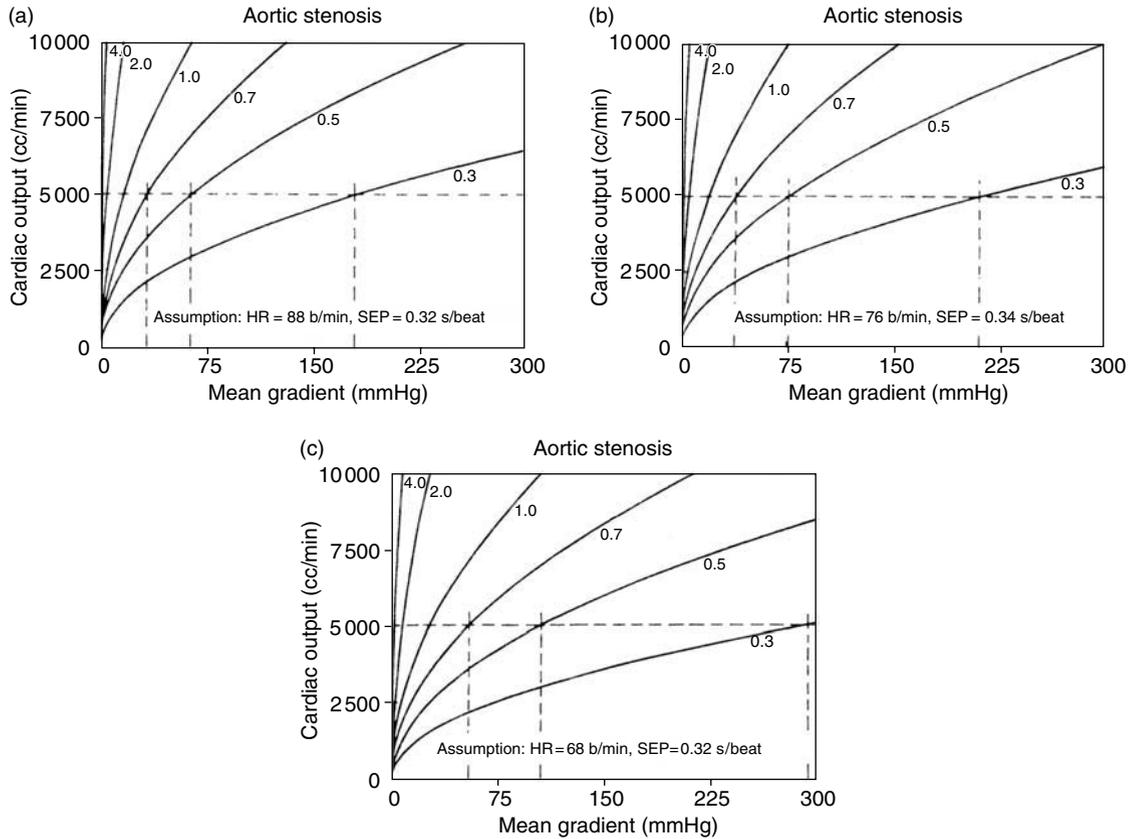
Fig. 5.9 The relationship of heart rate (HR), cardiac output (CO), aortic valve area, and systolic pressure gradient across the aortic valve is illustrated for patients with aortic stenosis. CO is plotted against the systolic pressure gradient for aortic valve areas ranging from 0.3–4.0 cm^2. (a) This plot illustrates these relationships for HR of 88 b/min and systolic ejection period (SEP) of 0.32 s/beat. (b) This plot illustrates these relationships for HR of 76 b/min and SEP of 0.34 s/beat. (c) This plot illustrates these relationships for HR of 68 b/min and SEP of 0.32 s/beat. Clearly, for a given CO and HR, systolic pressure gradient increases as aortic valve area decreases.

Furthermore, for a given CO and aortic valve area, systolic pressure gradient increases as HR decreases. Increases in HR in the range examined here have little effect on length of SEP. Therefore, for CO to remain constant as HR decreases, larger stroke volume (SV) must be ejected across stenotic aortic valve in relatively constant time period. This results in larger systolic pressure gradient. (From Carabello BA, Grossman W. Calcification of stenotic valve orifice areas. In: Baim DS, Grossman W (eds). *Cardiac Catheterization, Angiography and Intervention*, 5th edn. Baltimore: Williams & Wilkins, 1996:151–65, with permission.)

bradycardic states without prohibitive increases in mean LAP.

Contrary to what might be expected, decreasing afterload by reducing systemic vascular resistance does not always have a beneficial effect for patients with AS. A reduction in afterload should enhance LV ejection and thus increase SV. However, the impedance to LV ejection is largely due to the fixed outflow obstruction at the aortic valve orifice. Reductions in systemic vascular resistance (SVR) are offset by the large increases in the transvalvular gradient that accompany increased flow across the stenotic valve orifice. Thus, SVR reduction results in very little augmentation of CO in patients with significant AS. Furthermore, agents used to reduce afterload, such as nitroprusside and hydralazine,

decrease aortic diastolic pressure and compromise the tenuous subendocardial blood flow in these patients. In contrast, increases in afterload result in an elevation of LVEDV and LVEDP with maintenance of SV in patients with good ventricular function and some preload reserve. In patients with poor ventricular function, increasing afterload may result in a progressive decline in SV and EF secondary to afterload mismatch (see Fig. 5.6).

The term "critical aortic stenosis" commonly is used in association with severe aortic valve disease. This is a poorly defined term, but it is most appropriate when describing a pathophysiologic state rather than an absolute valve area. Critical AS exists when preload reserve is exhausted and EF is reduced such that further reductions in aortic valve area will produce increased pulmonary vascular congestion or further reductions in SV. Critical AS can exist with a larger valve area in patients with severe concomitant diastolic or systolic dysfunction or in patients with atrial fibrillation.

Anesthetic technique in AS

Goals

- Sinus rhythm is essential. Atrial contraction may contribute up to 40% of LV filling.
- Maintain heart rate at 70–90 b/min.
- Maintain a PCWP high enough to ensure adequate LVEDV; more full rather than less full.
- Maintain afterload. Decreases in diastolic blood pressure reduce coronary perfusion.
- Maintain contractility.

Preinduction

All patients should have adequate IV and central access. ECG monitoring should allow assessment of leads V_5, I, II, III, aV_R, aV_L, and aV_F. Baseline recording of all seven leads should be obtained for comparative purposes. Normally, two leads (II and V_5) are monitored simultaneously intraoperatively.

A radial artery catheter is placed with local anesthesia and adequate sedation before induction of anesthesia. A pulmonary artery catheter can be placed either before or after induction of anesthesia. All of the equipment and medications necessary for treatment of dysrhythmias must be available before placement of the pulmonary artery catheter. In particular, a defibrillator with demonstrated consistent synchronization to the patient's electrocardiogram (ECG) signal must be in the room if loss of sinus rhythm requires immediate cardioversion. Placement of the pulmonary artery catheter before induction allows optimization of preload and afterload before induction of anesthesia. Placement after induction is not associated with poor outcome and may be better tolerated by the compromised patient.

The presence of compensatory LV concentric hypertrophy will cause LV compliance to be considerably less than RV compliance. This will cause the right atrial pressure to underestimate the PCWP and LVEDP. Therefore, the peak A-wave pressure of the PCWP trace is used. The LVEDP measured at the time of cardiac catheterization is a useful guide as to the PCWP that will be necessary to obtain the end-diastolic volume that will optimize SV. In general, for patients with significant AS, a PCWP A-wave pressure of 15–25 mmHg is appropriate. In the absence of RV failure, the mean right atrial pressure will be 5–8 mmHg. If necessary, volume infusion before induction can optimize LVEDV.

Induction and maintenance

There is no one anesthetic technique superior to another. Induction agents must be chosen based upon the ability to achieve the anesthetic goals outlined above. Etomidate, barbiturates, or high dose narcotics are appropriate. Propofol may cause a severe reduction in blood pressure and should be used with great caution in patients with AS. A high dose narcotic induction is indicated in some critically ill patients. Generally, a balanced technique of narcotics and inhalational agents for maintenance of anesthesia is appropriate. Fentanyl (10–25 μg/kg) or sufentanil (2–5 μg/kg) can be used as the primary anesthetic for maintenance before CPB. These agents have no effect on myocardial contractility and cause a reduction in peripheral vascular resistance only through a diminution in central sympathetic tone. Compared with fentanyl, sufentanil is more likely to cause a fall in mean arterial pressure secondary to a reduced peripheral vascular resistance in patients with valvular heart disease. On

the other hand, patients with valvular heart disease receiving sufentanil are less likely to require supplemental anesthesia or vasodilator therapy for skin incision, sternotomy, sternal spread, or aortic manipulation.

After preoxygenation, with the patient breathing 100% oxygen, induction begins with a deliberate infusion of a hypnotic, midazolam, and fentanyl or sufentanil. Compared with patients with coronary artery disease, patients with valvular heart disease have a lower narcotic requirement to achieve unconsciousness. This is probably due to a lower CO with a relative greater distribution of output to the brain and spinal cord. After loss of consciousness, the hemodynamic response to insertion of an oral airway followed by insertion of a urinary catheter can gauge the need for additional narcotic to blunt the hemodynamic response to tracheal intubation. Laryngoscopy is performed carefully and should not be prolonged. If an upward trend in heart rate or blood pressure occurs, laryngoscopy should be terminated and additional narcotic administered. If there is poor visualization of the larynx, laryngoscopy should be terminated and intubating conditions improved by changing head position, using a stylet, or changing blades. This approach will help prevent long stimulating laryngoscopies that compromise hemodynamics. A TEE probe can be placed after tracheal intubation.

To optimize heart rate, the choice of muscle relaxant is critical. For patients who are poorly beta-blocked and for those not taking beta-blockers, fentanyl or sufentanil in combination with vecuronium is a good choice. Vecuronium 0.02 mg/kg or cisatracurium 0.04 mg/kg can be administered approximately 1–2 minutes before starting the narcotic infusion. As the patient loses consciousness, the remainder of the total dose of 0.1 mg/kg of vecuronium or 0.2 mg/kg of cisatracurium is administered, and controlled ventilation with 100% oxygen initiated. For patients who are well beta-blocked, fentanyl or sufentanil in combination with pancuronium works well. Sufentanil in combination with vecuronium or cisatracurium in a well beta-blocked patient may result in significant bradycardia. Pancuronium 0.02 mg/kg can be administered approximately 1–2 minutes before

starting the narcotic infusion. As the patient loses consciousness, the remainder of the 0.1 mg/kg dose is administered and controlled ventilation is initiated. Using this "priming dose" of neuromuscular blockade minimizes the risk of narcotic-induced rigidity without undue stress to the patient.

Bradycardia with hemodynamic compromise requires immediate treatment. A small dose of pancuronium (1–3 mg) can be effective if vecuronium was the neuromuscular blocking agent. Atropine is not a good choice for two reasons: its effect on heart rate, even in small doses (0.2 mg), is unpredictable; and tachycardia may be initiated by larger doses. Atropine, unlike β_1-adrenergic agents, increases heart rate without any reduction in the duration of systole. Thus, for equal increases in heart rate, atropine will cause a greater reduction in the duration of diastole and will compromise subendocardial perfusion to a greater degree than a β_1-adrenergic agent. Ephedrine (a direct- and indirect-acting β- and α-agonist) is a reliable agent to increase heart rate without compromising diastole. In addition, the augmentation in diastolic blood pressure obtained is beneficial when hypotension accompanies bradycardia.

Tachycardia requires aggressive treatment to avoid subendocardial ischemia and hemodynamic compromise. The first strategy should be to terminate any noxious stimuli and increase the depth of anesthesia if appropriate. Esmolol is an excellent agent to acutely reduce heart rate in a patient with AS. Esmolol is a β_1 selective agent with an elimination half-life of 9 minutes. This short half-life renders esmolol quite useful for patients with poor ventricular function or bronchospastic disease because, if it is not tolerated, therapy is terminated quickly. Furthermore, unlike longer acting beta-blockers, esmolol can be used aggressively in the pre-CPB period without fear that it will compromise termination of CPB.

If hypotension due to reduced peripheral vascular resistance occurs during induction, small doses of phenylephrine (40–120 μg) and volume infusion to increase preload to preinduction levels usually will correct the problem. TEE is very useful at this point. If TEE reveals a dilated, hypokinetic LV or if the patient fails to respond with a prompt increase

in aortic blood pressure, an inotropic agent may be indicated. Dobutamine 5–10 μg/kg/min is a reasonable choice because it is unlikely to cause tachycardia. IV nitroglycerin should be started to treat the elevated PCWP that inevitably accompanies this downward spiral. The infusion can be started at 0.15–0.30 μg/kg/min and titrated as necessary.

If surgical stimulation (skin incision, sternotomy, sternal spreading, or aortic manipulation) produces hypertension, additional doses of sufentanil (1–3 μg/kg) or fentanyl (5–15 μg/kg) may be necessary. If this fails to control the hypertension, the use of additional agents will be necessary. Vasodilation with increasing inhalational agents may resolve the issue. Alternatively, sodium nitroprusside can be titrated easily and terminated quickly. This makes it an ideal choice for treatment of transient elevations in peripheral vascular resistance. Although relatively large doses of nitroglycerin may be needed to control systemic hypertension, nitroglycerin is a better choice than nitroprusside for cases in which myocardial ischemia exists.

Benzodiazepines are an essential component of the anesthetic, and midazolam is the most commonly used. Doses range from 5 to 15 mg. Administration in conjunction with fentanyl or sufentanil may cause decreases in peripheral vascular resistance with subsequent hypotension. Therefore, caution is necessary. Midazolam in increments of 1–2 mg or lorazepam in increments of 0.5–1.0 mg are reasonable.

In recent years, there has been movement away from a pure high-dose narcotic anesthetic. Inhalational anesthetics are now common in all types of cardiac surgery. Nitrous oxide (N_2O) in association with high-dose opiates causes systolic dysfunction in patients with coronary artery disease, particularly those with an LVEDP > 5 mmHg. N_2O combined with high-dose opiates elevates pulmonary vascular resistance (PVR), particularly in the presence of pre-existing pulmonary hypertension. Because of the potential for altered myocardial oxygen balance in all patients with AS, and the presence of an elevated PVR in some patients, N_2O must be used with caution, if at all. Isoflurane is a potent vasodilator that causes little depression of systolic function. Sevoflurane and desflurane have similar effects. However, care must be taken to avoid decreases in peripheral vascular resistance and hypotension when they are used in patients with AS. Controversy exists regarding whether isoflurane in the presence of coronary stenosis is responsible for producing a coronary steal phenomena leading to ischemia. There may be beneficial effects of inhalational anesthetics as pharmacologic preconditioning agents. There is a growing body of evidence demonstrating that inhalational agents reduce the markers of myocardial injury after an ischemic-reperfusion injury.

Post-CPB management

After aortic valve replacement, the obstruction to forward flow is eliminated. With allograft replacement, the valve gradients are usually normal, and with mechanical valves there is a small peak gradient of 10–20 mmHg. The reduced transvalvular gradient allows the hypertrophied LV to significantly decrease left ventricular end systolic volume (LVESV); thus, augmenting SV and EF (see Fig. 5.6). In addition, the ventricle can now respond to further reductions in afterload with an increase in SV.

As with any procedure requiring cardioplegia, the LV systolic function may be compromised by inadequate myocardial protection during CPB. It may, therefore, be necessary to rely on inotropic agents for augmentation of systolic function despite the dramatic reduction in afterload. This is particularly true if there is coexisting coronary artery disease. Epinephrine 0.015–0.030 μg/kg/min, dopamine 1–5 μg/kg/min, or dobutamine 5–10 μg/kg/min are reasonable choices, providing inotropic support with little concomitant vasoconstriction and afterload increase.

Because there is no significant regression of concentric hypertrophy for 6–12 months after aortic valve replacement, the compliance characteristics of the LV will be unchanged in the post-CPB period. In fact, poor subendocardial myocardial protection during aortic cross-clamping may result in ischemic diastolic dysfunction. Sinus rhythm enhances filling. The peak A-wave pressure must be high enough to ensure adequate LVEDV. In general, because LVESV will be lower because of the reduction in impedance to ventricular ejection, LVEDV, and

therefore the A-wave pressure, need not be as high in the post-bypass period. A-wave pressures of 10–20 mmHg are usually adequate. Subendocardial perfusion will remain compromised in diastole and, therefore, aortic diastolic blood pressure must remain high enough to ensure perfusion.

Tachycardia remains detrimental because of its effects on subendocardial perfusion. Slower heart rates are now better tolerated because of the dramatic reduction in the transvalvular gradient with surgery.

Because the surgical procedure requires an aortotomy with subsequent repair, it is helpful to avoid hypertension, which places undue stress on the aortic suture line. The atrioventricular (AV) node lies proximal to the aortic valve annulus and may be transiently or permanently damaged after valve replacement. Ventricular pacing may be necessary.

Aortic regurgitation

Aortic regurgitation (AR) may result from damage to the aortic valve leaflets or from dilatation of the aortic root. Damage to the aortic valve leaflets results in a mechanical valve defect, whereas aortic root dilatation results in functional aortic valve impairment. AR may be acute or chronic in nature. Infective endocarditis with destruction of the valve leaflets is a cause of acute AR. There may be actual destruction of the valve leaflet by the infective process. Alternatively, the infective process may cause perforation of a leaflet or the presence of vegetations may prevent proper apposition of the leaflets.

Trauma with cusp rupture or laceration may result in acute AR. Aortic dissection may cause AR through a variety of mechanisms. Dilation of the proximal aortic root and valve annulus results in poor apposition of the leaflets and functional valvular incompetence. Dissection with intramural hematoma formation may distort the valve. Dissection can result in mechanical incompetence when the valvular annulus is involved.

Connective tissue diseases such as Marfan syndrome, Ellers–Danlos syndrome, and pseudoxanthoma elasticum produce chronic AR. Progressive aortic root dilation with subsequent dilation of the valve annulus results in functional AR. As time passes, the poorly apposed valve leaflets begin to bow, thicken, and shorten; resulting in worsening regurgitation. These patients may also suffer from mitral valve incompetence. A congenital bicuspid aortic valve is present in approximately 0.5% of the population. This condition is associated with AR. Bicuspid aortic valves with a genetic mutation in the fibrillin gene are seen in Marfan syndrome.

Inflammatory diseases of the aorta, such as syphilis, rheumatoid disease, ankylosing spondylitis, and Takayasu's aortitis, may produce chronic AR. These diseases cause distortion of the aortic root as well as destruction of valve cusps and annular support structures. MR is common in these conditions.

Aortic valve leaflet damage due to rheumatic fever is a common cause of chronic mechanical AR. However, isolated AR-secondary to rheumatic fever is rare. In rheumatic fever, there is infiltration of fibrous tissue in the valve cusps causing retraction. This results in poor valve apposition in diastole with subsequent regurgitation. At the same time, commissure fusion results in AS. Mitral valve involvement is common in rheumatic heart disease.

Pathophysiology and adaptation in AR

AR is a volume overload lesion that may be acute or chronic in nature. The extent of regurgitation depends on the diastolic pressure gradient between the aorta and the left ventricle, the time available for regurgitation (diastole), and the effective regurgitant orifice area. The pressure gradient is determined by the aortic diastolic pressure, ventricular early diastolic pressure, and ventricular compliance. Regurgitation ceases when the ventricular diastolic and aortic diastolic pressures equalize. The duration of diastole is inversely related to heart rate as demonstrated in Fig. 5.8.

Chronic volume overloading of the left ventricle results in eccentric ventricular hypertrophy or increased ventricular radius. The details of this process are summarized in Fig. 5.10a. Whereas both LVESV and LVEDV increase, LVEDV increases to a greater extent. This results in an enhanced SV with no need for an increased EF. The slope of the diastolic pressure–volume curve is little changed and compliance is only slightly increased. The entire pressure–volume loop is shifted to the right. This

(a)

(b)
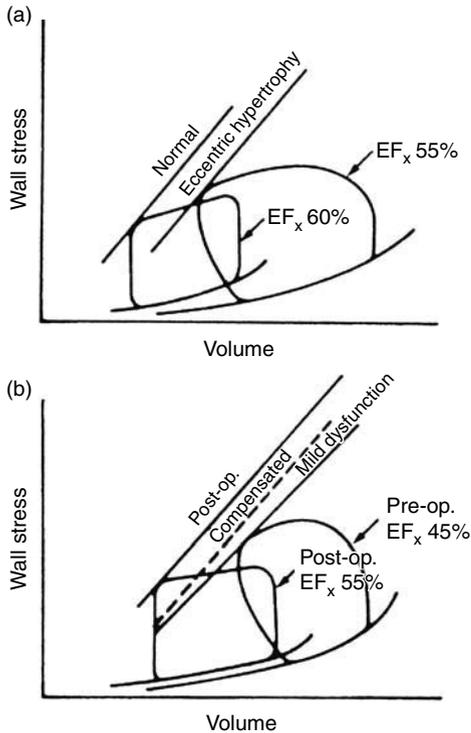
Fig. 5.10 Left ventricular wall stress–volume loops for patient with progressive aortic stenosis. (a) Wall stress–volume loops of normal ventricle and of ventricle having developed eccentric hypertrophy in response to chronic volume overload of aortic regurgitation (AR) are shown. The ventricle with eccentric hypertrophy has a reduced isovolumic contraction phase and has its entire wall stress–volume relationship shifted to the right. These adaptations allow the ventricle to deliver large stroke volume with nearly normal ejection fraction (EF) despite elevation of end-systolic wall stress. (b) Wall stress–volume relationships in a ventricle with chronic aortic regurgitation and mild systolic dysfunction. Progressive systolic dysfunction leads to exhaustion of preload reserve and elevation of wall stress due to large ventricular radius. This, in turn, results in reduced stroke volume (SV) and EF (EF = 45%). After surgical replacement of aortic valve, ventricular radius and wall stress are reduced and near-normal SV and EF exist despite the presence of systolic dysfunction (EF = 55%). (From Hurst JW. *The Heart*, 5th edn. New York: McGraw–Hill, 1985:818, with permission.)

rightward shift of the diastolic pressure–volume curve allows low diastolic pressures at very large end-diastolic volumes. The large increase in ventricular radius that accompanies eccentric hypertrophy elevates wall stress and stimulates some degree of concentric hypertrophy. This compensation is not complete and wall stress remains elevated both in end systole and end diastole (see Fig. 5.10a).

Unique LV pressure loading exists in AR, as illustrated in Fig. 5.10a. The isovolumic phase of ventricular systole is of very short duration and limited pressure generation. This allows a greater portion of myocardial energy expenditure directed toward ejecting a large volume and less toward overcoming impedance to begin ejection.

In acute AR, there is not ample time for compensatory eccentric hypertrophy to occur. Without increased diastolic compliance and the right shift of the pressure–volume loop, the regurgitated volume results in a very high LVEDP. Because LVEDP rises rapidly to equal aortic end-diastolic pressure, the gradient for regurgitation is abolished quickly. As a result, the aortic end-diastolic pressure generally is higher and the regurgitant volume generally is smaller in acute versus chronic AR. Ventricular dilation from acute AR may result in functional MR. For other patients, the rapid rise in diastolic pressure may result in early diastolic equalization of left atrial and LV pressures such that premature mitral valve closure occurs. In this setting, the PCWP or LAP will greatly underestimate the LVEDP.

In chronic AR, the increased compliance and the rightward shift of the diastolic pressure–volume curve allows passive filling of the left ventricle in early and mid-diastole. Therefore, LVEDV is maintained even without an atrial kick, except in end-stage AR, in which preload reserve is exhausted and the ventricle operates on the steep portion of its diastolic pressure volume curve (Fig. 5.10b).

In acute AR, increased ventricular compliance and a rightward shift of the diastolic pressure–volume curve are absent. In this setting, an atrial systole may be necessary to increase the left atrial to LV pressure gradient enough to allow filling of the left ventricle. If premature mitral valve closure

occurs due to rapid rise of LVDP, diastolic filling from the left atrium (LA) will be reduced.

Eccentric hypertrophy and the altered pressure–volume relationship allow large increases in LVEDV with minimal increases in LVEDP in patients with chronic AR. This affords a great deal of preload reserve. Stroke volume can be increased by preload augmentation without pulmonary congestion. In contrast, in acute AR preload reserve is nearly exhausted. Without adequate time for adaptation, the left ventricle operates on the steep portion of its diastolic pressure–volume curve.

The alterations in myocardial oxygen consumption in AR are shown in Table 5.3. Patients with chronic AR may remain symptom-free for many years despite progressive decreases in systolic function. The enormous preload reserve available to these patients allows preservation of SV by progressive increases in LVEDV in the face of declining contractile function. When preload reserve is exhausted, SV falls. At this point, systolic function is compromised and symptoms of reduced CO manifest (see Fig. 5.10b).

As contractility decreases, LVEDV increases: SV is maintained, but EF falls. EF will remain in the low normal range until significant systolic dysfunction

occurs. In fact, valve replacement is recommended for patients with AR without symptoms when ventricular dilation and a depressed EF are present.

As with AS, RV function is not directly affected by AR until pulmonary arterial hypertension develops. In chronic AR, ventricular dilation may lead to functional MR. This, in turn, may lead to a gradual elevation in left atrial and pulmonary artery pressures. If this situation persists, pulmonary arterial hypertension will soon develop. RV failure develops if the pulmonary arterial hypertension becomes severe.

In acute AR, functional MR from ventricular dilation is tolerated poorly. Acute ventricular dilation and functional MR leads to an immediate and profound elevation in LAP. Pulmonary vascular congestion with interstitial pulmonary edema rather than secondary pulmonary artery hypertension and RV failure ensues.

The relationship between heart rate and CO in AR is complex. Recall that the regurgitant volume is in large part determined by the length of diastole. Figure 5.8 illustrates the inverse relationship between heart rate and the length of diastole. Bradycardia (heart rate < 60 b/min) is detrimental in AR for several reasons. It increases the

Table 5.3 Myocardial oxygen consumption in aortic regurgitation.

Myocardial oxygen consumption is increased by:
- The large mass of myocardium
- The enormous volume of work done by the left ventricle. Volume work increases oxygen consumption, but to a much lesser extent than pressure work. The isovolumic contraction phase is highly energy consumptive. Because of the low aortic diastolic blood pressures present in AR, the isovolumic contraction phase is very brief and represents only a small portion of the total work done by the ventricle (see Fig. 5.10a). A greater portion of the total workload is devoted to the generation of volume ejection, which is an energy-efficient process
- Despite the development of eccentric hypertrophy and some degree of concentric hypertrophy, wall stress remains slightly elevated in both systole and diastole (see Fig. 5.10a). Recall that wall stress determines oxygen consumption in the ejection phase of ventricular contraction

Myocardial oxygen delivery is compromised by:
- The low diastolic aortic pressure characteristic of AR reduces the gradient for coronary blood flow (coronary perfusion pressure = aortic diastolic blood pressure − LVEDP). This is particularly true in acute AR, in which precipitous increases in LVEDP occur. Bradycardia can exacerbate the situation. Bradycardia increases the regurgitant volume and thus increases LVEDP
- In acute AR due to aortic dissection, one or both of the coronary ostia may be involved in the dissection. This may acutely and drastically reduce coronary blood flow

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AR, aortic regurgitation; LVEDP, left ventricular end-diastolic pressure.

regurgitant volume per beat, which tends to lower aortic diastolic blood pressure and increase LVEDP. This decreases the gradient for subendocardial oxygen delivery. Simultaneously, the large SV that accompanies bradycardia increases wall tension and oxygen consumption. Forward SV and CO fall because the regurgitant volume represents a large portion of the total SV (the regurgitant fraction is high).

With tachycardia, the regurgitant volume per beat falls, whereas the regurgitant volume per minute may remain unchanged. The relationship between regurgitant volume and total SV (the regurgitant fraction) does not remain constant as heart rate increases. Therefore, CO may decrease, remain unchanged, or increase with a heart rate increase. A change in rate of 75–85 b/min increases CO significantly. Further increases in heart rate from 85–110 b/min show a trend toward a slight additional increase in CO. Little additional change, or a slight decrease in CO, occurs when the heart rate is in excess of 110–120 b/min. Therefore, extremes of tachycardia offer no advantage over more moderate rates of 75–85 b/min in improving CO. Furthermore, in patients with coronary disease, the elevated heart rates increase demand and decrease oxygen supply.

Increased afterload is detrimental to patients with both acute and chronic AR because it increases the regurgitant volume per beat. Recall that one of the determinants of the regurgitant volume is the gradient between the aorta and the left ventricle in early diastole. It is important, then, to avoid agents and to blunt stimuli that increase afterload.

Efforts to actively decrease afterload in patients with AR are not uniformly helpful. In chronic AR, vasodilators benefit patients who have a depressed EF, high LVEDP, decreased forward CO, and high arterial pressure. Patients who do not meet these criteria may actually experience diminished forward CO with vasodilator therapy due to preload reduction from venodilation. In acute AR, vasodilator therapy is usually warranted. Recall that the absence of adequate ventricular compensation creates a very high LVEDP and that a low forward CO exists despite preserved systolic function. Afterload reduction will reduce LVEDP and increase forward CO. In addition, functional MR due to ventricular dilation improves in these patients with a reduction in ventricular size by vasodilators.

In properly selected patients, vasodilator therapy enhances ventricular performance in two ways. Reduced aortic impedance enhances systolic performance and the regurgitant volume is reduced by a reduction in the diastolic aortic to LV gradient. It is important to ensure that the reduction in aortic diastolic blood pressure that accompanies vasodilator therapy is not so severe as to jeopardize subendocardial perfusion.

Anesthetic technique in AR

Goals
- Maintain sinus rhythm (although this is not as important as in AS).
- Maintain heart rate at 75–85 b/min; faster better than slower.
- Avoid afterload increases; pursue afterload reduction in acute AR and in chronic AR when LVEDP and arterial blood pressure are elevated, and CO and EF are depressed.
- Maintain a PCWP high enough to guarantee adequate LVEDP.
- Maintain contractility.

Preinduction
The preinduction routine and monitoring is the same as for AS.

In chronic AR, a large LVEDV is necessary to ensure an adequate forward CO in the face of regurgitation. Because of the increased ventricular compliance and the right shift of the pressure–volume relationship, the peak A-wave pressure will differ little from mean PCWP. Likewise, LVEDV will be supplemented with only small increases in the mean PCWP. For patients with preserved LV function, a mean PCWP in the range of 10–15 mmHg will ensure optimal LVEDV. Serial COs obtained in conjunction with volume infusion will provide a Frank–Starling relationship curve to identify optimal preload.

For patients with depressed ventricular function who have exhausted preload reserve, optimal preload will occur with a peak A-wave pressure

in the range of 20–25 mmHg. For these patients, afterload reduction is indicated. Sodium nitroprusside is the agent of choice. It is easy to titrate owing to its very short half-life. Start the infusion at 0.15–0.30 μg/kg/min and titrated to effect with careful attention CO, arterial blood pressure, and LVEDP. Although nitroprusside is primarily an arterial vasodilator, it has some vasodilatory effects on the venous system. It is important not to let reductions in preload offset the beneficial effects of arterial dilation. If necessary, volume infusion can maintain PCWP in the range of 10–15 mmHg.

In acute AR in which premature closure of the mitral valve occurs, mean PCWP will underestimate LVEDP. When mitral incompetence from ventricular dilation occurs, mean PCWP will overestimate LVEDP in direct proportion to the amplitude and duration of the regurgitant V wave. These patients are very ill and may require pharmacologic stabilization before induction. Due to the lack of compensatory alterations in the pressure–volume relationship, these patients may have a PCWP in the range of 20–25 mmHg to maintain a low normal cardiac index. Afterload reduction with nitroprusside is indicated. Inotropic support should be added if the cardiac index remains depressed (<2.2 L/min/m^2) or functional MR persists due to a dilated ventricle. Either dopamine (1–5 μg/kg/min) or dobutamine (5–10 μg/kg/min) can be used; neither will cause an elevation of afterload.

Use of an intra-aortic balloon pump is contraindicated in AR because balloon inflation and augmentation of diastolic blood pressure will worsen the regurgitation.

Induction and maintenance

Induction of anesthesia can be accomplished with a number of agents as long as the primary hemodynamic goals are obtained. In stable patients, sodium thiopental or etomidate are appropriate. Alternatively, a high dose narcotic and benzodiazepine induction is safe. In the critically ill patient with acute AR, great caution is advised. Many of these patients require inotropic and vasodilatory support prior to induction of anesthesia. The addition of the anesthetic agents may reduce systemic blood pressure and inotropy to a critically dangerous level.

Muscle relaxants are chosen with optimization of heart rate in mind. In the absence of beta blockade, the vecuronium–fentanyl or vecuronium–sufentanil combination is a good choice if a small heart rate decrease is desired. The pancuronium–fentanyl or pancuronium–sufentanil combination is more likely to cause a heart rate increase, which is advantageous for those patients with bradycardia.

Bradycardia with hemodynamic compromise must be treated promptly. A small dose of pancuronium (1–3 mg) is often effective if vecuronium or cisatracurium has been used. Atropine 0.4–0.8 mg is a reasonable choice despite the risk of tachycardia because tachycardia is well tolerated by these patients. Ephedrine is a poor choice because the concomitant increase in afterload may be detrimental.

Hypotension must not be treated routinely with vasopressors because these arterial vasoconstricting agents may increase the regurgitant volume worsening the situation. If heart rate and preload are optimized, then augmentation of SV with an inotropic agent should be initiated. Dopamine 1–5 μg/kg/min or dobutamine 5–10 μg/kg/min will both augment CO without increasing afterload. When AR occurs in conjunction with an aortic dissection, inotropic agents may worsen the dissection by increasing shear forces on the aortic wall.

In emergency patients deemed at high-risk for aspiration, the induction sequence can be safely modified. Preoxygenation and cricoid pressure are indicated. Induction agents include etomidate 0.15–0.30 mg/kg, succinylcholine 1.0–1.5 mg/kg, in conjunction with fentanyl 10 μg/kg or sufentanil 1 μg/kg. Alternatively, sufentanil 5 μg/kg and succinylcholine 1.0–1.5 mg/kg can be used safely.

Post-CPB management

After aortic valve replacement for chronic AR, the impedance to ventricular ejection increases. The ventricle that has undergone compensation for a volume overload lesion is now faced with a relative pressure overload. The competent aortic valve causes an elevation of ventricular pressure during the isovolumic contraction phase (see Fig. 5.10b). The elimination of regurgitation via the competent valve greatly reduces the need for

a large total SV. Therefore, a greater proportion of total myocardial oxygen consumption goes toward the more energy-consumptive process of pressure generation to begin ejection and less toward volume ejection. Although there is an increase in LV pressure generation, wall stress does not increase substantially because ventricular radius is greatly reduced by elimination of the regurgitant volume. Nonetheless, if poor myocardial protection is obtained during bypass and aortic cross-clamping, or if depressed systolic function exists preoperatively, inotropic support of systolic function may be necessary in the post-bypass period. Epinephrine 0.015–0.030 μg/kg/min, dopamine 1–5 μg/kg/min, or dobutamine 5–10 μg/kg/min are good choices because they provide inotropic support with little vasoconstrictor activity at these doses.

After valve replacement in acute AR, the elimination of the regurgitant fraction allows the ventricle to maintain CO with a much lower LVEDV; therefore, LVEDP drops precipitously. Wall stress falls. Inotropic support may be necessary when preoperative systolic and diastolic dysfunction exists due to subendocardial ischemia or where myocardial preservation on bypass is poor. Epinephrine, dopamine, or dobutamine are good choices.

All LV diastolic filling occurs via the mitral valve when regurgitation is abolished. Therefore, atrial systole becomes more important in ensuring adequate LVEDV. Maintenance of sinus rhythm or AV sequential pacing becomes necessary. Bradycardia will be better tolerated in the post-bypass period.

In chronic AR, there are no significant alterations in the pressure–volume relationship and eccentric hypertrophy for 6–12 months after valve replacement (see Fig. 5.10b). Therefore, LVEDP will remain low, even for large LVEDV. This low LVEDP in combination with the elevation in aortic diastolic blood pressure will greatly improve myocardial oxygen delivery. The temptation when CO is low will be to use the large preload reserve available in these patients. Because ventricular pressure is elevated during the prolonged isovolumic contraction phase, wall stress for a given LVEDV will be greater in the post-bypass period. Efforts to increase preload to contend with poor systolic function or high afterload states will result in afterload mismatch and

declining systolic function. A mean PCWP or LAP of 10–15 mmHg usually is adequate. A better approach would be inotropic support with epinephrine or afterload reduction with sodium nitroprusside as described previously.

In acute AR, there is little or no alteration in the pressure–volume relationship or eccentric hypertrophy and postoperative preload reserve will resemble that of a normal ventricle.

Because the surgical procedure requires an aortotomy with subsequent repair, it is helpful to avoid hypertension, which places undue stress on the aortic suture line. The AV node lies proximal to the aortic valve annulus and may be transiently or permanently damaged after valve replacement. Ventricular pacing may be necessary.

The mitral valve

Anatomy
The mitral valve acquired its name in the sixteenth century because of its resemblance to a bishop's mitre. In a normal heart, the mitral valve separates the left ventricle from the LA, pulmonary circulation, and entire right side of the heart. The valve is bicuspid with an anterior and posterior leaflet. The anterior leaflet is the larger of the two leaflets, accounting for two-thirds of the surface area of the valve. The anterior leaflet base-to-coaptation distance is longer than that of the posterior leaflet. The posterior leaflet wraps around the anterior leaflet, accounting for only one-third of the valve's surface area and two-thirds of the annular circumference. The mitral annulus is a fibrous ring surrounding the mitral valve. The anterior leaflet portion of the annulus is part of the heart's fibrous skeleton. This skeleton also has a common attachment to the left coronary and noncoronary cusps of the aortic valve. The coaptation points of the anterior and posterior leaflets at the annulus are called the anterolateral and posteromedial commissures. The leaflets themselves are attached to the anterolateral and posteromedial papillary muscles via the chordae tendineae. During ventricular systole, the contraction of the papillary muscles prevent mitral leaflet prolapse. The American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists have

adopted the Carpentier classification of the mitral valve. This classification divides the three scallops of the posterior leaflet into P1, P2, and P3. The anterior leaflet is similarly divided into the three segments A1, A2, and A3, which oppose the corresponding scallops of the posterior valve. The coaptation of A1/P1 at the annulus form the anterolateral commissure. The coaptation of A3/P3 at the annulus form the posteromedial commissure.

Mitral stenosis

Mitral stenosis (MS) is almost always rheumatic in origin. Rheumatic fever results in fusion of the mitral valve apparatus in various locations. The site of valve apparatus involvement determines whether the valve will be primarily stenotic or incompetent in nature. Fusion of the cusps and commissures results in a stenotic valve orifice (Fig. 5.11a,b). The valve leaflets may become so rigid that they are incapable of closing, in which case MS and incompetence coexist.

Pathophysiology and adaptation in MS

The left ventricle in MS is typically under filled. The natural history of the disease is a gradual reduction in the mitral valve area from a normal of 4–6 cm^2 to <1 cm^2 over 3–4 decades. The length of diastole, the pressure gradient between the LA and the left ventricle and the mitral valve area, determine LV filling. As the mitral valve orifice decreases in size, there is a gradual increase in impedance to LV filling, and a pressure gradient develops across the valve such that LAP exceeds LV diastolic pressure.

Early in the disease process, complete LV filling occurs without an elevation of mean LAP if diastole is long enough and if an atrial systole exists. As the valve area decreases and the transvalvular gradient rises, a long diastole and an elevated mean LAP are necessary to ensure ventricular filling. Eventually, the valve orifice narrows to the point at which these compensatory mechanisms fail. The pressure–volume loop for MS is illustrated in Fig. 5.12.

Because MS presents a fixed resistance to ventricular inflow and because the atrial systole is of short duration, a large portion of the kinetic energy produced by atrial systole is dissipated in overcoming resistance to inflow. The role of atrial systole in
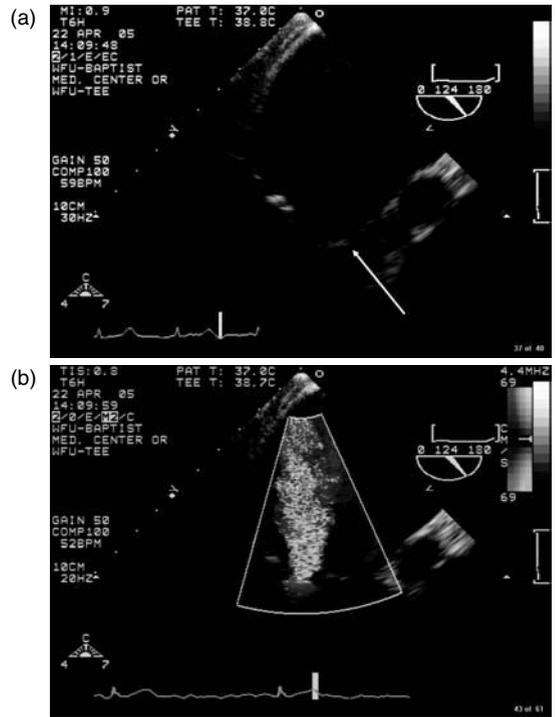
Fig. 5.11 (a) This is a patient with rheumatic mitral valve disease. There is commissural fusion with a classic "hockey stick" deformity of the anterior mitral valve leaflet (arrow) seen in diastole. (b) In systole this same patient now exhibits significant mitral regurgitation. The left atrium is severely dilated. Mixed lesions, mitral stenosis with regurgitation, are common in patients with rheumatic valvular disease.

augmenting LVEDV in MS is less dramatic than in AS but important nonetheless. At heart rates of 80–110 b/min, the loss of atrial systole results in a 20% decrease in diastolic flow per beat and CO in patients with moderate and severe MS. However, in moderate and severe MS, the presence of an atrial systole alone will not maximize LV filling, and an elevation of mean LAP is necessary.

The high LAP that develops as a result of the stenotic mitral valve orifice results in left atrial hypertrophy and left atrial distention. This distension results in the development of atrial dysrhythmias, the most common of which is atrial fibrillation. In severe MS, atrial fibrillation generally is the rule. When atrial systole is lost, diastolic flow is dependant on mean LAP. The higher the
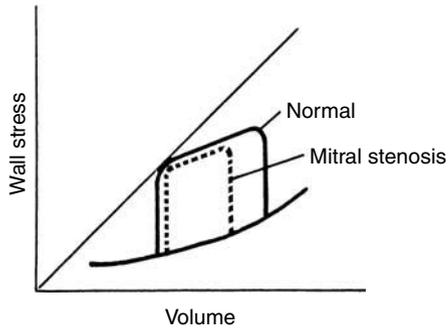
Fig. 5.12 Pressure–volume loop from a patient with mitral stenosis. The left-ventricular end-diastolic volume (LVEDV) is severely limited compared to a normal patient. This preload reduction results in reduced stroke volume and cardiac output. (From DiNardo JA. Anesthesia for valve replacement in patients with acquired valvular heart disease. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:109–40, with permission.)

mean LAP, the more complete the LV filling. Mean LAP is limited by the development of pulmonary congestion, and pressures >25 mmHg are rarely tolerated without symptoms. For a given valve area and LAP, ventricular inflow is determined by the length of diastole.

Ventricular diastolic function and compliance remain unchanged in MS. Despite this, preload reserve is severely limited in this lesion. Maximal LVEDV in moderate and severe MS is well below that seen in patients with normal mitral valves. Mean LAP must be elevated (often to the point of pulmonary congestion) to obtain an LVEDV large enough to meet baseline CO demands. Further increases in mean LAP only slightly augment LVEDV due to the large pressure gradient across the valve. In addition, this further elevation of mean LAP leads to progressive pulmonary congestion and pulmonary edema.

There are no special considerations regarding myocardial oxygen balance in patients with MS. It is important, however, to keep in mind the relationship between the length of diastole, aortic diastolic pressure, and LVEDP on subendocardial perfusion. It is also important to determine the extent of coronary artery disease in patients with MS and angina pectoris.

Myocardial fibrosis in the posterobasal region of the LV may result in segmental wall motion abnormalities and reduced systolic performance in patients with rheumatic MS. Patients with MS have normal indices of LV contractility, but have a reduced EF due to limited preload.

The prolonged elevations of LAP seen in progressive MS have profound effects on the pulmonary vasculature and RV function. Early in the disease, elevated LAP is transmitted to the pulmonary venous system, and there is reversible passive elevation of the pulmonary artery pressures while PVR remains normal (Fig. 5.13). RV function remains unchanged.

As the disease progresses, reactive changes occur in the pulmonary vasculature. Prolonged perivascular edema results in arterial intimal fibroelastosis and nonreversible elevations in PVR. Progression of this process presents a large increase in RV afterload or a "second stenosis" (see Fig. 5.13). The RV is poorly adapted to generate pressures that approach systemic. As a result, afterload mismatch occurs, the RV invariably fails, and the RV output falls. Peripheral edema and hepatic congestion ensue. RV failure and dilation also may lead to functional tricuspid regurgitation and worsening symptoms of right heart failure. In the steady-state, RV output and LV output must be equal. Therefore, LV output is limited by RV failure. Efforts to reduce RV afterload and improve RV output with nitroprusside significantly improve systemic output in patients with elevated PVR.

Figure 5.8 illustrates the reduction in diastolic filling time that accompanies an increase in heart rate. If CO is to remain constant as heart rate increases, then the flow rate across the mitral valve in diastole must increase. Recall that as flow rate increases across the stenotic valve, the gradient across the valve will increase by the square of the flow. Thus, the requirement for increased flow can result in prohibitive increases in mean LAP.

Figure 5.14(a–c) illustrates the effect of heart rate changes in MS. Higher heart rates can potentially improve CO when SV is small. However, in MS, the transvalvular gradient increases so dramatically with tachycardia that prohibits increases in mean LAP ensue. At slower rates, more diastolic filling
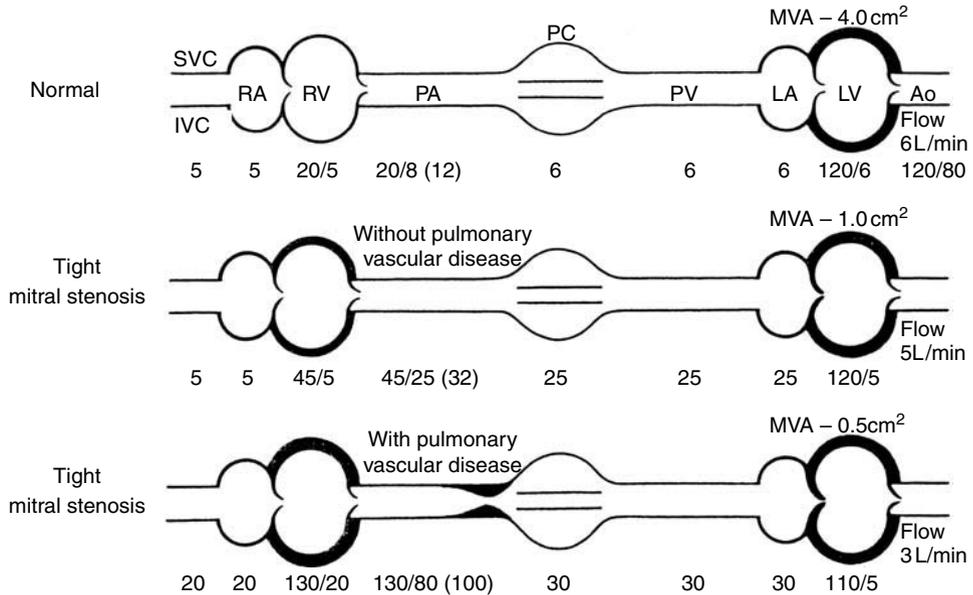
Fig. 5.13 Illustration of changes seen with progression of mitral stenosis (MS). Pressure in each of cardiac chambers and great vessels is indicated.

In MS without pulmonary vascular disease, there is reversible passive elevation of pulmonary vein (PV), pulmonary capillary (PC), and pulmonary artery (PA) pressures while pulmonary vascular resistance remains normal. These elevations are secondary to elevation of left atrium (LA) pressure, which is necessary to maintain left ventricle (LV) filling across stenotic mitral valve. Right ventricle (RV) pressure is elevated in response to elevated PA pressure, and RV concentric hypertrophy may result. RV systolic dysfunction usually is not present.

In MS with pulmonary vascular disease, PA pressure is elevated far in excess of LA, PC, and PV pressures because of the presence of pulmonary arterial occlusive disease with elevated pulmonary vascular resistance. This results in a second stenosis at the level of the PA. This second stenosis causes dramatic elevations in RV pressure. This RV pressure elevation may result in reduced RV stroke volume due to afterload mismatch and to tricuspid regurgitation due to RV dilation. Reduction in RV stroke volume results directly in a decrease in systemic cardiac output. Similar changes would be expected over time in patients with sustained elevations in LA pressure due to mitral regurgitation. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; MVA, mitral valve area; PA, pulmonary artery; PC, pulmonary capillary; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava. (From Grossman W. Profile of heart disease. In: Baim DS, Grossman W (eds). *Cardiac Catheterization, Angiography and Intervention*, 5th edn. Baltimore: Williams & Wilkins, 1996:735–56, with permission.)

time is available to augment LVEDV, but CO is compromised by bradycardia unless LVEDV is large. Large LVEDVs require a further increase in mean LAP as ventricular compliance diminishes at higher LVEDVs. For these reasons, heart rates between 70 and 90 b/min are optimal.

Most patients with moderate and severe MS are in atrial fibrillation. In these patients, control of heart rate is dependent on adequate control of the ventricular response rate to the fibrillating atrium. Drugs used to control the ventricular response rate by producing AV nodal block such as digoxin, diltiazem, and beta-blockers must be continued.

Patients with MS have severely limited preload reserve, as discussed previously. Some patients may have depressed systolic function due to posterobasal wall motion abnormalities. In addition, high baseline afterload states may limit SV in other patients. For these reasons, patients with MS tolerate large increases in afterload poorly because it is likely to cause afterload mismatch. LV afterload reduction is fraught with hazard because of the limited
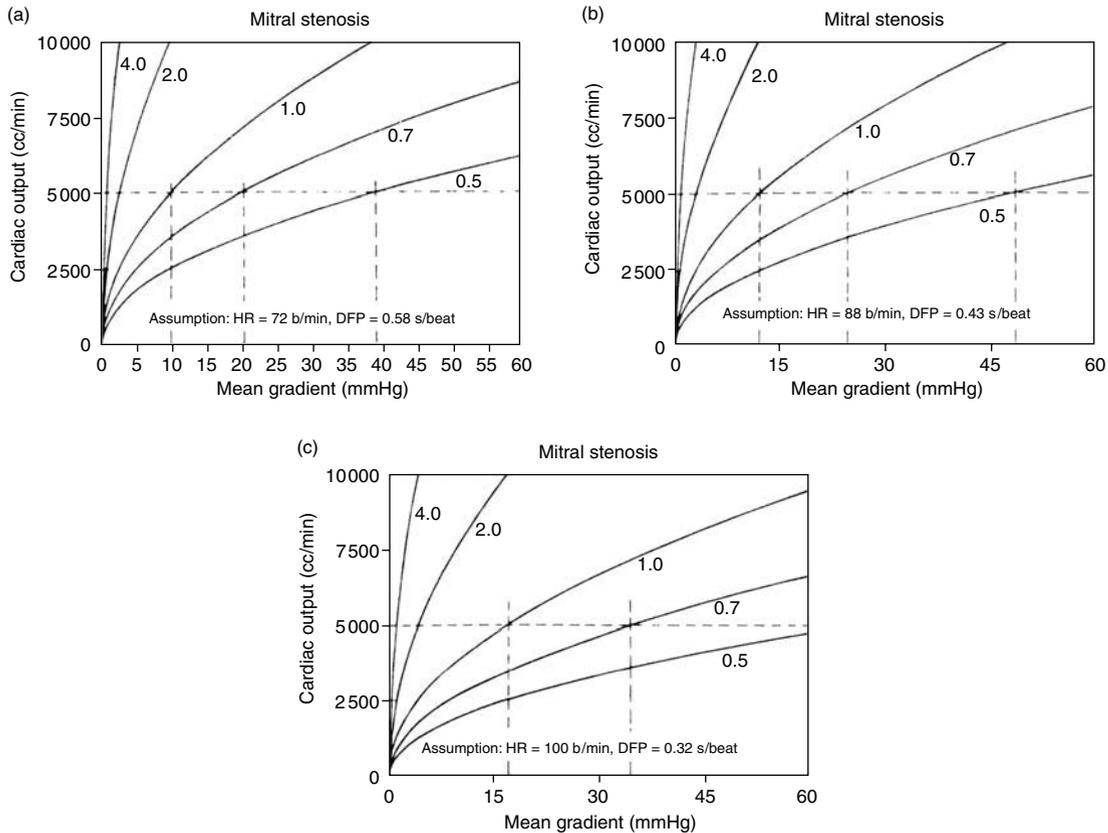
Fig. 5.14   The relationship of heart rate (HR), cardiac output (CO), mitral valve area, and diastolic pressure gradient across the mitral valve is illustrated for patients with mitral stenosis. CO is plotted against diastolic pressure gradient for mitral valve areas ranging from 0.5–4.0 cm^2. (a) Plot illustrates these relationships for HR of 72 b/min and diastolic filling period (DFP) of 0.58 s/beat. (b) Plot illustrates these relationships for HR of 88 b/min and DFP of 0.43 s/beat. (c) Plot illustrates these relationships for HR of 100 b/min and DFP of 0.32 s/beat.

It is clear that for given CO and HR, diastolic pressure gradient increases as mitral valve area decreases. Furthermore, for a given CO and mitral valve area, the diastolic pressure gradient increases as HR increases.

With CO constant, an increase in HR requires that a smaller volume cross the stenotic mitral valve during the DFP. This should result in reduction in diastolic pressure gradient. However, increases in HR in the range examined here progressively shorten the length of DFP. Reduction in DFP requires that volume move across stenotic mitral valve in less time, which increases diastolic pressure gradient. Shortening of DFP is the more important determinant of diastolic pressure gradient at HRs illustrated here. (From DiNardo JA. Anesthesia for valve replacement in patients with acquired valvular heart disease. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:109–40, with permission.)

preload reserve in these patients. Recall that after-load reduction will increase SV by reducing LVESV if LVEDV is maintained. Recall also that LVEDV is below normal in these patients and small decreases in mean LAP will result in large decreases in LVEDV

due to the mitral valve gradient. Because afterload reduction invariably results in some preload reduction due to venodilation, great care must be taken to maintain preload in these patients when afterload reducing agents are used.

Critical MS

The term "critical mitral stenosis" commonly describes mitral valve disease. Typically, it is used to describe patients with mitral valve areas <1.0 cm^2. As with AS, the term "critical MS" properly describes a specific pathophysiologic state, rather than an absolute valve area. Critical MS exists when LA pressure is elevated producing pulmonary venous congestion at rest. In the presence of diastolic and systolic dysfunction or poorly controlled atrial fibrillation or flutter, critical MS may exist with larger valve areas.

Anesthetic technique in MS

Goals

- Maintain sinus rhythm when possible; control ventricular rate in atrial fibrillation.
- Maintain heart rate at 70–90 b/min; slower better than faster.
- Maintain PCWP high enough to ensure as large an LVEDV as possible without pulmonary edema.
- Maintain a normal LV afterload; increases are poorly tolerated. Decreasing afterload is warranted when LV systolic function is poor and afterload is high. In this instance, preload must be maintained.
- Maintain contractility.
- When PVR is high and RV systolic performance is poor, RV afterload reduction will improve RV and LV output. Caution must be exercised so that excessive systemic vasodilation does not result.
- Avoid hypercarbia, hypoxemia, and acidemia that tend to cause pulmonary hypertension and may result in acute RV decompensation.

Preinduction

Standard monitoring and IV access is required. Although placement of a pulmonary artery catheter can be safely performed after the induction of general anesthesia, placement of the pulmonary artery catheter before induction allows recording baseline values and optimization of preload and afterload. The insertion distance necessary to obtain a wedge pressure trace is greater (5 cm more via the right internal jugular route) in patients with pulmonary hypertension than in normal patients. The risk of pulmonary artery perforation is greater in patients

with pulmonary hypertension. Pulmonary artery rupture may be due to eccentric balloon inflation forcing the catheter tip into the wall of vessel, vessel rupture from balloon over-inflation, or distal catheter migration during balloon deflation.

Patients in sinus rhythm will have a very large A wave on the PCWP trace, which can be used to estimate LVEDP. Patients in atrial fibrillation have no A wave, and mean PCWP can be used. It must be remembered that both the A-wave pressure and the mean PCWP will overestimate the LVEDP. The error is compounded (overestimated) with a smaller valve area and elevated heart rate. The cardiac catheterization report will provide information as to the relationship between mean PCWP and LVEDP in a given patient. In general, for patients with moderate to severe MS, a mean PCWP of 20–30 mmHg will optimize LVEPV. Some patients may present in heart failure and require diuresis preoperatively.

The pulmonary artery catheter allows calculation of PVR and measurement of pulmonary artery and central venous pressures (CVPs). This information is essential in treating RV afterload and improving RV systolic performance.

For patients with severe RV failure, pulmonary congestion, and systemic hypotension (systolic blood pressure below 90 mmHg), efforts to improve RV function with vasodilator therapy may be unsuccessful due to worsening systemic hypotension. For these patients, the addition of inotropic support is necessary. Dobutamine 5–10 μg/kg/min is a good choice because it has no α-adrenergic activity and little chronotropic activity, and it tends to reduce pulmonary artery pressures. Therefore, it will not exacerbate pulmonary artery hypertension or cause tachycardia. Other agents of benefit include epinephrine 0.03 μg/kg/min or milrinone 0.5 μg/kg/min.

Induction and maintenance

Adherence to the hemodynamic goals rather than a specific agent is the most important consideration in choosing an induction and maintenance plan for anesthesia.

Hypotension may be treated initially with volume infusion if PCWP has decreased and with cautious use of phenylephrine 40–80 μg. After preload and

heart rate are optimized, it may be necessary to use an inotropic agent. As discussed previously, dobutamine, epinephrine and milrinone are all appropriate choices.

If surgical stimulation (skin incision, sternotomy, sternal spreading, or aortic manipulation) produces hypertension, additional doses of sufentanil (1–2 μg/kg) or fentanyl (5–10 μg/kg) may be necessary. If this fails to control the hypertension, the use of additional agents will be necessary. Benzodiazepines and inhalational agents in combination with narcotics will cause vasodilation in patients and reduce blood pressure. Vasodilation with sodium nitroprusside can be titrated easily and terminated quickly. This makes it an ideal choice for treatment of transient elevations in peripheral vascular resistance.

Post-CPB management

After mitral valve replacement for MS, a small mean gradient of 2–5 mmHg usually exists across the prosthetic valve. Mechanical valves exhibit a small amount of regurgitant flow in systole (Fig. 5.15a,b). Repaired mitral valves may exhibit some residual mild regurgitation and stenosis. TEE allows the anesthesiologist and surgeon an excellent opportunity to evaluate the new valve structure and function. A full examination of the valve including color Doppler and pressure gradients is required. A dramatic improvement in LV filling via the LA after replacement or repair is expected. As a result, preload reserve is greatly improved. This makes LV afterload mismatch less likely and allows augmentation of CO via increases in preload even when preoperative systolic dysfunction exists. A mean PCWP or LAP of 10–15 mmHg usually is adequate to take advantage of this increased preload reserve.

Patients in atrial fibrillation with large left atria rarely convert to sinus rhythm postoperatively. Although the reduction in the transvalvular gradient allows greater hemodynamic tolerance with tachycardia, control of the ventricular response rate is important to allow adequate time in diastole to fill the LV.

The management of RV function and the pulmonary vasculature can be problematic in the post-bypass period. In all patients with elevated
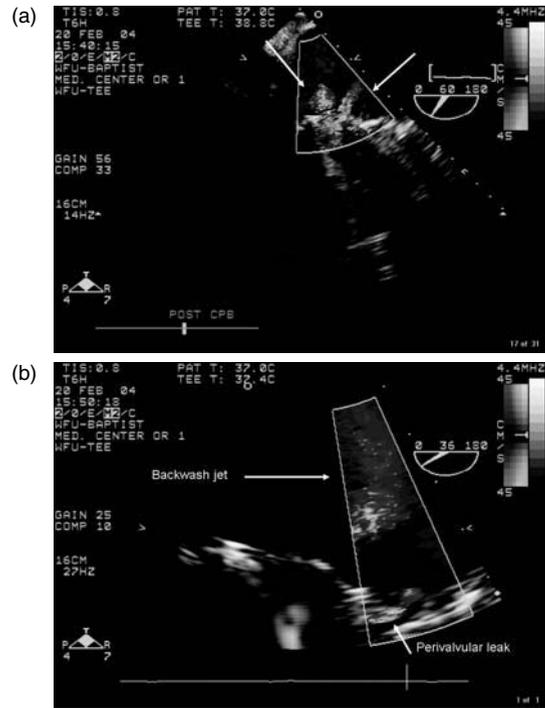
Fig. 5.15 (a) Replacement of the mitral valve with a St. Jude mechanical valve yields a characteristic regurgitant pattern. The regurgitant "flames" are normal backwash from the valve closure (arrows). (b) In this patient there is a significant perivalvular leak around the St. Jude valve (arrow). Note the normal regurgitant backwash next to the perivalvular leak.

pulmonary artery pressures, there will be a dramatic reduction in pulmonary artery pressures due to the reductions in the mean LAP and passive pulmonary congestion after valve replacement. Despite this, some patients will continue to have elevated PVR due to reversible (reactive pulmonary vasoconstriction) and nonreversible (morphologic changes in the pulmonary vasculature) causes. For these patients, careful management is necessary. LV SV depends on proper RV function. In RV failure, there is inadequate transit of blood to the left heart and CO falls. The hallmarks of this syndrome are a high right atrial pressure (RAP) (>10 mmHg) and PVR (over 150 dynes/s/cm^5), coupled with a low LAP (<5 mmHg) and cardiac index (<2.2 L/min/m^2). The clinician should aggressively strive to keep

PVR as low as possible by avoiding hypercarbia, hypoxemia, and acidemia, and by avoiding pulmonary vasoconstrictors. If pulmonary hypertension persists despite these efforts, then active pulmonary vasodilation will be necessary. Nitroglycerin has been shown to be effective in reducing pulmonary artery pressures and increasing pulmonary blood flow after mitral valve replacement. Nitroglycerin can be started at 0.15–0.30 µg/kg/min and titrated upward as needed. Sodium nitroprusside started at the same dosage and titrated upward also is effective. Other effective pulmonary vasodilators include inhaled nitric oxide (NO) and prostacyclin (PGI_2). These agents are discussed in detail in Chapter 7.

In some patients, inotropic support of the RV may be necessary in addition to pulmonary vasodilation. Inotropic support without increased PVR is ideal. Epinephrine 0.015–0.030 µg/kg/min, dopamine 1–5 µg/kg/min, or dobutamine 5–10 µg/kg/min all meet this goal. Increased doses of epinephrine and dopamine may result in progressive pulmonary vasoconstriction from increased α-adrenergic activity. In situations in which increasing demand for inotropic support is required, milrinone 0.5–0.75 µg/kg/min after a loading dose of 50–75 µg/kg may be added. Milrinone, a phosphodiesterase III inhibitor, provides potent inotropic support and pulmonary vasodilation. Isoproterenol, a potent β_1-agonist offers can improve inotropy and induce pulmonary vasodilation; however, isoproterenol is associated with an increase in heart rate, myocardial oxygen consumption, and the incidence of ventricular dysrhythmias, all of which may limit its usefulness. The combination of prostaglandin E_1 (PGE_1) and norepinephrine is effective in treating refractory pulmonary hypertension and RV failure after mitral valve replacement. PGE_1 is a potent pulmonary and systemic vasodilator. PGE_1 30–150 ng/kg/min is infused into the right heart in combination with norepinephrine in doses up to 1–2 µg/kg/min infused via a left atrial line. The norepinephrine is infused via the left atrial line to minimize its vasoconstricting effects on the pulmonary vasculature, provide inotropic support, and counteract the profound systemic vasodilatory effects of PGE_1. Management of RV dysfunction, including TEE findings are discussed in detail in Chapter 7.

A rare but potentially lethal complication of mitral valve replacement is ventricular disruption. This complication has been described after mitral valve replacement for a variety of lesions, but is most common in patients undergoing replacement for chronic MS. Three types of ventricular rupture are described. Type 1 involves rupture of the mitral annulus or of the ventricle at the atrioventricular junction due to a diseased annulus or posterior ventricular wall. Type 2 rupture occurs at the site of the excised papillary muscle due to surgically-induced thinning of the ventricular wall. Type 3 rupture or transverse mid-ventricular disruption (TMD) occurs midway between type 1 and 2 ruptures. Type 3 ruptures are secondary to a variety of causes. Endocardial injury from inadvertent surgical trauma or the valve prosthesis may be involved. Total excision of the mitral valve apparatus may result in loss of longitudinal support, which predisposes the ventricle to transverse disruption when ventricular dilation occurs.

Goals
- Maintain the ventricular response rate to atrial fibrillation below 100 b/min in absence of normal sinus rhythm.
- Maintain LAP high enough to take advantage of the increased preload reserve.
- Avoid pulmonary artery hypertension by treating hypercarbia, hypoxemia, and acidemia.
- Aggressively treat pulmonary artery hypertension with vasodilator therapy to avoid RV failure. If RV failure does occur, inotropic support of the RV and pulmonary vasodilation may be necessary.
- Maintain awareness of potential for LV rupture.

Mitral regurgitation (MR)
Any abnormality of the mitral valve apparatus may cause MR. The most common cause in the western countries is myxomatous mitral valve disease (Barlow syndrome). This condition is characterized by a prolapse of one or more valve segments into the LA. There is elongated or ruptured chordae, a thickened valve, and dilated annulus. Other causes include mechanical impairment due to
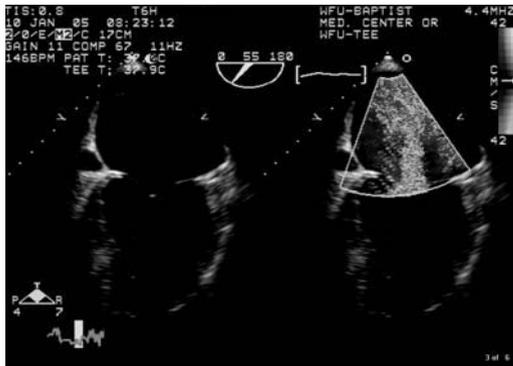
Fig. 5.16 Severe ischemic mitral regurgitation in the color compare mode. Note the dilated left ventricle and the central mitral regurgitation jet.

rheumatic fever, trauma, or infective endocarditis. Calcification of the valve annulus may result in mechanical impairment of leaflet apposition. Functional impairment of leaflet apposition due to annular dilation may result from ventricular dilation caused by ischemia or a dilated cardiomyopathy (Fig. 5.16). Mechanical impairment may result from rupture of the *chordae tendinae*. Infective endocarditis, rheumatic fever, trauma, or long-standing strain from mitral valve prolapse may result in *chordae tendinae* rupture.

Ischemia may cause ventricular wall motion abnormalities or papillary muscle dysfunction leading to regurgitation. The posterior papillary muscles are more vulnerable to ischemia than the anterior papillary muscles. This occurs because the posterior papillary muscle is supplied with blood solely from the posterior descending artery; whereas the anterior papillary muscle derives its blood supply from branches of both the left anterior descending and circumflex arteries. With continued ischemia, papillary muscle dysfunction may progress to necrosis and rupture of the papillary muscle. Classically, rupture of one or more of the papillary muscle heads from necrosis occurs 2–7 days after an inferior myocardial infarction. This leads to acute, severe MR.

Pathophysiology and adaptation in MR

MR is an LV volume overload lesion that can be either acute or chronic. In essence, a double-outlet left ventricle exists. There is a low-impedance outflow tract into the low-pressure LA via the incompetent mitral valve, and a high-impedance outflow tract into the high-pressure aorta via the aortic valve. The extent of regurgitation depends on the size of the mitral valve orifice, the time available for regurgitation (systole), and the pressure gradient between the LA and LV. The area of the mitral valve orifice is determined, in part, by the size of the LV. Dilation of the LV will result in distortion and enlargement of the valve orifice. Ventricular systolic pressure, LA pressure, and LA compliance all contribute to the valve gradient.

Regurgitant flow ceases when the LV and LA pressures equalize. Equalization of pressure will occur more rapidly when a small, noncompliant LA exists, because LA pressure will rise more rapidly than in a large compliant atrium. Equalization of pressure also occurs more rapidly when the impedance to LV ejection in the aorta is low. When aortic impedance is low, there is a larger forward SV, and equalization of pressure will occur quickly.

Chronic volume overloading of the left ventricle results in eccentric ventricular hypertrophy similar to that seen in AR. The results of this process are summarized in Fig. 5.17. As in AR, both LVESV and LVEDV increase, but LVEDV increases to a greater extent. This results in an enhanced SV with no need for an increased EF. The slope of the diastolic pressure–volume curve is little changed, and thus, compliance is only slightly increased. The entire pressure–volume loop is shifted to the right. This rightward shift of the diastolic pressure–volume curve allows low diastolic pressures at very large end-diastolic volumes. The large increase in ventricular radius that accompanies eccentric hypertrophy elevates wall stress and stimulates some degree of concentric hypertrophy. Unlike AR, this compensation is complete and wall stress is normalized in both end systole and end diastole (Fig. 5.17a).

Unique LV pressure loading exists in chronic MR, as illustrated in Fig. 5.17a. The isovolumic phase of ventricular systole is of very short duration and limited pressure generation. In fact, because the impedance to ejection into the LA is so low, the isovolumic phase is shorter and lower in pressure than that seen in AR. This allows a greater portion

(a)

(b)
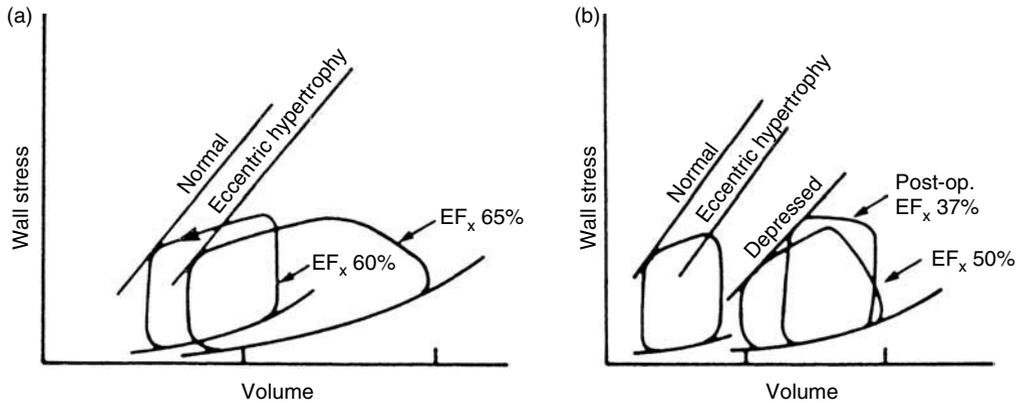
Fig. 5.17 Left ventricular wall stress–volume loops for a patient with progressive mitral regurgitation (MR). (a) Wall stress–volume loops of normal ventricle and of ventricle having developed eccentric hypertrophy in response to chronic volume overload of MR. The ventricle with eccentric hypertrophy has reduced isovolumic contraction phase and has its entire wall stress–volume relationship shifted to the right. The isovolumic contraction phase is even shorter than seen in aortic regurgitation (see Fig. 5.10). In addition, end-systolic wall stress is normalized. These adaptations allow the ventricle to deliver large stroke volume (SV) with high normal ejection fraction (EF). (b) Wall stress–volume relationships in ventricle with chronic mitral regurgitation and systolic dysfunction.

Low-impedance outflow tract to the left atrium provided by an incompetent mitral valve allows wall stress to remain low during early and late ventricular systole. Thus, despite the presence of systolic dysfunction, EF is maintained near normal (EF = 50%). After surgical replacement of mitral valve, the low-impedance outflow tract to the left atrium is abolished. This results in an elevation of wall stress during early and late systole. Under these loading conditions, afterload mismatch occurs and ventricular systolic dysfunction manifests as reduced EF (EF = 37%). Post-op., postoperative. (From Ross J Jr. Left ventricular function and the timing of surgical treatment in valvular heart disease. *Ann Intern Med* 1981;**94**:498–504, with permission.)

of myocardial energy expenditure directed toward ejecting a large volume and less toward overcoming impedance to begin ejection.

In chronic MR, the sustained high LAP results in left atrial hypertrophy and eventually left atrial distension. This distension results in the development of atrial dysrhythmias, the most common of which is atrial fibrillation. In severe MR, atrial fibrillation rather than sinus rhythm generally is the rule.

In acute MR, there is not ample time for ventricular eccentric hypertrophy to occur. As a result, the ventricle does not have the enormous preload reserve available in chronic MR. Of greater importance, is the status of the LA. In acute MR, a small, noncompliant LA exists. Regurgitation of volume into a small LA results in high LA pressures, which manifests as a regurgitant V wave. The height of the V wave does not quantify the regurgitant volume but rather is an indicator of the relationship between

regurgitant volume and LA compliance. Nonetheless, this elevation of LA pressure results in acute pulmonary congestion.

In chronic MR, as in AR, a large total SV is necessary to maintain forward SV when the regurgitant volume is large. An atrial kick is helpful in augmenting LVEDV; however, the increased compliance and rightward shift of the diastolic pressure–volume curve allows passive filling of the LV in early and mid-diastole when atrial fibrillation exists.

In acute MR, increased ventricular compliance and a rightward shift of the diastolic pressure–volume curve are absent. In this setting, an atrial systole may be necessary to increase the left atrial to LV pressure gradient enough to complete filling of the left ventricle via the LA.

In chronic MR, eccentric hypertrophy and a right shift in the pressure–volume curve allow large increases in LVEDV with minimal increases

in LVEDP. This affords a great deal of preload reserve. Unfortunately, the ventricular dilation that accompanies increases in LVEDV results in enlargement of the mitral annulus and an increase in the regurgitant fraction.

In contrast, in acute MR preload reserve is nearly exhausted. Without adequate time for adaptation, the left ventricle operates on the steep portion of its diastolic pressure–volume curve. Again, preload augmentation may result in ventricular dilation and a worsening of the regurgitation.

Myocardial oxygen consumption is altered in MR. There is an increase in oxygen consumption due to the large mass of myocardium that must be supplied with oxygen and the enormous volume work done by the left ventricle. Volume work increases oxygen consumption, but to a much lesser extent than pressure work. The isovolumic contraction phase is highly energy-consumptive. Because of the low impedance to ejection into the LA, the isovolumic contraction phase is very brief and represents only a small portion of the total work done by the ventricle (see Fig. 5.17a). A greater portion of the total workload is devoted to the generation of volume ejection, which is an energy efficient process.

In addition to the increased myocardial oxygen demands, oxygen supply is compromised when there are coexistent coronary artery stenoses. This is particularly important for patients with acute MR from papillary muscle rupture or dysfunction. Fortunately, unlike AR, aortic diastolic blood pressure is normal, which helps maintain the gradient for coronary blood flow. Further impairment of supply occurs because of the high LV end-diastolic pressures that accompany acute MR. In acute MR, eccentric hypertrophy has not had time to occur, and large LVEDV is accompanied by large LVEDP.

Patients with chronic MR may remain symptom-free for years despite progressive decreases in systolic function. The enormous preload reserve available to these patients allows maintenance of SV by progressive increases in LVEDV in the face of declining contractile function and increasing LVESV. When preload reserve is exhausted, further diminution in systolic function goes uncompensated and SV falls. At this point, symptoms of reduced CO and CHF appear (Fig. 5.17b). There is usually significant systolic impairment in patients with acute MR secondary to ischemia.

EF will greatly overestimate systolic function in MR because a portion of the SV is ejected backwards as mitral regurgitant volume. Recall that EF determinations are very afterload-dependent. In MR, the impedance to ejection via the incompetent mitral valve is low. Therefore, EF may remain in the normal range despite severe systolic dysfunction. This severe dysfunction may only become apparent after mitral valve repair or replacement when the low-impedance outflow tract is eliminated (see Fig. 5.17b).

The large, compliant LA that develops in chronic MR tends to shield the pulmonary circulation from elevated LA pressures. With time, however, pulmonary artery hypertension will develop from passive pulmonary venous distension. If LA pressures remain elevated over a long period, reactive changes occur in the pulmonary vasculature. Prolonged perivascular edema results in arterial intimal fibroelastosis and nonreversible elevations in pulmonary artery pressures and PVR. RV dysfunction from afterload mismatch may develop, as occurs in MS (see Fig. 5.13). In the most severe instances, tricuspid regurgitation from RV distension will complicate the picture. Pulmonary vasodilators may reduce RV afterload and improve RV output in patients with elevated PVR.

In acute MR the small, noncompliant LA is poorly adapted to shield the pulmonary vasculature from the regurgitant volume. Regurgitation of volume into the noncompliant LA results in profound and immediate elevation of LAP with a very large V wave. Pulmonary vascular congestion with interstitial pulmonary edema rather than secondary pulmonary artery hypertension is the issue here. RV systolic dysfunction may exist because reductions in posterior descending coronary artery perfusion severe enough to produce posterior papillary muscle dysfunction or infarction also may produce RV ischemia or infarction.

Bradycardia (heart rate < 60 b/min) is detrimental in MR because it prolongs systole, which increases the time available for regurgitation. In addition, bradycardia prolongs diastole allowing a large LVEDV to develop. This may result

in LV distension, particularly in acute MR, in which eccentric hypertrophy and pressure–volume compensation are absent. LV distension leads to enlargement of the mitral annulus and worsening regurgitation. Finally, when the regurgitant fraction is large (50–60%), total SV will be large but forward SV low. Elevating the heart rate enhances forward flow in this situation.

Efforts to increase heart rate into the optimal range of 80–100 b/min are balanced with the increased oxygen demand and decreased oxygen supply with tachycardia. This is particularly important for patients who have MR secondary to papillary muscle rupture or dysfunction from ischemia.

Most patients with moderate and severe MR are in atrial fibrillation. In these patients, control of heart rate is dependent on adequate control of the ventricular response rate to the fibrillating atrium. Drugs used to control the ventricular response rate at the AV node, such as digoxin, diltiazem, and beta-blockers, must be continued.

Increased afterload is poorly tolerated by patients with acute and chronic MR because it increases the regurgitant fraction. Increased afterload tends to increase the size of the LV by increasing LVESV, followed by a compensatory increase in LVEDV. This LV dilation increases the size of the mitral orifice. Increased afterload also increases the impedance to aortic ejection. This favors ejection into the LA via the lower impedance outflow tract.

Unlike AR, in which afterload reduction must be used selectively, afterload reduction is uniformly advantageous in both acute and chronic MR. Afterload reduction improves forward CO by promoting ejection via the aorta and reducing the regurgitant fraction. This is because the incompetent mitral valve provides such low impedance to ejection that any decrease in the impedance to ejection via the aortic valve will augment forward flow.

Anesthetic technique in MR

Goals
- Maintain sinus rhythm when possible.
- Maintain heart rate at 80–100 b/min; faster better than slower.
- Maintain end-diastolic PCWP high enough to guarantee a large LVEDV without ventricular distension and increased valve area.
- Decrease LV afterload; increases are poorly tolerated. Decreasing afterload will improve CO by decreasing regurgitation but preload must be maintained.
- Maintain contractility; there may be significant LV dysfunction.
- When PVR is high or when RV systolic dysfunction exists RV afterload reduction will improve RV and subsequently LV output. The concurrent systemic vasodilation also will directly reduce regurgitation.
- Avoid hypercarbia, hypoxemia, and acidemia which tend to cause pulmonary hypertension and may result in acute RV decompensation.

Premedication
For patients with acute MR, severe hemodynamic compromise usually is the rule. It is dangerous to sedate these patients before surgery. All sedatives and narcotics should be given with careful observation of the fully monitored patient. In chronic MR, the usual cautions are appropriate when considering premedication.

Preinduction
The V wave and the mean PCWP are not good estimates of LVEDP in patients with MR. Recall that the V wave occurs during early ventricular systole and quantifies the relationship between the regurgitant volume and left atrial compliance. The mean PCWP is skewed upward by a large V wave and will, therefore, overestimate the LVEDP by an amount proportional to the amplitude and duration of the V wave. The best estimate of LVEDP is the end-diastolic PCWP. In patients in sinus rhythm, this will be the A-wave pressure. In patients in atrial fibrillation, it will be the PCWP just before the onset of the V wave. The cardiac catheterization report will provide information regarding the optimal LVEDP in a given patient. The pulmonary artery catheter allows PVR to be calculated as well as measurement of the CVP. Therapy to reduce RV afterload and improve RV systolic performance cannot be initiated safely without this information.

In chronic MR, because of the increased ventricular compliance and the right shift in the pressure–volume relationship, LVEDV will be supplemented with only small increases in the mean PCWP. In patients with preserved LV function, a mean PCWP in the range of 10–15 mmHg will usually ensure optimal LVEDV. In patients with depressed ventricular function and exhausted preload reserve, PCWP will be in the range of 20–25 mmHg are sometimes required for optimal loading conditions.

In acute MR, there will be large V waves and LVEDP will be elevated because of the lack of compensatory atrial and ventricular enlargement. It may be necessary to have an end-diastolic PCWP of 20–25 mmHg to ensure an adequate LVEDV in patients with acute MR.

For patients in whom afterload reduction is required before induction, sodium nitroprusside is the agent of choice. It is easily titratable with a very short half-life. The infusion can be started at 0.15–0.30 μg/kg/min and titrated with careful attention paid to CO, arterial blood pressure, and PCWP. Nitroprusside is primarily an arterial vasodilator; however, it has vasodilatory effects on the venous system as well. It is important not to let reductions in preload offset the beneficial effects of arterial dilation. If necessary, volume infusion can maintain PCWP in the optimal range.

For patients with severe RV failure, pulmonary congestion, and systemic hypotension (systolic blood pressure < 90 mmHg), efforts to improve RV function and reduce regurgitation with vasodilator therapy may be unsuccessful due to worsening systemic hypotension. For these patients, the addition of inotropic support of the RV and LV is necessary. Dobutamine 5–10 μg/kg/min is a good choice because it has no α-adrenergic activity, little chronotropic activity and it tends to reduce pulmonary artery pressures. Therefore, it will not exacerbate pulmonary artery hypertension or increase LV afterload and regurgitation.

In patients with myocardial ischemia, efforts must be directed toward lowering LVEDP, decreasing ventricular radius, improving aortic diastolic blood pressure, and decreasing heart rate as much as is possible without worsening the regurgitant process. IV nitroglycerin is a mainstay of therapy.

Dobutamine 5–10 μg/kg/min is a good choice if an inotropic agent is necessary. It reduces LV radius and end-diastolic pressure while increasing aortic blood pressure and causing little change in heart rate. In patients with MR, the resultant reduction in wall stress and the valve orifice area will serve to decrease both myocardial oxygen consumption and the regurgitant volume. When pharmacologic interventions fail, the use of the intra-aortic balloon pump (IABP) may be indicated.

Induction and maintenance

Patients with chronic, stable MR usually tolerate induction without significant hemodynamic compromise. Etomidate, pentothal, ketamine, or propofol are all appropriate agents. Hypotension may be treated with vasopressors; however, caution is urged because in some patients, increasing afterload will increase the regurgitant volume which worsens the situation. In all patients heart rate and preload must be optimal. If inotropic support is required, dobutamine 5–10 μg/kg/min can augment CO without increasing afterload or worsening pulmonary artery hypertension.

Many patients with acute MR from myocardial ischemia or infarction will be in cardiogenic shock with possible respiratory distress from pulmonary vascular congestion. These patients may arrive from the cardiac catheterization laboratory or ICU intubated, on inotropes, and supported with an IABP. Narcotics, small dose benzodiazepines, and muscle relaxants are appropriate in this group of patients. In nonintubated patients with acute MR, the induction sequence should be modified to account for the hemodynamic condition and the higher risk of aspiration. After preoxygenation and with cricoid pressure applied, etomidate 0.15–0.30 mg/kg, succinylcholine 1.0–1.5 mg/kg, in conjunction with fentanyl 10 μg/kg or sufentanil 1 μg/kg can be administered. Alternatively, sufentanil 5 μg/kg and succinylcholine 1.0–1.5 mg/kg can be used.

Post-CPB management

Repaired mitral valves may exhibit some residual mild regurgitation and stenosis. TEE is essential in evaluating valvular repairs.

After mitral valve replacement or repair for chronic MR, the ventricle is now faced with a relative pressure overload. The competent mitral valve eliminates the low-impedance outflow into the LA. Ejection of the SV is now directed out the high-impedance outflow tract into the aorta. This causes a substantial elevation of ventricular pressure during the isovolumic contraction phase. The elimination of regurgitation by the competent valve greatly reduces the need for a large total SV. Therefore, a greater proportion of total myocardial oxygen consumption goes toward the more energy-consumptive process of pressure generation to begin ejection and less toward volume ejection. There is an elevation of early and late systolic wall stress. This occurs despite the dramatic reduction in ventricular radius that accompanies elimination of the regurgitant volume (see Fig. 5.17b). This results in a state of afterload mismatch such that postoperative systolic function is compromised. The temptation when CO is low will be to use the large preload reserve available in these patients. Because ventricular pressure is already elevated, during the prolonged isovolumic contraction phase wall stress for a given LVEDV will be greater in the post-bypass period. Efforts to increase preload to contend with poor systolic function or high afterload states will only worsen afterload mismatch. A mean PCWP or LAP of 10–15 mmHg usually is adequate.

For these reasons, particularly if poor myocardial protection is obtained during bypass and aortic cross-clamping or if depressed systolic function exists preoperatively, management of these patients post-CPB is challenging. The mainstays of therapy are afterload reduction and inotropic support of systolic function. The goal of vasodilator therapy is to reduce afterload.

An inotrope is indicated when systolic blood pressure is low (<90 mmHg) and the cardiac index is low (<2.0 L/min/m^2). Epinephrine 0.015–0.030 μg/kg/min is a good choice because it is a potent inotrope with little vasoconstrictor activity at this dose. When afterload reduction is needed, as determined by a high SVR or mean aortic pressure, nitroprusside can be added. It is easily titratable with a short half-life. The infusion can be started at 0.15–0.3 μg/kg/min and titrated

with careful attention paid to cardiac index, arterial blood pressure, and PCWP. Volume infusion may be necessary to keep PCWP in the optimal range. If the PCWP remains elevated (>18 mmHg) with inotrope infusion, then nitroglycerin started at 0.15–0.30 μg/kg/min and titrated upward is the vasodilator of choice. Alternatively, a phosphodiesterase inhibitor can be used. Milrinone provides both inotropy and vasodilation.

The management of RV function and the pulmonary vasculature can be problematic in the post-bypass period. Management of this problem is described in detail in the section on MS.

Patients in atrial fibrillation with large left atria will rarely convert to sinus rhythm postoperatively. Therefore, the ventricular response rate will have to be controlled. Bradycardia is better tolerated after replacement of the incompetent mitral valve than before replacement.

Goals
- Maintain the ventricular response rate to atrial fibrillation <100 b/min if sinus rhythm cannot be maintained.
- Avoid reliance on a large LVEDV; wall stress will be greatly elevated and systolic function may decline.
- Aggressively use inotropic support and afterload reduction of the LV.
- Avoid pulmonary artery hypertension by treating hypercarbia, hypoxemia, and acidemia.
- Aggressively treat pulmonary artery hypertension with vasodilator therapy to avoid RV failure. If RV failure does occur, inotropic support of the RV and pulmonary vasodilation may be necessary.

The tricuspid valve

The tricuspid valve (TV) consists of anterior, posterior, and septal cusps tethered by chordae tendinae and papillary muscles all suspended by a fibromuscular annulus. The commissures of the TV are not as well defined as those of the mitral valve. The orifice is larger than that of the mitral valve and is triangular in shape, as compared to the saddle-shape of the mitral valve. The anterior leaflet is the largest and is tethered to the

Table 5.4 The primary and secondary causes of tricuspid insufficiency.

Primary	Secondary
Infective endocarditis	Myocardial ischemia/ infarction
Carcinoid tumor	
Rheumatic heart disease	Cor pulmonale
Trauma	Pulmonary embolism
Papillary muscle dysfunction	Left heart failure
Fen-Phen valvulopathy	Pulmonic stenosis
Ebstein anomaly	Pulmonary hypertension
Connective tissue disorders	Mitral insufficiency
	Pulmonary artery catheter/pacemaker

Fig. 5.18 A mid-esophageal four-chamber view transesophageal echocardiographic image demonstrating severe tricuspid regurgitation. Note the large right atrium and the bulging intra-atrial septum indicating high right atrial pressures (arrow).

anterior papillary muscle which arises from the moderator band. The moderator band is composed of muscular tissue arising from the intraventricular septum and can sometimes be seen on the echocardiogram. The posterior leaflet is the smallest and is anchored by the posterior papillary muscle. The septal leaflet attaches to the ventricular septum and is in very close proximity to the bundle of His.

Tricuspid valvular disease is almost always regurgitant in nature. The defect may be either functional or anatomic. The result is RV dilation, elevation of RV systolic and diastolic pressures, and tricuspid annular dilatation. Left-sided valvular lesions with pulmonary hypertension, RV infarction, pacemaker malfunction, or RV failure from any cause can result in tricuspid regurgitation (TR). Other causes of tricuspid abnormalities include rheumatic valvulitis, endocarditis, carcinoid, radiation therapy, trauma, or congenital lesions. Ebstein's anomaly is seen when the TV is displaced toward the apex in the RV (Table 5.4). Tricuspid stenosis (TS) is less common and most likely secondary to rheumatic heart disease. Other causes of TS include congenital abnormalities or endocarditis. Right atrial masses may act as functional stenotic lesions and impede TV inflow.

There is a giant a wave on the CVP waveform in TS, and abnormal c and v waves with TR. TEE is most helpful in the diagnosis of TS and TR (Fig. 5.18). It is common for TR to present in conjunction with other valvular heart lesions (i.e. MS

or MR). If there is RV failure, the medical prognosis is worse. The anesthetic management should consider the degree of RV failure. Most frequently, the surgical intervention for TR is a repair with a ring annuloplasty.

The pulmonary valve

The pulmonary valve (PV) is anterior and superior to the aortic valve. Similar to the aortic valve, it is trileaflet and semilunar, consisting of anterior, left and right leaflets. The plane of the valve is roughly perpendicular in orientation to the aortic valve. The pulmonic valve is isolated from the other three heart valves by the infundibulum. Pulmonary valvular disease is usually congenital in nature. Stenosis is more common than regurgitation although a wide spectrum of pathology is possible (Fig. 5.19). Congenital pulmonary stenosis is usually treated with balloon valvuloplasty. Mild pulmonary regurgitation occurs in nearly all cardiac surgical patients in whom a pulmonary artery catheter has been placed. Significant pulmonary regurgitation is rare, and is usually well tolerated. In some patients, RV dysfunction may occur secondary to pulmonary regurgitation and should be surgically corrected. Pulmonary allografts are usually chosen when replacing a pulmonary

Fig. 5.19 Transesophageal echocardiography (TEE) color compare image of severe pulmonary artery aneurysm with pulmonary hypertension and mild pulmonary insufficiency. On the left image the aneurysm is indicated by the arrow. In the right image, the pulmonary insufficiency is seen with color Doppler. LA, left atrium; PA, pulmonary artery; PR, pulmonary regurgitation; RA, right atrium; RV, right ventricle.

valve; pulmonary valvular repair is typically not performed.

Multiple valve lesions

It is not uncommon for patients with valvular heart disease to have both a stenotic and regurgitant process affecting one valve or to have involvement of two or more valves. There are several important points to keep in mind when evaluating patients with multiple valve lesions.

It is possible for a valve to be stenotic and incompetent; however, a severely stenotic valve can allow only minimal regurgitation because of the profound reduction in valve area. Likewise, a severely incompetent valve can offer only minimal impedance to flow across its large area. It is possible for a prosthetic valve to possess high-grade stenosis and regurgitation if it has a large perivalvular leak.

When a valve is not clearly primarily stenotic or incompetent, it is necessary to determine which lesion has the most pronounced effect on the patient's hemodynamics. If a patient with MS and MR has a large LVEDV, it follows that MR is the predominant lesion. Likewise, if a patient with AS and AR is found to have a normal LVEDV with left atrial enlargement and a large A-wave pressure, it follows that AS is the predominant lesion.

When two valves are involved, it is necessary to know which features of each lesion exacerbate or ameliorate the effects of the other lesions.

AR and MS
The under-loading of the LV characteristic of MS will be offset by the regurgitation of the aortic valve lesion. Increased LAP and pulmonary artery hypertension characteristic of MS will be present. The increased heart rate so beneficial in AR will cause precipitous increases in LAP with subsequent pulmonary congestion. Therapy for both RV and LV afterload reduction will be necessary.

AS and MS
The LV under-loading characteristic of MS will severely limit the preload reserve of the LV because LV compliance in AS will be diminished, LAP will have to be greatly elevated to ensure adequate filling of the LV with the gradient across the mitral valve. This will exacerbate pulmonary congestion. LV afterload reduction will be poorly tolerated because of the large gradient across the aortic valve and the limited ability to increase LVEDV. Efforts to reduce RV afterload will be severely limited by the concomitant systemic vasodilation.

AR and MR
The pathophysiology of LV volume overload will be predominant. Efforts to reduce LV afterload will be of benefit in the management of both lesions. Likewise, a relatively fast heart rate will be advantageous. High LAP and pulmonary artery hypertension not normally seen in AR may be a feature here. If the MR is secondary to ventricular dilation from AR, then only replacement of the aortic valve will be necessary.

AS and MR
High ventricular pressure in AS will cause dramatic MR if the mitral valve is incompetent. The combination of concentric and eccentric hypertrophy will allow the LV to maintain a relatively large SV. With a larger than normal preload reserve available, some LV afterload reduction might be

tolerated in an effort to reduce regurgitation if the AS is mild. Efforts to increase heart rate to reduce the regurgitant process will have detrimental effects on the subendocardial perfusion of the hypertrophied LV. Pulmonary congestion and pulmonary artery hypertension with RV failure are likely. Reduction of pulmonary arterial pressure will be difficult for patients with severe AS, because the concomitant systemic vasodilation may result in profound systemic hypotension. In instances in which MR is mild to moderate and AS is severe, replacement of the aortic valve may reduce ventricular pressures and ventricular dilatation such that mitral valve replacement or repair is unnecessary.

Pulmonary autograft for aortic valve replacement

In some patients with aortic valve disease, moving the pulmonary valve to the aortic position and implantation of a pulmonary homograft is beneficial (Ross procedure). In children, the pulmonary autograft will increase in size as the child grows and there is no need for anticoagulation. Hemodynamics seen across the new aortic valve are excellent and the development of new AR is low. The freedom from autograft replacement is approximately 50–75% at 20 years. This procedure is technically more complicated and requires an extended CPB time.

Table 5.5 Indications for aortic valve replacement. (Reprinted with permission from Bonow RO, Carabello BA, Chatterjee K *et al*. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Valvular Heart Disease). *J Am Coll Cardiol* 2006;**48**:e1–148.)

Class I

1 AVR is indicated for symptomatic patients with severe AS (*Level of evidence: B*)

2 AVR is indicated for patients with severe AS undergoing coronary artery bypass graft surgery (CABG) (*Level of evidence: C*)

3 AVR is indicated for patients with severe AS undergoing surgery on the aorta or other heart valves (*Level of evidence: C*)

4 AVR is recommended for patients with severe AS and LV systolic dysfunction (ejection fraction <0.50) (*Level of evidence: C*)

Class IIa

AVR is reasonable for patients with moderate AS undergoing CABG or surgery on the aorta or other heart valves (see Sections on Combined multiple valve disease and on AVR in patients undergoing CABG) (*Level of evidence: B*)

Class IIb

1 AVR may be considered for asymptomatic patients with severe AS and abnormal response to exercise (e.g. development of symptoms or asymptomatic hypotension) (*Level of evidence: C*)

2 AVR may be considered for adults with severe asymptomatic AS if there is a high likelihood of rapid progression (age, calcification, and CAD) or if surgery might be delayed at the time of symptom onset (*Level of evidence: C*)

3 AVR may be considered in patients undergoing CABG who have mild AS when there is evidence, such as moderate to severe valve calcification, that progression may be rapid (*Level of evidence: C*)

4 AVR may be considered for asymptomatic patients with extremely severe AS (aortic valve area less than 0.6 cm^2, mean gradient >60 mmHg, and jet velocity >5.0 m/s) when the patient's expected operative mortality is 1.0% or less (*Level of evidence: C*)

Class III

AVR is not useful for the prevention of sudden death in asymptomatic patients with AS who have none of the findings listed under the class IIa/IIb recommendations (*Level of evidence: B*)

AS, aortic stenosis; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CAD, coronary artery disease; LV, left ventricle.

Previously undiagnosed valve disease found during CABG

Occasionally, patients presenting for CABG are found to have significant AS during the TEE examination. The new lesion should be fully evaluated by TEE and the indications for replacement are the same as in any other patient (Table 5.5). If the AS is moderate to severe, the aortic valve should be replaced. Controversy exists when mild AS is uncovered.

MR is also a common unexpected finding in patients having CABG surgery. The MR requires full evaluation by TEE. If there is a structural defect such as valve prolapse or flail, the valve should be repaired or replaced. Ischemic MR is due to LV remodeling and apical tenting of the chordae. The MR jet us usually central in nature as compared to the more eccentric MR jets seen with either restrictive disease or valve prolapse. Severe ischemic MR should be surgically corrected. Controversy exists about mild to moderate ischemic MR. Ischemic MR

Table 5.6 Indications for mitral valve surgery. (Reprinted with permission from Bonow RO, Carabello BA, Chatterjee K *et al*. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Valvular Heart Disease). *J Am Coll Cardiol* 2006;**48**:e1–148.)

Class I

1 MV surgery is recommended for the symptomatic patient with acute severe MR (*Level of evidence: B*)

2 MV surgery is beneficial for patients with chronic severe MR and NYHA functional class II, III, or IV symptoms in the absence of severe LV dysfunction (severe LV dysfunction is defined as ejection fraction <0.30) and/or end-systolic dimension >55 mm (*Level of evidence: B*)

3 MV surgery is beneficial for asymptomatic patients with chronic severe MR and mild to moderate LV dysfunction, ejection fraction 0.30–0.60, and/or end-systolic dimension ≥40 mm (*Level of evidence: B*)

4 MV repair is recommended over MV replacement in the majority of patients with severe chronic MR who require surgery, and patients should be referred to surgical centers experienced in MV repair (*Level of evidence: C*)

Class IIa

1 MV repair is reasonable in experienced surgical centers for asymptomatic patients with chronic severe MR with preserved LV function (ejection fraction >0.60 and end-systolic dimension <40 mm) in whom the likelihood of successful repair without residual MR is >90% (*Level of evidence: B*)

2 MV surgery is reasonable for asymptomatic patients with chronic severe MR, preserved LV function, and new onset of atrial fibrillation (*Level of evidence: C*)

3 MV surgery is reasonable for asymptomatic patients with chronic severe MR, preserved LV function, and pulmonary hypertension (pulmonary artery systolic pressure >50 mmHg at rest or >60 mmHg with exercise) (*Level of evidence: C*)

4 MV surgery is reasonable for patients with chronic severe MR due to a primary abnormality of the mitral apparatus and NYHA functional class III–IV symptoms and severe LV dysfunction (ejection fraction <0.30 and/or end-systolic dimension >55 mm) in whom MV repair is highly likely (*Level of evidence: C*)

Class IIb

MV repair may be considered for patients with chronic severe secondary MR due to severe LV dysfunction (ejection fraction <0.30) who have persistent NYHA functional class III–IV symptoms despite optimal therapy for heart failure, including biventricular pacing (*Level of evidence: C*)

Class III

1 MV surgery is not indicated for asymptomatic patients with MR and preserved LV function (ejection fraction >0.60 and end-systolic dimension <40 mm) in whom significant doubt about the feasibility of repair exists (*Level of evidence: C*)

2 Isolated MV surgery is not indicated for patients with mild or moderate MR (*Level of evidence: C*)

LV, left ventricular; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association.
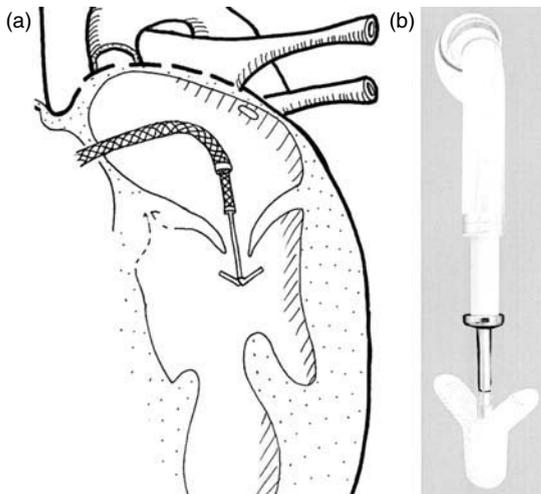
Fig. 5.20 (a) Schematic of the endovascular repair system guide catheter across the atrial septum. The clip delivery system is positioned through the guide. The clip is in the open position in the left ventricle, ready to be retracted to grasp the mitral leaflets. (b) The distal end of the delivery system and the polyester-covered clip shown in the open position. (From St. Goar FG, Fann JL, Komtebedde J *et al*. Endovascular edge-to-edge mitral valve repair: short term results in a porcine model. *Circulation* 2003;**108**:1990–3, with permission.)

is dynamic and is responsive to pharmacologic alterations in loading conditions and LV remodeling. The indications for mitral valve repair or replacement are given in Table 5.6.

Alternatives to surgical repair

For some patients, alternatives to surgical repair exist. Techniques are now available for percutaneous replacement of the pulmonary and aortic valve. There is active work on percutaneous endovascular end-to-edge repair of the mitral valve (Fig. 5.20a,b). The coronary sinus wraps around the mitral valve and allows an opportunity for positioning of an annular constraint device, which may reduce mitral annular size and MR (Fig. 5.21). Finally, there is some enthusiasm for
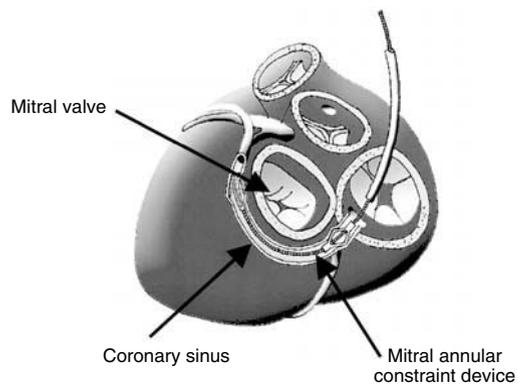
Fig. 5.21 The position of the mitral annular constraint device in the coronary sinus and its relation to the posterior aspect of the mitral valve. Elements of the device, including proximal and distal anchors and an intervening cable, are depicted. (From Kaye DM, Byrne M, Alferness C, Power J. Feasibility and short-term efficacy of percutaneous mitral annular reduction for the therapy of heart failure-induced mitral regurgitation. *Circulation* 2003;**108**:1795–7, with permission.)

a surgical edge-to-edge annuloplasty of the mitral valve (Alfieri stitch); although late outcome data suggest that long-term benefit is lacking. In any case, the techniques and indications for percutaneous repair and replacement of valvular heart disease will likely only increase in the next years.

Suggested reading

Bonow RO, Carabello BA, Chatterjee K *et al*. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. *J Am Coll Cardiol* 2006;**48**: 1–148.

Carabello BA. Is it ever too late to operate on the patient with valvular heart disease? *J Am Coll Cardiol* 2004;**44**:376–83.

Rahimtoola SH. Choice of prosthetic heart valve for adult patients. *J Am Coll Cardiol* 2003;**41**:893–904.

Rahimtoola SH. The year in valvular heart disease. *J Am Coll Cardiol* 2005;**45**:111–22.

Vahanian A, Acar C. Percutaneous valve procedures: what is the future? *Curr Opin Cardiol* 2005;**20**:100–6.

CHAPTER 6

Congenital Heart Disease

The incidence of congenital heart is approximately 7–10 per 1000 live births. Environmental factors such as drugs, viral infection, maternal diabetes, or maternal alcohol abuse may account for specific lesions. Most congenital heart defects are the result of an interaction of genetic predisposition and environmental factors.

The anesthesiologist who cares for patients with congenital heart disease (CHD) faces myriad challenges in the perioperative management of these complex individuals. In major pediatric cardiac centers, almost every lesion is amenable to surgical intervention. The pathophysiology of a wide variety of congenital heart defects can be best understood by applying certain basic principles to each patient. This chapter outlines those principles. The anesthesiologist who understands the dynamics of these lesions and the planned surgical intervention will be able to conduct an appropriate anesthetic. Although younger, smaller, and sicker patients are presenting for more complex, innovative surgical treatment, it is encouraging and impressive that there has been a concomitant decrease in surgical and anesthetic morbidity and mortality.

Pediatric cardiovascular physiology

Dramatic circulatory changes occur within minutes of birth, there and continue over the first few days and weeks of life. These changes have profound effects on neonatal cardiovascular physiology. It is not coincidental that 50% of the neonates born with CHD will become ill enough during the first days or weeks of life to require medical or surgical intervention. Optimal anesthetic management of the neonate with CHD must be based on a firm understanding of these developmental changes.

Fetal circulation

The placenta provides gas exchange in the fetus. Changes at birth are directly related to the exclusion of the placenta and the establishment of the lungs as the unit of gas exchange. Fetal circulatory channels shunt blood away from the lung, resulting in a parallel circuit in which both ventricles supply systemic circulation. This parallel circulation permits normal fetal growth and development even in fetuses with cardiac malformations. Fetal shunts permit alternate pathways and provide adequate systemic blood flow.

Oxygenated blood from the placenta returns to the fetus via the umbilical vein, which enter the portal venous system (Fig. 6.1). The ductus venosus connects the left portal vein to the left hepatic vein at its junction with the inferior vena cava (IVC). This allows approximately 50% of umbilical venous blood to bypass the hepatic sinuses. The remainder of umbilical venous flow passes through the liver and enters the IVC via the hepatic veins. Fetal IVC blood is a combination of blood from the lower fetal body, umbilical vein, and hepatic veins. The stream of blood from the ductus venosus has a higher velocity in the IVC than the stream from
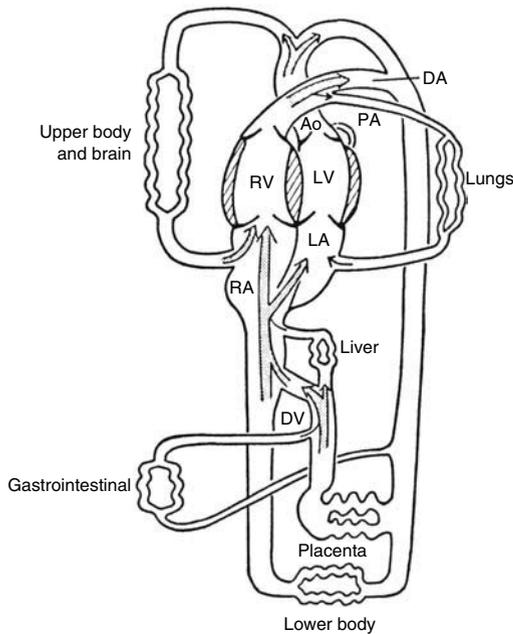
Fig. 6.1 Schematic of the fetal circulation. Ao, aorta; DA, ductus arteriosus; DV, ductus venosus; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

the lower body and hepatic veins. This higher velocity facilitates delivery of this higher oxygen content blood across the foramen ovale (FO) into the left atrium (LA).

IVC blood enters the right atrium (RA) and due to the position of the Eustachian valve, Chiari network, and FO enters the LA during 80% of the cardiac cycle. During the other 20% (atrial systole) IVC blood crosses the tricuspid valve and enters the right ventricle (RV). The overwhelming majority of superior vena cava (SVC) crosses the tricuspid valve and enters the RV as well. Blood from the RV is ejected into the pulmonary artery (PA). Approximately 10–15% of blood from the PA passes through the lungs to reach the LA the rest is shunted to the distal aorta via the ductus arteriosus (DA). As a result, two-thirds of total fetal cardiac output is provided by the RV with the remaining one-third provided via the left ventricle (LV).

The dynamics of shunting at the level of the ductus venosus, FO, and DA result in preferential delivery of the most highly oxygenated blood to the coronary and cerebral circulations. Obviously, this preferential delivery of oxygenated blood is compromised *in utero* by cardiac lesions that prevent or reduce LV output.

At birth, a series circulation is established in which each ventricle pumps into a specific vascular bed (RV to PA; LV to aorta). The removal of the placenta and the initiation of alveolar ventilation at birth have the immediate effect of establishing this series circulation. To maintain the adult series circulation, the fetal channels must be closed. Complex neurochemical and hormonal influences affect the closing of these fetal shunts. Acidosis, sepsis, hypothermia, hypoxia, and hypercarbia may cause reopening of the shunts and persistence of the fetal circulation (PFC). Most neonates who are critically ill from CHD have one or more of these inciting factors at the time of presentation. In some instances, persistence of fetal circulatory channels may be beneficial or even mandatory for survival.

Closure of the ductus arteriosus

In the fetus, patency of the ductus arteriosus (DA) is maintained by high levels of prostaglandin (prostacyclin (PGI_2) and prostaglandin E1 (PGE_1)). There are two stages of ductal closure in the newborn: functional closure and permanent anatomic closure. Functional closure occurs by contraction of the smooth muscle of the ductal wall and usually occurs within the first day of life. An increase in partial pressure of oxygen (PO_2) and a decrease in prostaglandins contribute to functional closure. Oxygen is a dose-dependent ductal constrictor that acts by increasing the rate of oxidative phosphorylation within smooth muscle cells. In addition, the response to oxygen may be age-related; full-term neonates have a more dramatic response to oxygen than an immature newborn. Norepinephrine and epinephrine, by changing pulmonary and systemic vascular resistances, may secondarily contribute to ductal closure. Acetylcholine has a direct constrictor effect on ductal tissue. Permanent anatomic closure of the duct usually is accomplished by 2–3 weeks of life in the normal full-term neonate. The lumen is sealed by fibrous connective tissue, leaving the vestigial structure, known as the ligamentum arteriosum (Fig. 6.2a–c).
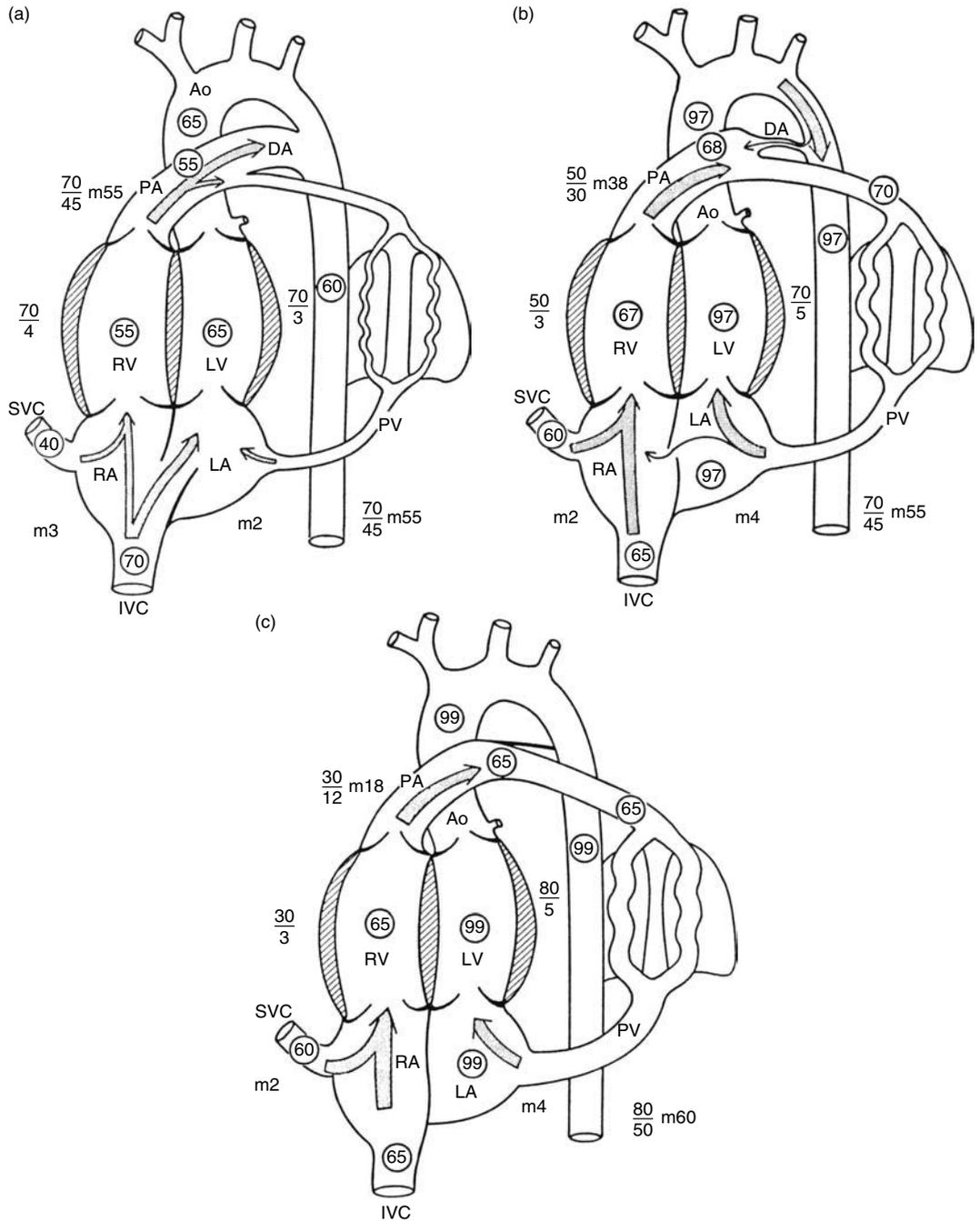
Fig. 6.2 Hemodynamics of the fetus and neonate. Circled figures are oxygen saturations. Systolic, diastolic, and mean (m) pressures appear near their respective chambers and vessels. (a) Circulation of the term fetus. (b) Transitional circulation less than 1 day after birth.

(c) Circulation several days after birth. Ao, aorta; DA, ductus arteriosus; DV, ductus venosus; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

Survival of some neonates with congenital cardiac lesions is dependent on ductal patency. Because functional closure is a reversible event, the use of PGE_1 infusions ($0.01–0.05\,\mu g/kg/min$) has been one of the major medical advances in stabilization of neonates with ductal-dependent heart lesions. Preterm neonates are at risk of delayed ductal closure. This may be due to decreased degradation of PGE_1, increased production of PGE_1, or diminished sensitivity to the ductal constricting effects of oxygen. In instances in which delayed ductal closure is disadvantageous, prostaglandin inhibitors such as indomethacin ($0.1–0.3\,mg/kg$ orally (PO) or intravenously (IV)) have been used successfully to promote ductal closure and establish normal patterns of pulmonary blood flow.

Closure of the foramen ovale

In utero, the right atrial pressure is higher than left atrial pressure (LAP) IVC blood flows in such a manner as to keep the foramen ovale (FO) open. Removal of the placenta causes a significant decrease in venous return to the right heart, causing a decrease in right atrial pressure. In addition, ventilation causes a marked increase in pulmonary arterial and venous blood flow resulting in an increase in LAP. This elevation of left atrial relative to right atrial pressure causes the flap-like valve of the FO to functionally close. In instances in which right atrial pressure remains elevated, right-to-left (R–L) shunting may persist. Functional closure usually progresses to anatomic closure. However, probe patency of the FO may persist in 30% of normal adults and 50% of children younger than 5 years of age.

Closure of the ductus venosus

The umbilical vessels constrict strongly after mechanical stimulation and high oxygen tensions facilitate this process. The resultant decrease in umbilical venous blood flow causes passive closure of the ductus venosus. The ductus venosus does not appear to be as sensitive as the DA to the arterial partial pressure of oxygen (Pa_{O_2}), the arterial partial pressure of carbon dioxide (Pa_{CO_2}), or pH. High levels of norepinephrine also cause constriction. The ductus venosus is functionally closed by 1 week of life and anatomically closed by 3 months. The remaining structure is the ligamentum venosum.

In addition to the establishment of the adult series circulation, dramatic alterations in pulmonary circulation, cardiac output and distribution, myocardial performance, and myocardial cell growth and hypertrophy continue to occur during the first weeks, months, and even years of life. In the presence of CHD, these changes may be pathologically affected.

Pulmonary vascular changes

The fetus has low pulmonary blood flow secondary to a high pulmonary vascular resistance (PVR). The minimal blood flow that reaches the pulmonary bed has a very low Pa_{O_2}, which may cause hypoxic pulmonary vasoconstriction and contributes to the elevated pulmonary resistance seen in the fetus. Morphologic examinations of the small arteries of the fetal and newborn lung show a thick medial smooth muscle layer. The fetal pulmonary vasculature is reactive to a number of stimulants. Vasoconstriction is induced by decreases in Pa_{O_2}, pH, and leukotrienes. Acetylcholine, histamine, bradykinin, PGE_1, PGE_2, PGI_2 (prostacyclin), and prostaglandin D_2 and β-adrenergic catecholamines are potent vasodilators of fetal pulmonary vessels.

At birth, alveolar ventilation commences. This reduces mechanical compression of small pulmonary vessels and increases Pa_{O_2}. The result is a dramatic reduction in PVR. During the following weeks and months, remodeling of the pulmonary vessels occurs; the most notable change is a thinning of the medial smooth muscle layer. By 6 months of life, this process results in reduction of PVR to near normal adult levels. The normal process of postnatal pulmonary maturation may be altered significantly by pathologic conditions, such as those associated with CHD.

Myocardial performance in the neonate

In utero, the RV has a cardiac output of approximately $330\,mL/kg/min$ compared with the LV output of $170\,mL/kg/min$. At birth, both RV and LV eject an output of approximately $350\,mL/kg/min$.

This requires minimal stroke volume increase for the RV but a considerable increase in stroke volume for the LV. The high output state of the newborn effectively limits further increases in cardiac output. This high output state decreases to about 150 mL/kg/min by 8–10 weeks of life.

Myocardial morphology and performance is notably different in the neonate. These differences are summarized as follows:

- *Afterload mismatch.* The neonatal heart is more susceptible to afterload mismatch, and therefore, stroke volume is poorly maintained in the face of increasing outflow resistance.
- *Limited preload reserve.* The neonatal heart has limited preload reserve. Augmentation of stroke volume via the Frank–Starling mechanism is limited as compared with an adult.
- *Reduced contractile capacity.* Neonatal cardiac cells contain more water and fewer contractile elements than mature myocardium.
- *Reduced ventricular compliance.* The compliance of the neonatal myocardium is reduced because a deficiency of elastic elements parallels the deficiency of contractile elements.
- *Increased intraventricular dependence.* Changes in ventricular pressure are transmitted to the opposite ventricle via the ventricular septum more readily in the immature myocardium. Left ventricular diastolic filling is disproportionately impaired in the neonate by high right ventricular end-diastolic pressure. This is due to a leftward shift of the intraventricular septum and a reduction in left ventricular distensibility. Right ventricular diastolic filling is impaired to an equal extent by high left ventricular end-diastolic pressure in neonates. This enhanced ventricular interaction is caused by reduced ventricular compliance and because, at birth, the LV and RV are of equal mass. The increased volume and pressure load experienced by the LV after birth produces relative LV hypertrophy. The normal adult LV to RV mass ratio of 2:1 is not seen until several months after birth.
- *Incomplete autonomic innervation.* Sympathetic innervation, which is responsible for increasing heart rate and contractility, is incompletely developed at birth. As a result, local myocardial release of norepinephrine contributes less to increases in contractility than do increases in circulating catecholamine levels. For this reason, inotropic agents such as dopamine, the effects of which are partially mediated through release of norepinephrine from myocardial nerve endings, may have to be used in higher doses to be effective in younger patients. On the other hand, the parasympathetic system, which reflexly slows the heart, is fully functional at birth.
- *Immature myocardial metabolism.* The neonatal myocardium is more dependent on anaerobic metabolism than the adult heart. This may have a somewhat protective effect, making the neonatal myocardium more tolerant to the effects of hypoxia.

Pathophysiology of CHD

While some congenital heart defects involve purely obstructive or regurgitant valvular lesions, the presence of shunts (both physiologic and anatomic) is the hallmark of CHD. Anesthetic management of the patient with CHD is dependent on a clear understanding of:

- The concepts of shunting (both physiologic and anatomic), single ventricle physiology, and intercirculatory mixing.
- The types of anatomic shunts and the dynamics of the anatomic shunting process.
- The effects of congenital lesions on the development of the pulmonary vascular system.
- The factors that influence pulmonary and systemic vascular resistance.
- The factors responsible for producing myocardial ischemia.

The concepts of shunting, single ventricle physiology, and intercirculatory mixing

Shunting
Shunting is the process whereby venous return into one circulatory system is recirculated through the arterial outflow of the same circulatory system. Flow of blood from the systemic venous atrium or RA to the aorta produces recirculation

of systemic venous blood. Flow of blood from the pulmonary venous atrium or LA to the PA produces recirculation of pulmonary venous blood. Recirculation of blood produces a physiologic shunt. Recirculation of pulmonary venous blood produces a physiologic left-to-right (L–R), whereas recirculation of systemic venous blood produces a physiologic R–L shunt. A physiologic R–L or L–R shunt commonly is the result of an anatomic R–L or L–R shunt. In an anatomic shunt, blood moves from one circulatory system to the other via a communication at the level of the cardiac chambers or great vessels. Physiologic shunts can exist in the absence of an anatomic shunt. Transposition physiology is the primary example of this process.

Effective blood flow is the quantity of venous blood from one circulatory system reaching the arterial system of the other circulatory system. Effective pulmonary blood flow is the volume of systemic venous blood reaching the pulmonary circulation, whereas effective systemic blood flow is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary blood flow and effective systemic blood flows are the flows necessary to maintain life. Effective pulmonary blood flow and effective systemic blood flow are always equal, no matter how complex the lesions. Effective blood flow usually is the result of a normal pathway through the heart, but it may occur as the result of an anatomic R–L or L–R shunt.

Total pulmonary blood flow (Q_P) is the sum of effective pulmonary blood flow and recirculated pulmonary blood flow. Total systemic blood flow (Q_S) is the sum of effective systemic blood flow and recirculated systemic blood flow. Total pulmonary blood flow and total systemic blood flow do not have to be equal. Therefore, it is best to think of recirculated flow (physiologic shunt flow) as the extra, noneffective flow superimposed on the nutritive effective blood flow. These concepts are illustrated in Figs 6.3 and 6.4.

Single ventricle physiology

Single ventricle physiology is used to describe the situation wherein complete mixing of pulmonary venous and systemic venous blood occurs

at the atrial or ventricular level and the ventricle(s) then distribute output to both the systemic and pulmonary beds. As a result of this physiology the:

- Ventricular output is the sum of pulmonary blood flow (Q_p) and systemic blood flow (Q_S).
- Distribution of systemic and pulmonary blood flow is dependent on the relative resistances to flow (both intra and extracardiac) into the two parallel circuits.
- Oxygen saturations are the same in the aorta and the PA.
- This physiology can exist in patients with one well-developed ventricle and one hypoplastic ventricle as well as in patients with two well-formed ventricles.

In the case of a single anatomic ventricle there is always obstruction to either pulmonary or systemic blood flow as the result of complete or near complete obstruction to inflow and/or outflow from the hypoplastic ventricle. In this circumstance there must be a source of both systemic and pulmonary blood flow to assure post-natal survival. In some instances of a single anatomic ventricle, a direct connection between the aorta and the PA via a patent ductus arteriosus (PDA) is the sole source of systemic blood flow (hypoplastic left heart syndrome (HLHS)) or of pulmonary blood flow (pulmonary atresia with intact ventricular septum or PA/IVS). This is known as ductal dependent circulation. In other instances of a single anatomic ventricle, intracardiac pathways provide both systemic and pulmonary blood flow without the necessity of a PDA. This is the case in tricuspid atresia (TA) with normally related great vessels, a nonrestrictive ventricular septal defect (VSD) and minimal or absent pulmonary stenosis.

Single ventricle physiology can exist in the presence of two well-formed anatomic ventricles when there is complete or near complete obstruction to outflow from one on the ventricles:

- Tetralogy of Fallot (TOF) with PA where pulmonary blood flow is supplied via a PDA or major aortopulmonary collateral arteries (MAPCAs).
- Truncus arteriosus.
- Severe neonatal aortic stenosis and interrupted aortic arch; in both lesions a substantial portion of systemic blood flow is supplied via a PDA.
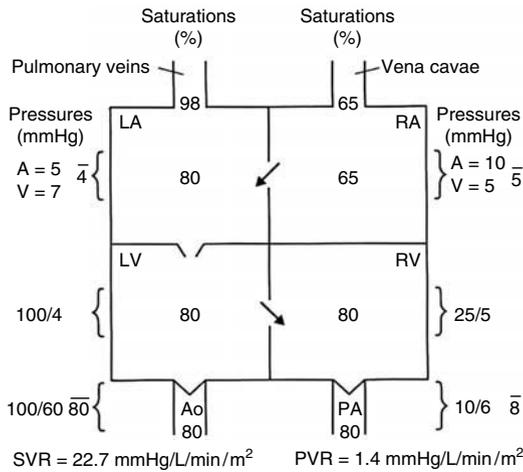
Fig. 6.3 Depiction of saturations, pressures, and blood flows in type 1B tricuspid atresia with a mildly restrictive atrial septal defect (ASD), a small restrictive ventricular septal defect (VSD), and mild pulmonic stenosis (PS). Complete mixing or blending occurs at the atrial level. This complete mixing is the consequence of an obligatory physiologic and anatomic right-to-left (R–L) shunting across the ASD. Effective pulmonary and effective systemic blood flow are equal (1.5 L/min/m^2). Effective systemic blood flow occurs via a normal pathway through the heart. Effective pulmonary blood flow is the result of an anatomic R–L shunt at the atrial level and an anatomic left-to-right (L–R) shunt at the ventricular level. This illustrates the concept that when complete outflow obstruction exists and there is obligatory anatomic shunting, a downstream anatomic shunt must

exist to deliver blood back to the obstructed circuit. Total pulmonary blood flow (Q_P) is 2.8 L/min/m^2 and is the sum of effective pulmonary blood flow (1.5 L/min/m^2) and a physiologic and anatomic L–R shunt (1.3 L/min/m^2) at the VSD. Total systemic blood flow (Q_S) is 3.3 L/min/m^2 and is the sum of effective systemic blood flow (1.5 L/min/m^2) and a physiologic and anatomic R–L shunt (1.8 L/min/m^2) at the ASD.

In this depiction, there is a small pressure gradient at the atrial level and a large pressure gradient at the ventricular level. In addition, there is a small additional gradient at the level of the pulmonic valve. Ao, aorta; LA, left atrium; LV, left ventricle; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; SVR, systemic vascular resistance.

● Heterotaxy syndrome where there are components of systemic venous (SVC, IVC, hepatic veins, azygous veins) and pulmonary venous return to both right and left sided atria. In addition, atrial morphology is ambiguous.

Despite the fact that patients with totally anomalous pulmonary venous return (TAPVR) have complete mixing of pulmonary and systemic venous blood at the atrial level they do not manifest the other features necessary to create single ventricle physiology. This holds true as well for lesions in which a common atrial or ventricular chamber exists due to bidirectional (both L–R and R–L) anatomic shunting across a large defect (atrial septal or ventricular septal) and where there is

no obstruction to ventricular outflow. Table 6.1 lists a number of single ventricle physiology lesions.

All patients with single ventricle physiology who have severe hypoplasia of one ventricle will ultimately be staged down the single ventricle pathway to Fontan physiology. This will be discussed in detail later. Patients with single ventricle physiology and two well-formed ventricles will be able to undergo a two-ventricle repair. In some cases the two-ventricle repair will be complete. In others, significant residual lesions (VSD, aortopulmonary collaterals) may remain.

With single ventricle physiology, the arterial saturation (SaO_2) will be determined by the relative volumes and saturations of pulmonary venous and
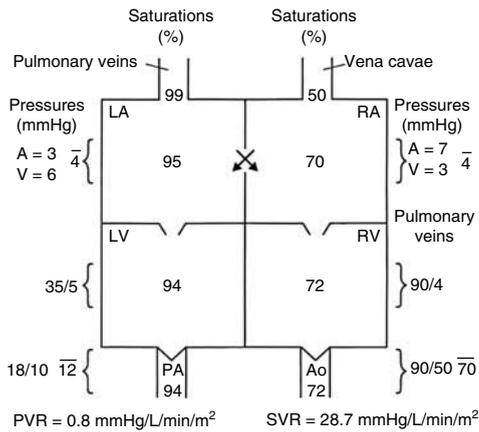
Fig. 6.4   Depiction of saturations, pressures, and blood flows in transposition of the great arteries with a nonrestrictive atrial septal defect (ASD) and a small left ventricular outflow tract gradient. Intercirculatory mixing occurs at the atrial level. Effective pulmonary and effective systemic blood flows are equal ($1.1\,\text{L/min/m}^2$) and are the result of a bidirectional anatomic shunt at the atrial level. The physiologic L–R shunt is $9.0\,\text{L/min/m}^2$; this represents blood recirculated from the pulmonary veins to the pulmonary artery. The physiologic R–L shunt is $1.2\,\text{L/min/m}^2$; this represents blood recirculated from the systemic veins to the aorta. Total pulmonary blood flow ($Q_P = 10.1\,\text{L/min/m}^2$) is almost five times total systemic blood flow ($Q_S = 2.3\,\text{L/min/m}^2$). The bulk of pulmonary blood flow is recirculated pulmonary venous blood. In this depiction, pulmonary vascular resistance is low (approximately 1/35 of systemic vascular resistance) and there is a small (17 mmHg peak to peak) gradient from the left ventricle to the pulmonary artery. These findings are compatible with the high pulmonary blood flow depicted. Ao, aorta; LA, left atrium; LV, left ventricle; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; SVR, systemic vascular resistance.
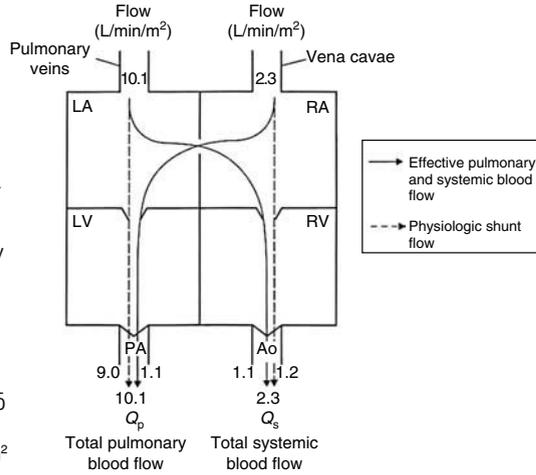
systemic venous blood flows that have mixed and reach the aorta. This is summarized in the following equation:

$$\text{Aortic saturation} = \big[(\text{systemic venous saturation})$$
$$\times (\text{total systemic venous blood flow})$$
$$+ (\text{pulmonary venous saturation})$$
$$\times (\text{total pulmonary venous blood flow})\big]$$
$$\div \big[\text{total systemic venous blood flow}$$
$$+ \text{total pulmonary venous blood flow}\big].$$

This is illustrated in Fig. 6.3 where:

$$\text{Sa}_{O_2} = [(65)(3.3) + (98)(2.8)]/(3.3 + 2.8) = 80\%$$

From this equation, it is apparent that with single ventricle physiology, three variables will determine arterial saturation:

1 *The ratio of total pulmonary to total systemic blood flow ($Q_p:Q_s$).* A greater proportion of the mixed blood will consist of saturated blood (pulmonary venous blood) than of desaturated blood (systemic venous blood) when $Q_p:Q_s$ is high. Figure 6.5 demonstrates the increase in arterial saturation that occurs with increases in pulmonary blood flow relative to systemic blood flow. Figure 6.5 also demonstrates that an arterial saturation approaching 100% is possible only with an extremely large $Q_p:Q_s$.

2 *Systemic venous saturation.* For a given $Q_P:Q_S$ and pulmonary venous saturation, a decrease in systemic venous saturation will result in a decreased arterial saturation. Decreases in systemic venous saturation occur as the result of decreases in systemic oxygen delivery or increases in systemic oxygen consumption. Recall that systemic oxygen delivery is the product of systemic blood flow and arterial oxygen content. Arterial oxygen content is dependent on the hemoglobin concentration and the arterial saturation.

Table 6.1 Anatomic subtypes of single ventricle physiology.

	Aortic blood flow from	Pulmonary artery blood flow from
HLHS	PDA	RV
Severe neonate aortic stenosis	PDA	RV
IAA	LV (proximal) PDA (distal)	RV
PA/IVS	LV	PDA
Tetralogy of Fallot with pulmonary atresia	LV	PDA, MAPCAs
Tricuspid atresia, NRGA, with pulmonary atresia (type 1A)	LV	PDA, MAPCAs
Tricuspid atresia, NRGA, with restrictive VSD and pulmonary stenosis (type 1B)	LV	LV thru VSD to RV
Tricuspid atresia, NRGA, with non-restrictive VSD and no pulmonary stenosis (type 1C)	LV	LV thru VSD to RV
Tricuspid atresia, D-TGA, with non-restrictive VSD and pulmonary atresia (type 2A)	LV thru VSD to RV	PDA, MAPCAs
Tricuspid atresia, D-TGA, with non-restrictive VSD and pulmonary stenosis (type 2B)	LV thru VSD to RV	LV
Tricuspid atresia, D-TGA, with non-restrictive VSD and no pulmonary stenosis (type 2C)	LV thru VSD to RV	LV
Tricuspid atresia, D-loop ventricles, L-TGA, subpulmonic stenosis (type 3A)	LV	LV thru VSD to RV
Tricuspid atresia, L-loop ventricles, L-TGA, subaortic stenosis (type 3B)	LV thru VSD to RV	LV
Truncus arteriosus	LV and RV	Aorta
DILV, NRGA	LV	LV thru VSD to BVF
DILV, L-loop ventricles, L-TGA, restrictive BVF	LV thru VSD to BVF, PDA	LV

BVF, bulboventricular foramen; D, dextro; DILV, double inlet left ventricle; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; L, levo; LV, left ventricle; MAPCAs, multiple aortopulmonary collateral arteries; NRGA, normally related great arteries; PA/IVS, pulmonary atresia with intact ventricular septum; PDA, patent ductus arteriosus; RV, right ventricle; TGA, transposition of the great arteries; VSD, ventricular septal defect.

3 *Pulmonary venous saturation.* In the absence of large intrapulmonary shunts and/or V/Q mismatch, pulmonary venous saturation should be close to 100% breathing room air. In the presence of pulmonary parenchymal disease, pulmonary venous saturation may be reduced. The V/Q mismatch component of pulmonary venous desaturation will be largely eliminated with a fractional inspired oxygen concentration (Fio_2) of 1.0 while the intrapulmonary shunt contribution will not be
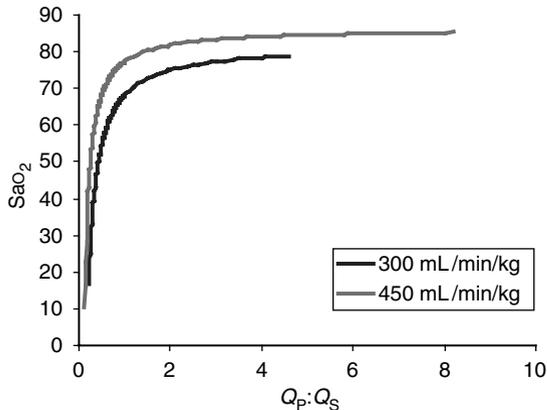
Fig. 6.5 Graph of systemic Sao_2 versus $Q_P{:}Q_S$ for two different systemic ventricular outputs (300 mL/kg/min and 450 mL/kg/min) in single ventricle physiology. In this example oxygen (o_2) consumption is assumed to be 9 mL/kg/min and $Spvo_2 = 95\%$. It is clear that Sao_2 peaks at or near a $Q_P{:}Q_S$ of 1:1. Further increases in $Q_P{:}Q_S$ produce minimal to no increases in Sao_2.

eliminated. For any given systemic venous saturation and $Q_P{:}Q_S$ a reduction in pulmonary venous saturation will result in a decreased arterial saturation.

Intercirculatory mixing

Intercirculatory mixing is the unique situation that exists in transposition of the great arteries (TGA) (see Fig. 6.4). In TGA, two parallel circulations exist due to the existence of atrioventricular (AV) concordance (RA to RV, LA to LV) and ventriculoarterial discordance (RV to aorta, LV to PA). This produces a parallel rather than a normal series circulation. In this arrangement, blood flow will consist of parallel recirculation of pulmonary venous blood in the pulmonary circuit and systemic venous blood in the systemic circuit. Therefore, the physiologic shunt or the percentage of venous blood from one system that recirculates in the arterial outflow of the same system is 100% for both circuits. Unless there are one or more communications (atrial septal defect (ASD), patent foramen ovale (PFO), VSD, PDA) between the parallel circuits to allow intercirculatory mixing, this lesion is incompatible with life.

An anatomic R–L shunt is necessary to provide effective pulmonary blood flow, whereas an anatomic L–R shunt is necessary to provide effective systemic blood flow. Effective pulmonary blood flow, effective systemic blood flow, and the volume of intercirculatory mixing must always be equal. Total systemic blood flow is the sum of recirculated systemic venous blood plus effective systemic blood flow. Likewise, total pulmonary blood flow is the sum of recirculated pulmonary venous blood plus effective pulmonary blood flow. Recirculated blood makes up the largest portion of total pulmonary and total systemic blood flow with effective blood flows contributing only a small portion of the total flows. This is particularly true in the pulmonary circuit where the total pulmonary blood flow (Q_P) and the volume of the pulmonary circuit (LA to LV to PA) is 2–3 times larger than the total systemic blood flow (Q_S) and the volume of the systemic circuit (RA to RV to aorta). The net result is transposition physiology, in which the PA oxygen saturation is greater than the aortic oxygen saturation.

Arterial saturation (Sao_2) will be determined by the relative volumes and saturations of the recirculated systemic and effective systemic venous blood flows reaching the aorta. This is summarized in the following equation:

Aortic saturation $= [$(systemic venous saturation)

$\times$ (recirculated systemic venous blood flow)

$+$ (pulmonary venous saturation)

$\times$ (effective systemic venous blood flow)$]$

$\div [$total systemic venous blood flow$]$.

This is illustrated in Fig. 6.4 where:

$Sao_2 = [(50)(1.2) + (99)(1.1)]/2.3 = 73\%$.

Obviously, the greater the effective systemic blood flow (intercirculatory mixing) relative to the recirculated systemic blood flow, the greater the aortic saturation. For a given amount of intercirculatory mixing and total systemic blood flow, a decrease in systemic venous or pulmonary venous saturation will result in a decrease in arterial saturation.

Table 6.2 Simple shunts (no obstructive lesions).

	Restrictive (small communication)	Nonrestrictive (large communication)
	1 Large shunt pressure gradient	**1** Small shunt pressure gradient
	2 Direction and magnitude of shunt are relatively independent of PVR:SVR	**2** Direction and magnitude of shunt are largely dependent on PVR:SVR
	3 Shunt is less subject to control by ventilatory or pharmacologic interventions	**3** Shunt is subject to control by ventilatory or pharmacologic interventions
	Examples: Small VSD, small PDA, modified Blalock–Taussig shunt, small ASD	*Examples:* Large VSD, large PDA, CAVC

ASD, atrial septal defect; CAVC, complete atrioventricular canal defect; PDA, patent ductus arteriosus; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; VSD, ventricular septal defect.

Classification of anatomic shunts

Anatomic shunts can be characterized as simple or complex.

Simple shunts

In an anatomic shunt, a communication (orifice) exists between pulmonary and arterial vessels or heart chambers (Table 6.2). In a simple shunt, there is no fixed obstruction to outflow from the vessels or chambers involved in the shunt. When the shunt orifice is small (restrictive shunt), a large pressure gradient exists across the orifice, and variations in outflow resistance (PVR; and systemic vascular resistance (SVR)) have little effect on shunt magnitude and direction. In this instance, the magnitude of the shunt is affected by the size of the shunt orifice. However, when the shunt orifice is large, the shunt becomes nonrestrictive, and the outflow resistance becomes the primary determinant of the magnitude and direction of shunting. These shunts, in which the ratio of PVR to SVR determines the magnitude of shunting, are known as dependent shunts. When the communication is very large, no pressure gradient exists between the vessels or chambers involved. In this instance, bidirectional shunting occurs, resulting in complete mixing and a functionally common chamber. Net systemic and pulmonary blood flow is then determined by the ratio of systemic to PVR (Fig. 6.6a–c).

Complex shunts

In complex anatomic shunt lesions there is obstruction to outflow in addition to a shunt orifice (Table 6.3). The obstruction may be at the valvular, subvalvular, or supravalvular level. The obstruction may be fixed (as with valvular or infundibular stenosis) or variable (as with dynamic infundibular obstruction). In complex shunts, outflow resistance is a combination of the resistance across the obstructive lesions and the resistance across the pulmonary or systemic vascular bed (Fig. 6.7). When an obstruction is severe, the SVR or PVR distal to the obstruction will have little effect on shunt magnitude or direction.

TOF is a good example of a complex shunt in which there is partial obstruction to outflow. There is a fixed component of right ventricular outflow obstruction in TOF secondary to infundibular, valvular, and possibly supravalvular obstruction. A dynamic component of right ventricular obstruction is produced by changes in the caliber of the right ventricular infundibulum. These two components of right ventricular outflow obstruction can produce a R–L shunt. Because right ventricular outflow obstruction is incomplete, increases in PVR will also increase the total right ventricular outflow resistance and increase R–L shunting. Similarly, a decrease in SVR relative to PVR will increase R–L shunting
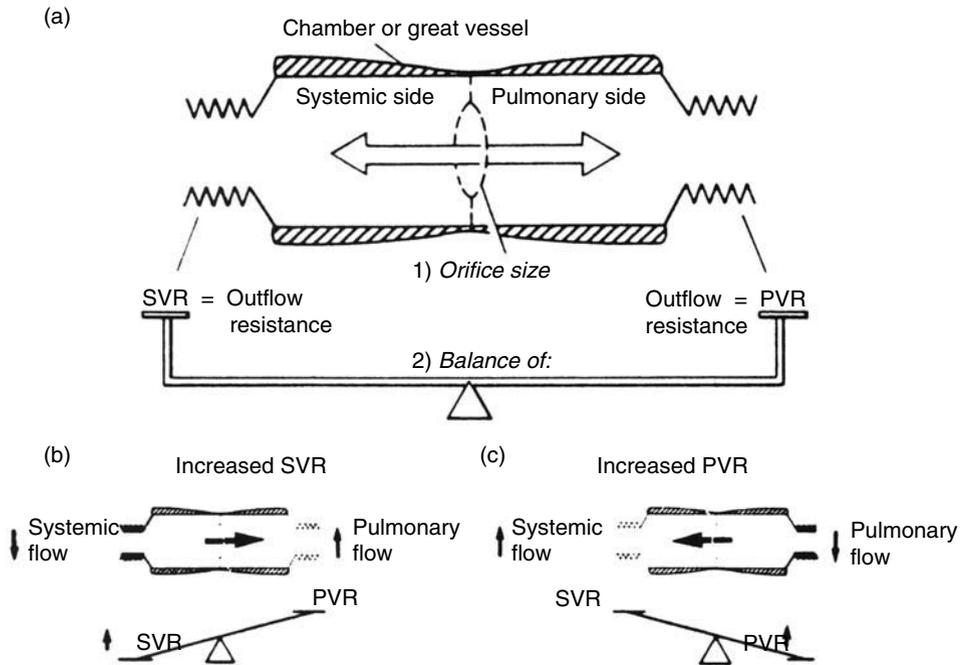
Fig. 6.6 Influence of orifice size and the pulmonary vascular resistance:systemic vascular resistance (PVR:SVR) ratio on the magnitude and direction of a dependant shunt. (a) PVR and SVR are balanced resulting in equal pulmonary and systemic blood flows.

(b) PVR is reduced relative to SVR, resulting in an increase in pulmonary blood flow and a decrease in systemic blood flow. (c) PVR is elevated relative to SVR, resulting in a decrease in pulmonary blood flow and an increase in systemic blood flow.

Table 6.3 Complex shunts (shunt and downstream obstructive lesion).

Partial outflow obstruction	Complete outflow obstruction
1 Shunt magnitude and direction is largely fixed due to the obstruction	**1** Shunt magnitude and direction is totally fixed
2 Shunt dependence on PVR:SVR is inversely related to the severity of the obstructive lesion	**2** All flow is thru the shunt, independent of PVR:SVR
3 Shunt pressure gradient is determined by both the shunt orifice and the obstructive lesion	**3** Shunt pressure gradient is determined only by the shunt orifice
Examples: TOF, VSD and pulmonary stenosis, VSD with coarctation	*Examples:* Tricuspid atresia, mitral atresia, pulmonary atresia, aortic atresia

PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Systemic obstruction

Pulmonary obstruction
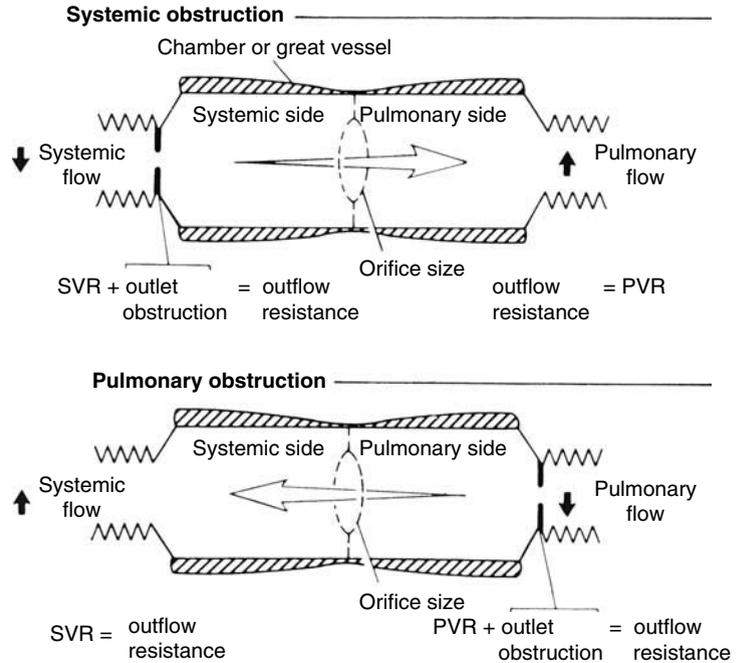
Fig. 6.7 Influence of orifice size and total outflow resistance on the magnitude and direction of a complex shunt. Total outflow resistance will be a combination of pulmonary vascular resistance (PVR) or systemic vascular resistance (SVR) and the resistance offered by the obstructive lesion.

without any increase in right ventricular outflow resistance.

Another form of complex shunt is present in patients who have single ventricle physiology. In these lesions, changes in SVR or PVR play no role in determining shunt magnitude or direction. The entire shunt flow is fixed and obligatory across the communication and complete mixing results. For flow of this mixed blood to reach the obstructed circuit, an additional downstream shunt, such as a VSD or PDA must be present. The downstream shunt may be simple or complex and is dependant on the ratio of PVR to SVR.

These concepts are critical to a clear understanding of the pathophysiology involved in patients with CHD. Describing a lesion as cyanotic or acyanotic may be misleading and simplistic. For example, in a patient with TOF, there may be minimal valvular or infundibular obstruction to pulmonary blood flow at baseline, and the patient may not be cyanotic. In fact, this type of patient ("pink Tet") may have a large L–R shunt through the VSD with increased pulmonary blood flow. During anesthesia, hypercarbia and hypoxemia may develop resulting in

an increase in both PVR and the dynamic component of infundibular obstruction. This will produce a net R–L shunt and cyanosis ("Tet spell"). Similarly, a cyanotic episode (a net R–L shunt) may be precipitated in the same patient by the SVR reduction that accompanies a febrile illness.

Pulmonary vascular pathophysiology

Pulmonary vascular occlusive disease (PVOD) may occur as the result of congenital heart lesions. Unfortunately of late PVOD has been used as an abbreviation for pulmonary veno-occlusive disease, a different process. PVOD as described in the context of CHD produces obstruction to pulmonary blood flow due to structural changes in the pulmonary vasculature. The morphologic changes have three components: increased muscularity of small pulmonary arteries, small artery intimal hyperplasia, scarring, and thrombosis and reduced numbers of intra-acinar arteries. These changes produce progressive obstruction to pulmonary blood flow and result in progressive and irreversible elevations of PVR and PA pressure. These changes may be graded morphologically

using lung biopsy or angiographically using the PA angiogram. Ultimately, these changes elevate PVR and reduce pulmonary blood flow. The increased muscularity of the small pulmonary arteries that accompanies development of PVOD enhances the response of the pulmonary vasculature to pulmonary vasoconstrictors.

The stimulus for development of PVOD is exposure of the pulmonary vascular system (both *in utero* and after birth) to abnormal pressure and flow patterns associated with CHD. In particular, three categories of abnormalities predispose the development of PVOD:

1 Exposure of the pulmonary vascular circuit to systemic arterial pressures and high pulmonary blood flows. Patients for whom the pulmonary vasculature is exposed to high flows and systemic arterial pressures typically have very early development of PVOD. This classically occurs in the presence of a large (nonrestrictive) VSD.

2 Exposure of the pulmonary vascular circuit to high pulmonary blood flow in the absence of high PA pressures. The progression of PVOD is typically much slower in this situation than when PA pressure is also elevated. A large ASD or a small (restrictive) PDA are examples of this type of lesion.

3 Obstruction of pulmonary venous drainage. This will lead to elevation of pulmonary arterial pressure and will predispose to development of PVOD. Pulmonary venous obstruction may result from stenotic pulmonary veins, which can exist in TAPVR or cor triatriatum. Pulmonary venous obstruction also may occur as the result of high LAPs (mitral atresia, congenital aortic stenosis, severe coarctation of the aorta) or high right atrial pressures (TAPVR).

Control of PVR

Alterations in PVR may be an important determinant of shunt magnitude and direction in some shunt lesions. Furthermore, the patient with CHD is likely to have an enhanced response of the pulmonary vasculature to vasoconstricting substances. It is therefore necessary to be familiar with the interventions that will alter PVR in the patient with CHD:

• *Pao_2*. Both alveolar hypoxia and arterial hypoxemia induce pulmonary vasoconstriction. A Pao_2 lower than 50 mmHg increases PVR over a wide range of arterial pH; however, this effect is enhanced when pH is lower than 7.40. Conversely, high levels of inspired oxygen can reduce an elevated PVR.

• *$Paco_2$*. Hypercarbia increases PVR, independent of changes in arterial pH. Hypocarbia, on the other hand, reduces PVR only through production of an alkalosis. In fact, reliable reductions in PVR and increases in pulmonary blood flow and Pao_2 are seen in children with R–L shunts when hyperventilation to a $Paco_2$ near 20 mmHg and a pH near 7.60 is obtained. Similarly, post-cardiopulmonary bypass (CPB) hyperventilation to a $Paco_2$ of 20–33 mmHg and a pH of 7.50–7.56 in patients with preoperative pulmonary hypertension results in a reduction in PVR when compared with ventilation that produces normocarbia or hypercarbia.

• *pH*. Both respiratory and metabolic alkalosis reduce PVR, whereas both respiratory and metabolic acidosis increase PVR.

• *Variation in lung volumes*. At small lung volumes, atelectasis results in compression of extra-alveolar vessels, whereas at high lung volumes, hyperinflation of alveoli results in compression of intra-alveolar vessels. Therefore, PVR is normally lowest at lung volumes at or near the functional residual capacity. Positive end-expiratory pressure (PEEP) may cause an increase in PVR by increasing alveolar pressure through hyperinflation. However, in situations in which PEEP works to recruit atelectatic alveoli and increase arterial Pao_2, a decrease in PVR generally is seen.

• *Anesthetic agents*. This topic will be discussed at length in the section on anesthetic agents.

• *Vasodilator agents*. Most IV pulmonary vasodilators (PGE_1, nitroglycerin, sodium nitroprusside, and tolazoline) induce systemic vasodilation as well. A number of inhaled agents (of which nitric oxide (NO) is the prototype) capable of providing selective pulmonary vasodilatation are now available. NO generated by endothelial NO synthase (eNOS) is an endogenous vasodilator. A wide variety of substances that increase intracellular calcium stimulate production of NO from L-arginine via eNOS. After it has been formed, NO diffuses from endothelium to vascular smooth muscle (VSM), where it binds to and activates guanylate cyclase to produce cyclic

guanosine monophosphate (cGMP). cGMP acts as a second messenger to catalyze reactions that lead to a reduction of VSM calcium by reduced calcium influx, increased calcium efflux, and reduced release of intracellular calcium. This produces relaxation of VSM and vasodilation. NO is involved in modulation of basal VSM tone as well. This modulation capacity is lost in vessels in which endothelium is removed or damaged.

Inhaled NO selectively reduces pulmonary hypertension and improves ventilation/perfusion matching in a variety of disease states. Pulmonary selectivity is based on three characteristics of NO:
- Its gaseous state allows delivery to ventilated alveoli by inhalation.
- Its small size and lipophilicity allows ready diffusion into the appropriate cells.
- Its avid binding to and rapid inactivation by hemoglobin prevents systemic vasodilatation. NO binds to oxyhemoglobin (Fe^{2+}) to form nitrosylhemoglobin which is rapidly converted to methemoglobin (Fe^{3+}) and NO_3^-.

Inhaled NO has been used to treat pulmonary hypertension in both the pre- and post-CPB period in a variety of congenital heart lesions and in treatment for persistent pulmonary hypertension of the newborn. Generally, approximately 20–40 ppm inhaled NO has been used. Some caution is warranted because both NO dependency and rebound pulmonary hypertension following NO discontinuation has been reported. No may not be effective in treating pulmonary hypertension when there is a downstream obstruction to pulmonary blood flow such as:
- Pulmonary vein obstruction.
- LA hypertension from LV dysfunction or mitral valve disease.
- A small LV where an increase in pulmonary venous return is likely to elevate LAP.

In these situations NO is unlikely to reduce pulmonary artery pressure (PAP) and will likely cause interstitial pulmonary edema.

An alternative to inhaled NO is aerosolized prostacyclin (PGI_2) and aerosolized PGE_1. PGI_2 and its analogues (iloprost, epoprostenol or Flolan) and PGE_1 act by binding to prostacyclin receptors and activating cyclic adenosine monophosphate

(cAMP). This activates protein kinase A, which leads to a reduction of VSM intracellular calcium, causing vasorelaxation. PGI_2 also stimulates endothelial release of NO. Aerosolized PGI_2 (2–50 ng/kg/min) is useful in selectively lowering PVR after congenital cardiac surgery. There is less experience with aerosolized PGE_1 but at doses of 150–300 ng/kg/min it has been proved useful in treatment of neonatal respiratory failure.

Sildenafil is cGMP-specific phosphodiesterase (PDE_5) inhibitor that also works to increase cGMP levels. Oral, IV, and aerosolized sildenafil is effective in reducing PVR.

Sympathetic nervous system stimulation
Sympathetic stimulation results in increases in both pulmonary and systemic vascular resistance. In children with PA medial hypertrophy, this may result in a hyperactive pulmonary vasoconstrictor response. Blunting of sympathetic outflow during a stress response attenuates increases in PVR in children predisposed to pulmonary hypertension.

In summary, control of ventilation with manipulation of Pa_{O_2}, Pa_{CO_2}, pH, and lung volumes are the best methods for altering PVR independently of SVR. A combination of a high inspired Fi_{O_2}, a Pa_{O_2} higher than 60 mmHg, a Pa_{CO_2} of 30–35 mmHg, a pH of 7.50–7.60, and low inspiratory pressures without high levels of PEEP, will produce reliable reductions in PVR. Conversely, a reduced Fi_{O_2}, a Pa_{O_2} of 50–60 mmHg, a Pa_{CO_2} of 45–55 mmHg, and the application of PEEP, can be used to increase PVR. Inhaled NO and prostacyclin are valuable selective pulmonary vasodilators in some patients.

Myocardial ischemia
Patients with CHD are more at risk for the development of subendocardial ischemia than is commonly appreciated. In some congenital lesions there are abnormalities in the coronary circulation predisposing to ischemia but in many others forms of CHD ischemia occurs in the presence of normal coronary arteries secondary to myocardial oxygen supply and demand imbalance.

Subendocardial perfusion is largely determined by coronary perfusion pressure (CPP), which is

the mean aortic diastolic pressure minus the ventricular end-diastolic pressure. In addition the time interval available for perfusion (predominately diastole) is critical. As a result, the relationship between heart rate, diastolic blood pressure, and ventricular end-diastolic pressure will determine whether subendocardial ischemia occurs. These factors as they apply to patients with CHD are considered below.

Aortic diastolic pressure

Subendocardial perfusion in a ventricle with systemic pressure occurs predominately in early diastole. In normal children, some subendocardial perfusion of the pulmonary or RV can occur in systole as well as in diastole because pulmonary ventricular systolic pressure is low. However, in many congenital lesions systolic pressure in both ventricles is systemic, and in some cases the pulmonary ventricle may have suprasystemic pressures. As a result perfusion of both ventricles may be dependent on the rapid increase in early diastolic flow.

Aortic diastolic pressure, which is normally low in neonates and infants, is further compromised in single ventricle physiology lesions because these lesions promote diastolic runoff of aortic blood into the lower resistance pulmonary circuit. The subgroup of patients with ductal dependent systemic blood and patients with truncus arteriosus are particularly at risk for enhanced aortic diastolic runoff. In addition, coronary perfusion is further compromised in patients with HLHS because the coronary ostia are perfused retrograde down a segment of atretic ascending aorta.

Subendocardial pressure

Subendocardial pressure is elevated and subendocardial perfusion is compromised in the presence of elevated ventricular end-diastolic pressure. Elevated end-diastolic pressure may be the result of impaired diastolic function (both reduced ventricular compliance and impaired ventricular relaxation), impaired systolic function, increased ventricular end-diastolic volume, or a combination of all three. For example, elevated ventricular end-diastolic pressure occurs as the result of the ventricular volume overload that accompanies single ventricle lesions, lesions with a high $Q_P:Q_S$, and regurgitant AV and semilunar valve lesions. The ventricular hypertrophy that accompanies pressure overload lesions is particularly detrimental to subendocardial perfusion. Ventricular hypertrophy reduces ventricular compliance and elevates ventricular end-diastolic pressure. In addition, the extravascular compressive forces that accompany a high external pressure workload further compromise myocardial perfusion by reducing transmural coronary vascular reserve (CVR). CVR is the ratio of hyperemic myocardial blood flow to baseline myocardial blood flow.

Heart rate

The duration of diastole diminishes geometrically as heart rate increases while the duration of systole remains relatively constant. As a result, the time available for diastolic coronary artery perfusion falls as heart rate increases. Consequently, a higher diastolic pressure is necessary to maintain subendocardial perfusion at higher heart rates. Hence, subendocardial perfusion is maintained in the presence of a low diastolic blood pressure if the heart rate is slower. In an infant with HLHS and an aortic diastolic pressure of 25 mmHg a heart rate of 130–140 b/min may well be tolerated without evidence of subendocardial ischemia whereas it is unlikely that a heart rate of 170–180 b/min will be tolerated at the same diastolic pressure.

Anatomic coronary artery lesions

Anatomic coronary artery abnormalities complicate the management of patients with a number of congenital cardiac lesions such as PA/IVS and Williams–Beurin syndrome.

Preoperative evaluation

Psychological considerations

The anesthesiologist who evaluates the patient with CHD must be aware of the considerable effect that appropriate psychological preparation may have during the preoperative and postoperative period.

The pediatric patient has unique psychological concerns that depend on age and previous surgical and anesthetic experience. In addition, the effect that serious heart disease has on parents and other family members cannot be minimized and must be addressed sensitively during the preoperative evaluation. Although neonates require no psychological preparation, the perioperative process can overwhelm the parents.

The preoperative psychological preparation must be appropriate to the age of the patient. Fear of separation from parents ("stranger anxiety") can be manifest in the infant at 8–12 months with an intense aversion to strangers. Very few toddlers, even if playful and cooperative in the presence of the parent, will leave their parent happily to go to the operating room. Older children have fears of disfigurement or that they will "wake up" or feel pain during and after surgery. Even the withdrawn, seemingly complacent adolescent often is in great turmoil regarding impending surgery. Previous surgery and anesthesia will influence even a young child's ability to cope with the newest operative experience. Psychological issues influence not only the conduct of the physical examination but also how much detail is discussed with parents in the presence of the patient. Obtaining informed consent from the parent in the presence of a school-aged child may create undue stress for the child. On the other hand, weak promises of "no needles" or little discussion about what the child can expect is equally unpleasant and counterproductive. Most experienced pediatric anesthesiologists, aware of the spectrum and unpredictability of children's behavior, prudently plan for alternative approaches to physical examination and, most importantly, how to pleasantly and safely separate the child from the parent for the induction of anesthesia.

Clinical history

Clinical history should include medications, allergies, past hospitalizations and operations (including prior anesthetic experiences), and a thorough review of systems. Performance of age-appropriate activities will aid in the evaluation of cardiac function and reserve. The infant in cardiac failure will manifest symptoms of low cardiac reserve during feeding. A parent might report that sweating, tiring, dyspnea, and circumoral cyanosis during feeding. The observation by a parent that the patient cannot keep the same pace as siblings often is a reliable clinical sign that cyanosis or congestive heart failure is worsening. Frequent pulmonary infections may occur as a result of increased pulmonary blood flow in otherwise asymptomatic patients. Cardiac catheterization data may be several months old by the time the patient presents for surgery, and the newly observed clinical signs may more accurately reflect the patient's current cardiac status.

Physical examination

Interpretation of vital signs is age-specific. Heart rate decreases and blood pressure increases with age (Figs 6.8 and 6.9). Growth curves also are useful. Congestive heart failure will sequentially inhibit age-appropriate gains in weight, height and head circumference. It is not unusual for patients with severe congestive heart failure to weigh less at 4 months of age than at birth. Interestingly, cyanotic children often do not manifest this failure to thrive.

Physical examination may reveal cyanosis, clubbing, or signs of congestive heart failure similar to those seen in adults (hepatomegaly, ascites, edema, or tachypnea). Rales may not be heard in infants and children with congestive heart failure, and the degree of heart failure may be determined more reliably by some of the signs and symptoms outlined above. Cyanosis is visibly detectable when the deoxyhemoglobin concentration is >5 g/dL and anemia masks detection of cyanosis. Differentiation between congestive heart failure and a upper respiratory tract infection can be difficult. The physical examination in both conditions may show mild tachypnea, wheezing, and upper airway congestion. Abnormal laboratory findings may help distinguish between the two. The decision to proceed to surgery may be necessary even when the differentiation between worsening congestive heart failure and a respiratory tract infection cannot be made with certainty.
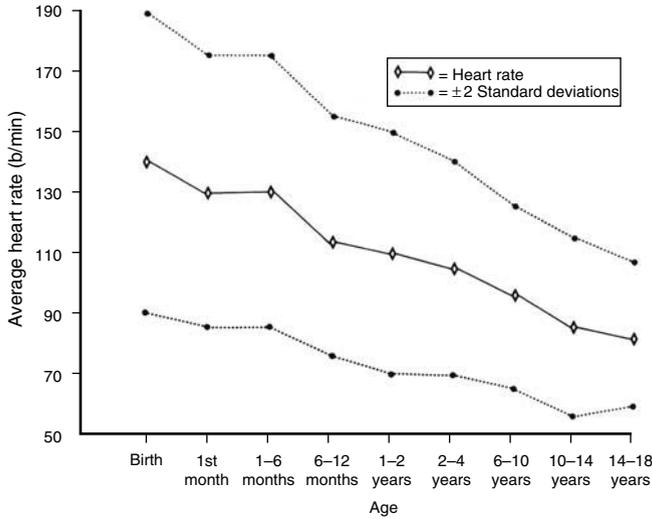
Fig. 6.8 Variation in average heart rate with age.
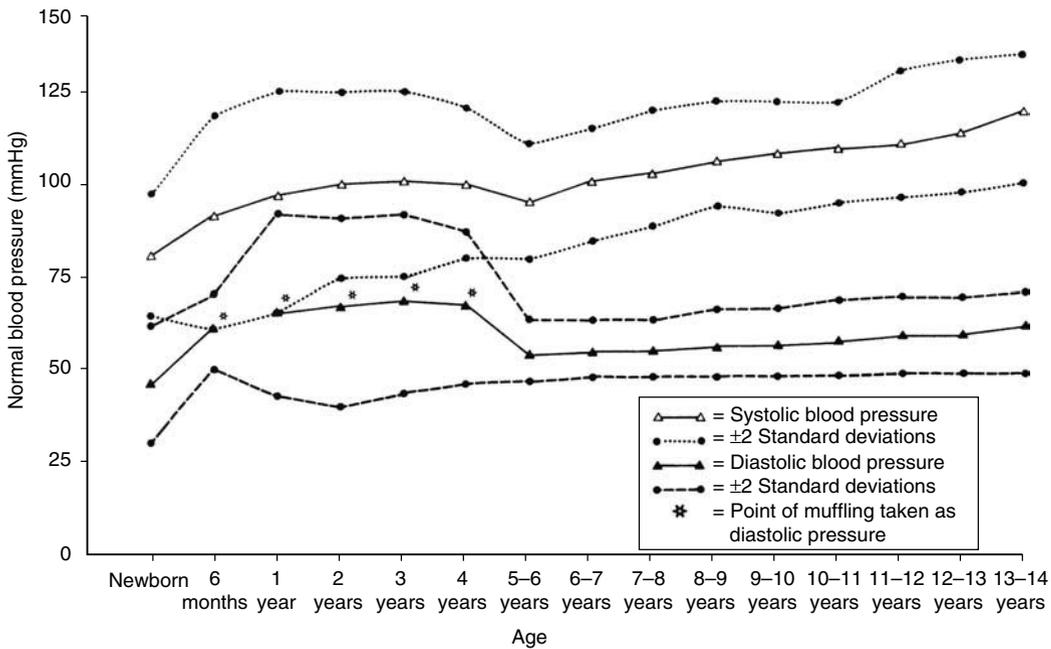
Fig. 6.9 Variation in normal blood pressure with age.

Physical examination should include an evaluation of the limitations to vascular access and monitoring sites. A child who has undergone a previous palliative shunt procedure may have a diminished pulse or unobtainable blood pressure in the arm in which the subclavian artery has been incorporated into the shunt. This obviously has implications for arterial catheter placement, blood pressure monitoring, and use of pulse oximetry during surgery. Finally, the child who has undergone multiple palliative procedures may have poor venous access, which will influence the mode of induction.

Approximately 8% of children with CHD have other congenital abnormalities. Preoperative evaluation must define these defects. For example, conotruncal lesions (TOF, interrupted aortic arch, truncus arteriosus, VSDs) are commonly associated with a 22q11.2 chromosomal deletion. This defect is associated with DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndromes. These syndromes are associated with hypocalcemia, immunodeficiency, facial dysmorphia, palate anomalies, velopharyngeal dysfunction, renal anomalies, and speech and feeding disorders. ASDs, VSDs, and TOF are seen in children with VACTERL (vertebral, vascular, anal, cardiac, tracheoesophageal, renal, and limb anomalies) and CHARGE (coloboma, heart anomaly, choanal atresia, retardation, and genital and ear anomalies) association. Tracheal stenosis must be considered in patients with VATER (vertebral defects, imperforate anus, transesophageal fistula, and radial and renal dysplasia) association who have undergone tracheoesophageal fistula repair. The incidence of CHD (primarily AV canal defects) in patients with trisomy 21 is approximately 50%. As they age these patients may present with problematic airways due to a large tongue and atlanto-occipital instability.

Laboratory data

A review of pertinent laboratory data and correlation with the clinical findings is necessary. The child in congestive heart failure may have mild iron deficiency because of chronically increased metabolic needs. The cyanotic child will be erythrocytotic in direct relation to the degree of arterial desaturation. Hematocrit levels higher than 65% are associated with a marked increase in blood viscosity. To avoid possible neurologic sequalae from such extreme viscosity, exchange transfusion should be considered before surgery. This is especially important if the proposed surgery is palliative and CPB with hemodilution is not employed. Patients with severe cyanosis and anemia may require transfusion. Cyanosis also affects the coagulation process, and it is not unusual to observe prolongation of prothrombin time (PT), partial thromboplastin time (PTT), and bleeding times. Thrombocytopenia or

functional platelet defects also may exist. In the face of reoperation with extensive dissection, the anesthesiologist should plan adequate blood component therapy for each patient.

Plasma electrolyte concentrations should be screened, especially in patients receiving digitalis and diuretic therapy. Hypocalcemia may be observed in patients with congestive heart failure as well as patients with DiGeorge syndrome. Severe congestive heart failure may be accompanied by jitteriness and irritability. It is important to rule out hypoglycemia as an alternative cause of these findings.

The chest radiograph serves to confirm other clinical and diagnostic findings, such as cardiomegaly, the quantity of pulmonary blood flow, previous surgical procedures, and the presence of acute pulmonary infections. The electrocardiogram (ECG) similarly confirms chamber enlargement and the presence of dysrhythmias. Review of the catheterization and echocardiographic data is critical to a clear understanding of the pathophysiology and surgical plan. The following information should be obtained routinely from a review of the catheterization data:

- *Anatomic diagnosis.*
- *Interpretation of saturation data.* Saturation step-ups or step-downs between vessels and chambers are used to detect shunts. Likewise, saturation data are used to calculate the ratio of pulmonary to systemic blood flow (Q_P:Q_S). Saturation data also are used to differentiate intrapulmonary shunting and V/Q mismatch (atelectasis, hypoventilation, pulmonary disease) from intracardiac shunting.
- *Interpretation of pressure data.* Pressure data are used to compare right and left heart pressures and systemic and pulmonary arterial pressures. In addition, pressure gradients across valve and shunt orifices are measured. Pressure data can be used to assess ventricular diastolic function (distensibility and compliance).
- *Interpretation of angiographic data.* Cineangiograms can be used to assess ventricular wall motion (systolic function) and to assess intracardiac and great vessel blood flow patterns.
- *Functional status and location of prior surgical interventions.* This information will allow intelligent

decisions regarding monitor placement and anesthetic management to be made.

• *Effect of interventions.* Interventions made in the catheterization laboratory to palliate congenital heart lesions (balloon valvuloplasty, balloon septostomy, balloon angioplasty) are common. The effects of these interventions on the underlying lesion must be assessed. Furthermore, a trial of 100% inspired oxygen or NO may be used to assess the reversible component of PA hypertension.

Two-dimensional echocardiography has revolutionized the field of pediatric cardiology over the last decade. Unlike adults, who may have limited transthoracic echocardiographic windows, images in pediatric patients are easily obtained. Most neonates proceed to surgery without catheterization studies. In rare instances catheterization is necessary to clearly delineate coronary or aortopulmonary collateral anatomy. Although angiocardiographic studies often complement echocardiographic findings, it is not unusual for the echocardiographic data to be a superior diagnostic tool and offer the surgeon more valuable anatomic information.

Preoperative preparation

The routine preoperative preparation of the anesthesia equipment is not noticeably different for the pediatric patient. It is important to have various-sized airway equipment so that there can be quick selection of appropriate airways, masks, and endotracheal tubes. A pediatric circle system with humidification can be used for older children. The resistance to airflow created by the unidirectional valves is not an issue for patients receiving mechanical ventilation. Generally, pressure-limited ventilation is used to avoid inadvertent barotrauma. This mode of ventilation requires vigilance in that changes in chest wall or lung compliance will lead to instantaneous changes in tidal volumes.

Appropriate emergency medications should be available in doses consistent with the patient's weight (Tables 6.4 and 6.5). For critically ill patients and patients with marginal reserve, selected infusions should be prepared in anticipation of their use. Careful attention should be paid to dosages because

Table 6.4 Vasoactive agents.

Agent	Dosage (IV)
Calcium chloride	10–20 mg/kg
Calcium gluconate	50–100 mg/kg
Epinephrine	0.05–0.50 µg/kg/min
Norepinephrine	0.05–0.50 µg/kg/min
Phenylephrine	0.1–0.50 µg/kg/min
Isoproteronol	0.01–0.05 µg/kg/min
Dobutamine	5–10 µg/kg/min
Dopamine	3–15 µg/kg/min
Milrinone	Bolus 50 µg/kg then 0.3–1.0 µg/kg/min
Nitroglycerin	0.5–5.0 µg/kg/min
Nitroprusside	0.5–5.0 µg/kg/min
Fenoldopam	0.1–0.5 µg/kg/min
PGE$_1$	Initiate at 0.05–0.10 µg/kg/min then 0.01–0.05 µg/kg/min

IV, intravenous; PGE$_1$, prostaglandin E$_1$.

Table 6.5 Antiarrythmic agents.

Agent	Dosage (IV)
Lidocaine	Bolus 1 mg/kg then 20–50 µg/kg/min
Procainamide	Bolus 2–5 mg/kg then 20–50 µg/kg/min
Diltiazem	Bolus 0.1–0.2 mg/kg then 1–3 µg/kg/min
Amiodarone	Slow bolus of 2–5 mg/kg with extreme caution in neonates/infants then 7 µg/kg/min
Esmolol	Bolus 300–500 µg/kg then 50–300 µg/kg/min
Adenosine	50–200 µg/kg
Magnesium	10–25 mg/kg

IV, intravenous.

the dose per kilogram may vary significantly from those used for adults.

Appropriate IV catheters are placed with air-trap filters in line to avoid the potential for air embolism in every patient (not just those with R–L shunts).

Preoperative fluid therapy

Preoperative fluid and NPO (nothing by mouth) orders are routinely geared to the age-specific needs of the pediatric patient. Generally speaking the rule of two, four, six, eight can be used as the NPO interval for neonates, infants and children with CHD:

- Two hours for clear liquids.
- Four hours for breast milk.
- Six hours for formula.
- Eight hours for solid food.

Obviously, in the absence of IV hydration infants should remain NPO for the shortest possible interval. Because dehydration may have potentially deleterious effects on hemodynamics or on the degree of blood viscosity in the polycythemic patient, IV hydration with maintenance fluids before surgery should be considered for certain patients (i.e. cyanotic patients with hematocrit levels of 60% or higher).

Maintenance caloric requirements in the awake neonate and infant are 100 kcal/kg/day or 4 kcal/kg/h. This caloric requirement can be met with glucose 25 g/kg/day or 1 g/kg/h. From a practical point of view this glucose requirement can be met with 10% dextrose (100 mg/mL) administered at maintenance volume replacement rate of 4 mL/kg/h. Ten percent dextrose administered at half this rate (2 mL/kg/h) is usually sufficient to meet the caloric requirements of an anesthetized infant while avoiding both the hyper- and hypoglycemia that can be detrimental to neurologic outcome following deep hypothermic circulatory arrest (DHCA). These dextrose infusions should be discontinued prior to commencement of CPB as CPB generally produces mild hyperglycemia. Some patients receive nutritional support as part of medical stabilization prior to surgery. High calorie total parenteral nutrition and intralipid therapy should be discontinued and replaced with a 10% dextrose infusion several hours prior to transport to the operating room. Continued administration of these high calorie infusions makes intraoperative serum glucose management problematic. In these patients, higher dextrose infusion rates may be necessary pre-CPB to avoid rebound hypoglycemia.

Preoperative medications

Premedication prior to induction can be used to facilitate a number of objectives. In older children it can be used to alleviate anxiety prior to an IV or inhalation induction. In younger children, premedication can ease separation of the child from the parents. In infants, judicious premedication alone, or in combination with inhaled nitrous oxide can greatly simplify placement of an IV catheter. One must always consider how stressful it is to parents to see their child being taken to the operating room crying or upset.

Current induction techniques do not justify routine administration of atropine or glycopyrrolate either IV or intramuscularly (IM) as a premedicant. Midazolam 1.0 mg/kg (20 mg as a maximum dose) orally in infants and younger children who have not had prior cardiac surgery is useful. In patients who have undergone previous operative procedures midazolam alone may be insufficient. These patients are remarkably tolerant to midazolam as the result of either heightened anxiety or previous intra- and postoperative exposure to benzodiazepines. Oral ketamine (3–5 mg/kg for infants, 5–10 mg/kg for children >1 year old) can be given in conjunction with the midazolam to these patients. In circumstances in which the child will not take oral medication the IM route can be used. Ketamine 2–3 mg/kg and glycopyrrolate (8–10 μg/kg) alone or in combination with midazolam 0.1 mg/kg is appropriate.

Age-appropriate premedication dosages are outlined in Table 6.6. Premedication requires individualization of dosage to avoid respiratory depression. Lower doses are best used for smaller children and children in congestive heart failure. Premedication should always be administered and assessed in the continuous presence of the anesthesiologist. Older children may opt for placement of an IV.

Digoxin, diuretics, and angiotensin-converting enzyme (ACE) inhibitors are generally withheld

Table 6.6 Premedication guidelines.

Age	Medication
0–6 months	None or Midazolam 0.5–1.0 mg/kg PO or Midazolam 0.5–1.0 mg/kg PO Ketamine 3–5 mg/kg
6–12 months	None or Midazolam 0.5–1.0 mg/kg PO or Midazolam 0.5–1.0 mg/kg PO Ketamine 3–5 mg/kg
>12 months	Midazolam 0.5–1.0 mg/kg PO or Midazolam 0.5–1.0 mg/kg PO Ketamine 5–10 mg/kg or Pentobarbital 4 mg/kg PO Meperidine 3 mg/kg or Midazolam 0.5–1.0 mg/kg PO Meperidine 3 mg/kg or Ketamine 3 mg/kg Midazolam 0.1 mg/kg IM Glycopyrrolate 8–10 μg/kg

IM, intramuscular; PO, by mouth.

the morning of surgery. ACE inhibitors exacerbate hypotension occurring with anesthetic induction. Inotrope and prostaglandin infusions are continued into the operative period for critically ill neonates and children.

Monitoring

If the infant or child is awake or minimally sedated, application of multiple monitors can prevent a smooth induction, even for an initially calm patient. Minimizing stimulation, including distracting discussion in the operating room, will avoid disturbing the child. Ideally, preinduction monitoring should include a noninvasive automated blood pressure cuff, ECG, pulse oximeter, and an end-tidal carbon dioxide monitor. In some cases, a pulse oximeter and an ECG may be all that is practical in the early stages of induction. Other monitors are then quickly added as induction progresses.

ECG and blood pressure

A 5-lead ECG with leads II and V$_5$ displayed allows rhythm and ischemia monitoring. Intra-arterial access is obtained following induction, however many neonates who have been medically stabilized in the intensive care unit (ICU) preoperatively will have an arterial catheter in place. Generally, percutaneous arterial access can be accomplished in even the smallest neonates. Radial and femoral arteries are the sites most commonly utilized. Posterior tibial and dorsalis pedis arteries may be used as well; however these sites often do not reflect central aortic pressure during and immediately following hypothermic CPB in neonates and infants. Brachial arteries are not used given the high risk of distal limb ischemia. Consideration is given to any previous or proposed surgical procedure which may compromise the reliability of ipsilateral upper extremity intra-arterial pressure monitoring such as a Blalock–Taussig shunt, modified Blalock–Taussig shunt, subclavian artery patch repair of aortic coarctation, or sacrifice of an aberrant subclavian artery. Previous catheterization procedures particularly those of an interventional nature may result in femoral or iliac artery occlusion. Occasionally, surgical access to a peripheral artery is necessary.

Umbilical artery catheters may be used intraoperatively but are generally replaced with a peripheral arterial catheter and removed postoperatively. Blood pressure monitoring consists of an intra-arterial catheter as well as upper and lower extremity noninvasive blood pressure cuffs. This arrangement allows detection of residual coarctation or aortic arch/isthmus obstruction via comparison of upper and lower extremity blood pressures.

Systemic oxygen saturation

Oxygen saturation (Sa$_{O_2}$) monitoring is accomplished with pulse oximeter probes on both an upper and a lower extremity; these can be placed in pre- and post-ductal locations if the physiology warrants.

End-tidal carbon dioxide

End-tidal carbon dioxide (ET_{CO_2}) monitoring is routinely employed with the caveat that the difference between Pa_{CO_2} and ET_{CO_2} will vary as physiologic dead space varies and that in some circumstances the difference may be large ($>10–15$ torr). Any acute reduction in pulmonary blood flow (decreased cardiac output, pulmonary embolus, increased physiologic intracardiac R–L shunting) will increase this gradient. In patients with single ventricle physiology (most commonly those with HLHS or truncus arteriosus) with high $Q_P{:}Q_S$ prior to initiation of CPB, the right PA may be partially, or completely, occluded by the surgeon to mechanically limit pulmonary blood flow. This maneuver dramatically increases physiologic dead space and ET_{CO_2} will vastly underestimate Pa_{CO_2}.

Central venous pressure (CVP)

Percutaneous central venous access offers numerous advantages and can be reliably obtained even in small neonates. The use of ultrasound both real-time and off-line has helped improve the successful placement rate to 90–95% in neonates. The preferred access sites are the internal jugular and femoral veins. Four-French 5 cm double lumen catheters are available for use in neonates and infants, 5-French 5 cm double lumen catheters are available for use in young children and 6–9-French catheters are available for use in older children. Preoperative use of PA catheters for pediatric patients is uncommon. In patients where postoperative assessment of PAP is important the surgeon may choose to place a transthoracic PA catheter.

Central venous access is not without risks particularly in neonates and infants and therefore the decision to place a percutaneous central venous catheter must involve consideration of the relative risks and benefits. In particular, the risk of internal jugular or SVC thrombosis must be considered as this complication can be devastating in patients who are to be staged to a superior cavopulmonary connection. The relative risk and benefits of central venous cannulation are outlined in Table 6.7. The risk of thrombosis and infection can be reduced by maintaining a heparin infusion (2 units/h) through the central line lumens postoperatively and by

Table 6.7 Advantages and disadvantages of central venous pressure monitoring in neonates, infants and children.

Advantages
- Central venous pressure monitoring
- Infusion site for vasoactive and inotropic agents
- Infusion site for blood products and intravascular volume replacement
- Sampling of SVC blood for measurement of SVC oxygenation saturation to determine the adequacy of cardiac output and to determine $Q_P{:}Q_S$ (internal jugular)
- Cardiac rhythm analysis (detection of cannon A waves may accompany loss of atrial-ventricular synchrony)
- Detection of inadequate SVC drainage leading to cerebral venous hypertension during CPB (internal jugular)

Disadvantages
- Pneumothorax (internal jugular)
- Hematoma with vascular or tracheal compression/displacement
- Thoracic duct injury (left internal jugular)
- Air embolus
- Internal jugular and/or SVC thrombosis
- Femoral vein thrombosis
- Infection

CPB, cardiopulmonary bypass; SVC, superior vena cava.

removing the lines as soon as possible (typically 1–2 days).

In some institutions neonates and infants are managed prior to CPB without central venous lines. Transthoracic intracardiac lines (RA, LA, PA) placed by the surgeon prior to termination of CPB can be used for pressure monitoring, infusion of vasoactive and inotropic agents, and blood product and volume replacement. In older children particularly those undergoing reoperation with adhesion of the aorta or of the RV to PA conduit to the sternum large bore central venous catheters are used in conjunction with a rapid infusion system. In these children, transthoracic intracardiac lines while suitable for pressure monitoring and infusion of drugs are insufficient for rapid volume replacement.

Temperature

Rectal, esophageal and tympanic membrane temperatures are monitored for all CPB cases.

Rectal temperature is considered a peripheral temperature site and equilibration of rectal temperature with tympanic and esophageal temperature serves as the best index of homogenous somatic cooling and rewarming. Rectal temperature lags behind esophageal and tympanic membrane temperature during both cooling and rewarming. Both esophageal and tympanic membrane are core temperature monitoring sites and temperature changes at these sites generally mirror brain temperature changes. Even so, esophageal and tympanic membrane temperatures may over- or under-estimate brain temperature by as much as 5°C during cooling and rewarming. This observation underscores the importance of providing an adequately long period of core cooling prior to commencement of low-flow CPB or DHCA. The likelihood that target brain temperature (15–18°C) will be reached is greatly increased if core cooling is utilized to bring tympanic, esophageal, and rectal temperatures to this target temperature.

Near infra-red spectroscopy

This is an evolving technology that holds promise as a real-time, on-line monitor of cerebral tissue oxygenation. All commercially available NIRS devices utilize continuous wave (cwNIRS) reflectance technology. With this technology the transmission and detection optodes are placed a few centimeters (3–6 cm) apart on the same side of the head. There are two closely placed (1–2 cm apart) detection optodes. The more proximal optode receives light, which passes primarily through extracranial tissue (skin, bone) while the distal optode receives light, which also passes through brain tissue. The difference between the two signals represents light passing through brain tissue.

Near infra-red spectroscopy (NIRS) technology is particularly suited to analysis of cerebral tissue oxygenation because wavelengths of light in the near infra-red range (650–900 nm) contain photons capable of penetrating tissue far enough to reach the cerebral cortex and because the peak absorption spectra of the chromophores best suited to reflect tissue oxygenation – oxyhemoglobin (HbO_2), deoxyhemoglobin (Hb), and oxidized cytochrome aa3 (CytOx) reside in this wavelength range.

Cerebral oxygen saturation (ScO_2) as measured by NIRS is the combined oxygen saturation of an uncertain mix of arterioles, capillaries, and venules. Commercially available NIRS monitors assume that ScO_2 represents contributions of cerebral arterial and venous blood in a ratio of 25:75 with the contribution of capillary blood felt to be negligible. Traditional pulse oximetry differs in this respect from NIRS because it is capable of isolating and measuring the arteriole component by gating measurements to pulsatility.

Investigations utilizing NIRS devices in neonates and infants are limited and both normal and critical values for cerebral oxygenation have yet to be determined. Nonetheless, it is clear that the technology has an emerging role in detecting cerebral deoxygenation and in guiding appropriate corrective interventions.

Transcranial Doppler

The role of Transcranial Doppler (TCD) monitoring in the care of pediatric cardiac surgical patients is evolving. TCD allows measurement of cerebral blood flow velocity as well as detection of cerebral microemboli and is a technology ideally suited to use in neonates and infants. The thin skull of neonates/infants combined with a low-frequency ultrasonic transducer allows transmission of ultrasonic energy into brain tissue with little signal attenuation. Placement of a 2 MHz pulsed wave (PW) Doppler probe over the temporal bone allows the ultrasonic signal to be aligned parallel to the proximal (M1) segment of the middle cerebral artery (MCA). The ability of PW Doppler to be gated to a specific depth allows determination of blood flow velocity in the MCA just distal to the takeoff of the anterior cerebral artery. This PW Doppler interrogation yields a velocity spectrum in the MCA for each cardiac cycle. Integration of the area under the velocity spectrum yields the time-velocity integral (TVI) in units of cm/cardiac cycle. The product of vessel TVI and vessel cross-sectional area (units of cm^2) is flow (units of cm^3/cardiac cycle). If it is assumed that MCA cross-sectional area remains constant than there is a linear relationship between TVI and MCA blood flow. Normal TCD velocity values in various patient subgroups (cyanotic versus

noncyanotic, age, following DHCA), and under various CPB conditions (hematocrit, flow, pressure, acid-base status, temperature) have yet to be determined. TCD determination of cerebral blood may prove useful as a continuous surveillance monitor for detection of inadequate flow or obstructed cerebral venous drainage during CPB.

Cerebral microemboli produce transient increases in reflected Doppler energy as compared to the background Doppler spectra. These high intensity transient signals (HITS) can be counted by the TCD microprocessor and displayed as microembolic events per hour. Due to their higher reflective capacity gaseous emboli can be detected over a greater distance than particulate emboli and as a result have a higher sample velocity length (the product of emboli duration and velocity). At present, cerebral emboli detection with TCD requires the constant attention of a skilled observer because TCD technology alone lacks sufficient sensitivity and specificity to distinguish between gaseous brain emboli, particulate brain emboli and artifacts. TCD emboli detection is being investigated as tool to refine post-CPB de-airing routines and to reduce the number of cannulation and perfusion related inatrogenic embolic events.

Transesophageal echocardiography (TEE)

7.5 MHz multiplane probes are available for intraoperative use in neonates and infants. These probes possess two-dimensional continuous wave Doppler, PW Doppler, color Doppler, and M-mode capability. Although intraoperative TEE can be performed safely in the smallest patients (2.5–3.5 kg) caution must be exercised as the presence of the probe in the esophagus may cause tracheal and bronchial compression with compromise of ventilation, inadvertent tracheal extubation, right main stem bronchial intubation, esophageal perforation, aortic arch compression with loss of distal perfusion, and compression of the LA resulting in left atrial hypertension or compromise of ventricular filling. In particular, ante- or retroflexion of the probe must be performed with caution in small patients.

Intraoperative TEE has a major impact on post-CPB decision making (such as return to CPB to repair residual lesions) in approximately

15% of cases when it is used nonselectively. Some institutions use intraoperative TEE selectively (approximately 30–40% of CPB cases) in cases involving repair of a semilunar or AV valve, complex ventricular outflow tract reconstructions, and for delineation of complicated anatomy that cannot be completely delineated with transthoracic echocardiography preoperatively. In the subset of patients undergoing valve repair and outflow tract reconstruction TEE provides the best immediate assessment of the adequacy of the operative procedure and if necessary directs its revision. TEE is not helpful in assessment of residual arch obstruction following stage 1 repairs as this area is poorly visualized. While detection of retained intracardiac air is certainly facilitated by use of intraoperative TEE it remains to be determined what role the technology will play in improving cardiac de-airing algorithms particularly in neonates and infants.

The role of TEE in the detection of residual VSDs following repair of both simple and complex defects deserves some discussion. Residual defects <3 mm are detectable by TEE but generally do not require immediate reoperation as they are hemodynamically insignificant. The majority (75%) of these small defects are not present at the time of hospital discharge as determined by transthoracic echocardiography. Residual defects >3 mm detected by TEE require immediate reoperation only if they are associated with intraoperative hemodynamic (elevated LAP and/or PAP in the presence of good ventricular function) and oximetric (Q_P:Q_S > 1.5:1 or RA to PA oxygen saturation step-up with $FiO_2 \leq 0.5$) evidence that they are significant.

Airway management

Fundamental to the anesthetic care of every patient with CHD is good airway management. As discussed previously, PVR is altered by changes in ventilatory pattern, PaO_2, $PaCO_2$, and pH. Changes in PVR may dramatically affect shunt magnitude and direction as well as cardiovascular function and stability. Therefore, prompt control of the airway and of ventilation will allow optimal pulmonary blood flow in each patient.

Children with high pulmonary blood flow particularly those with interstitial pulmonary edema have

surprisingly poor lung compliance necessitating higher than expected airway pressures. Care must be taken not to insufflate the stomach during mask ventilation. The relatively large occiput of infants and small children will cause the head to flex forward; placement of a small roll under the neck or shoulders will allow the head to remain in the neutral position. Placement of an oral airway in neonates and infants will greatly facilitate mask ventilation by pulling the large tongue away from the pharyngeal wall. In children <10–12 years old nasal endotracheal tubes are generally utilized as they provide better stability intra- and postoperatively. This is particularly important in patients undergoing intraoperative TEE examinations. Denitrogenation of the lungs is recommended prior to induction in all patients including those in whom high inspired oxygen concentrations might temporarily reduce PVR and compromise systemic perfusion.

In patients with high venous pressure and cyanosis, such as those with a bidirectional Glenn shunt or Fontan, nasal endotracheal tubes must be passed cautiously as substantial nasal bleeding can be initiated. Uncuffed endotracheal tubes with a leak at or near 25–30 cm H_2O are generally used in children <6–8 years of age. Consideration is given to use of a cuffed endotracheal tube in patients where poor pulmonary compliance secondary to lung water, chest wall edema, or abdominal distention are anticipated to compromise minute ventilation. In these patients temporary inflation of the cuff will allow higher airway pressures to be utilized as needed.

Anesthesia induction and maintenance

Induction of anesthesia

A variety of induction techniques provide hemodynamic stability and improved arterial oxygen saturation in patients with cyanotic heart disease. Sevoflurane, halothane, isoflurane, and fentanyl/midazolam do not change $Q_P{:}Q_S$ in children with ASDs and VSDs when cautiously administered with 100% oxygen. Sevoflurane (1 MAC) and fentanyl/midazolam have no significant effect on

myocardial function in patients with a single ventricle. Halothane (1 and 1.5 MAC) depresses cardiac index and contractility more than comparable levels of sevoflurane, isoflurane, and fentanyl/midazolam anesthesia. In addition, halothane anesthesia may result in more severe hypotension and emergent drug use than sevoflurane anesthesia in children with CHD.

No one anesthetic induction technique is suitable for all patients with CHD. The patient's age, cardiopulmonary function, degree of cyanosis, and emotional state all play a role in the selection of an anesthetic technique. IV administration of induction agents clearly affords the greatest flexibility in terms of drug selection and drug titration and allows prompt control of the airway. IV induction is the preferred technique in patients with severely impaired ventricular systolic function and in patients with systemic or suprasystemic PA pressures.

Mask induction

Mask induction of anesthesia can be accomplished safely in the subset of children without severe cardio-respiratory compromise. However, reduced pulmonary blood flow in cyanotic patients will prolong the length of induction and the interval during which the airway is only partially controlled. In addition, in these patients even short intervals of airway obstruction or hypoventilation may result in hypoxemia. Sevoflurane and halothane are the inhalation induction agents of choice. Sevoflurane causes less myocardial depression, hypotension and bradycardia than halothane. Isoflurane and particularly desflurane are unsuitable agents as their pungency causes copious secretions, airway irritation, and laryngospasm.

IV induction

High-dose synthetic narcotics in combination with pancuronium (0.1 mg/kg) is commonly used for IV induction in neonates and infants. The vagolytic and sympathomimetic effects of pancuronium counteract the vagotonic effect of synthetic opioids. In patients with a low aortic diastolic blood pressure and a high baseline heart rate vecuronium (0.1 mg/kg) or cisatracurium (0.2 mg/kg) may be

used without affecting heart rate. In older children with mild to moderately depressed systolic function lower doses of a synthetic opioid can be used in conjunction with etomidate (0.1–0.3 mg/kg).

Ketamine (1–2 mg/kg) is a useful induction agent. For patients with both normal and elevated baseline PVR, ketamine causes minimal increases in PA pressure as long as the airway and ventilation are supported. The tachycardia and increase in SVR induced by ketamine makes it unfavorable for use in patients with systemic outflow tract obstructive lesions.

The myocardial depressive and vasodilatory effects of propofol and thiopental make them unsuitable as induction agents except in patients with simple shunt lesions in whom cardiovascular function is preserved.

An alternative to IV induction in patients with difficult peripheral IV access is IM induction with ketamine (3–5 mg/kg), succinylcholine (2–5 mg/kg), and glycopyrrolate (8–10 μg/kg). Glycopyrrolate is recommended to reduce the airway secretions associated with ketamine administration and to prevent the bradycardia that may accompany succinylcholine administration. The dose of succinylcholine per kg body weight is highest in infants. This technique provides prompt induction and immediate control of the airway with tracheal intubation. It is useful in circumstances where it is anticipated that initial IV access will have to be obtained via the internal or external jugular vein or the femoral vein. This technique is hampered by the fact that the short duration of action of succinylcholine limits the period of patient immobility. An alternative technique combines IM ketamine (3–5 mg/kg), glycopyrrolate (8–10 μg/kg), and rocuronium (1.0 mg/kg). This technique is hampered by the slightly longer time interval until attainment of adequate intubating conditions with rocuronium.

Maintenance of anesthesia

Anesthesia is generally maintained using a synthetic opioid (fentanyl or sufentanil) based technique. These opioids may be used in high doses (25–100 μg/kg fentanyl or 2.5–10.0 μg/kg sufentanil) or in low to moderate doses (5–25 μg/kg fentanyl or 0.5–2.5 μg/kg sufentanil). In either instance these opioids are used in combination with an inhalation agent (generally isoflurane 0.5–1.0% or sevoflurane 1.0–2.0%) or a benzodiazepine (generally midazolam 0.05–0.10 mg/kg). Caution must be exercised because the combination of narcotics and benzodiazepines is synergistic in reducing SVR. The high-dose technique is particularly useful in neonates and infants. Patients in this age group presenting for surgery often have significant ventricular pressure and/or volume overload. In addition, many of these patients have tenuous subendocardial and systemic perfusion secondary to runoff into the pulmonary circulation and the associated low aortic diastolic blood pressure. Given the limited contractile reserve available in the immature myocardium, it is not surprising that the myocardial depressive and systemic vasodilatory effects of inhalation agents and the synergistic vasodilatory effects of benzodiazepines and opioids may be poorly tolerated in this patien group.

There are unique considerations for maintenance of anesthesia during CPB. Light anesthesia, particularly during cooling and rewarming, may lead to elevated SVR requiring a reduction in pump flow rate which compromises both somatic perfusion and the efficiency of CPB cooling and rewarming. Subclinical shivering due to inadequate neuromuscular blockade and light anesthesia are avoidable causes of increased systemic oxygen consumption. Increased systemic oxygen consumption during CPB will manifest as a lower than acceptable venous saturation (<65%) at what should be an adequate CPB flow rate for the patient. Furthermore, for a membrane oxygenator at or near its maximum flow capacity, a low venous saturation may result in a lower than acceptable arterial saturation on CPB.

Lower doses of opioid in conjunction with an inhalation agent or benzodiazepine are suitable for older patients with better cardiovascular reserve. In fact, carefully selected patients (>1 year old, no pulmonary hypertension, benign past medical history) undergoing simple ASD or VSD closure are candidates for immediate tracheal extubation in the operating room or in the ICU within 2–3 hours.

Specific lesions

This section discusses specific lesions and the anesthetic considerations applicable to their management.

Ventricular septal defects

Anatomy

An opening in the ventricular septum that permits communication between the RV and LV is a Ventricular septal defects (VSD). Such communications may exist in one or more locations in the ventricular septum. As illustrated in Fig. 6.10, VSD can be classified by their location in the septum.

Subpulmonary or supracristal defects
These are located in the infundibular septum just below the aortic valve. Subpulmonary lesions may be associated with aortic insufficiency due to a lack of support for the right coronary cusp of the aortic valve and prolapse of this leaflet.

Membranous or perimembranous defects
These defects comprise approximately 80% of all VSDs and are located in the subaortic region of

Fig. 6.10 Location of ventricular septal defects. AV, atrioventricular.

the membranous septum. These defects are located near or under the septal leaflet of the TV, and communicate with the LV just below the aortic valve. These defects are commonly partially closed by a collection of tricuspid valve and membranous septal tissue giving an aneurysmal appearance to the septum.

Conoventricular defects
These defects involve the same area as perimembranous defects but have extension anteriorly and superiorly in the septum.

Inlet or canal-type defects
These defects involve the posterior septum near the AV valves.

Muscular defects
These defects are located in the lower trabecular septum and may appear deceptively small on inspection from the right ventricular aspect of the septum due to heavy trabeculation. These defects may be apical, midmuscular, anterior, or posterior.

Physiology

A VSD is an example of a simple shunt. The size of the defect is the critical determinant of the magnitude of shunting. If the defect is small (restrictive shunt), flow through the defect will be limited and there will be a large pressure gradient across the defect. However, as the orifice becomes larger (approximating the size of the aortic valve orifice) and the pressure gradient across the orifice decreases, the magnitude and direction of shunting becomes more dependent on the relative resistances of the systemic and pulmonary vascular beds.

Because the ratio of PVR to SVR is normally 1:10–1:20, VSDs generally result in production of a L–R shunt. In some instances, however, the ratio of PVR to SVR may be higher, resulting in near-normal pulmonary blood flow or, in extreme cases, production of a R–L shunt.

The infant with a large VSD may have near-normal pulmonary blood flow as a result of high PVR present at birth. By the second week of life, PVR begins to fall to near-normal levels and pulmonary blood flow increases dramatically.
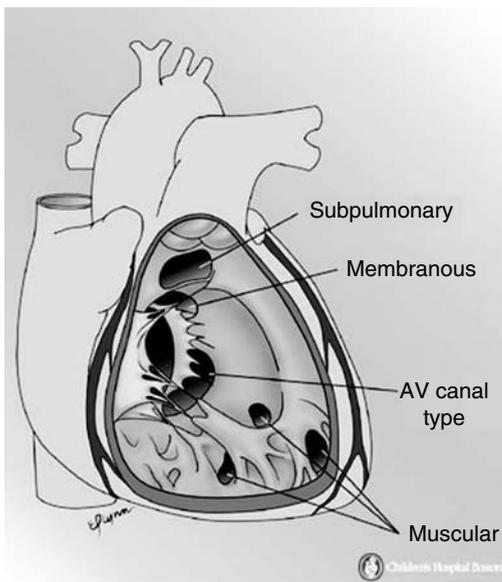
Continued decreases in PVR after birth may be delayed by the elevated LAP that accompanies increased pulmonary blood flow.

Large VSDs predispose the development of PVOD during the first few years of life due to exposure of the pulmonary vasculature to high flows and systemic blood pressures. The increases in PVR that accompany PVOD will ultimately produce bidirectional and R–L shunts. Patients with advanced PVOD and markedly increased PVR (Eisenmenger's complex) generally are not candidates for VSD closure, because closure will result in an enormous increase in RV afterload and RV afterload mismatch. For this reason, large VSDs (Q_p:Q_s > 2:1) are corrected early in childhood.

An increase in LA volume and pressure parallels the increase in pulmonary blood flow seen with a large VSD. The resultant pulmonary venous congestion increases the work of breathing, decreases pulmonary compliance, and increases airway resistance. All of these factors predispose recurrent pulmonary infections. LV end-diastolic volumes are increased in parallel with the increase in pulmonary blood flow. RV end-diastolic volumes are often not increased because shunting from the LV across the VSD into the RV occurs in systole.

In VSDs with a large L–R shunt, systemic blood flow is maintained at the expense of a large volume load on both the RV and LV. This limits the capacity of the patient to meet increased cardiac output demands and may result in pulmonary and systemic venous congestion at rest. The timing of surgery often is dictated by failure of medical therapy to control this congestion.

Surgical therapy

VSDs generally are closed with a patch via a variety of approaches, depending on their location. To avoid postoperative compromise of a small ventricle, with its poor compliance and limited capacity for tension development, a ventriculotomy to approach and correct VSDs should be avoided. Many defects are approachable through the RA and tricuspid valve, aorta, or PA. However, in some instances, a right ventriculotomy may be the necessary approach. Less commonly, assessment and closure of some muscular defects will require a left ventriculotomy. Because a left ventriculotomy may seriously compromise myocardial function in the infant, palliation with PA banding may be preferable to a left ventriculotomy for small infants. Nonoperative device closure of muscular VSDs remote from AV or semilunar valves is possible in the cardiac catheterization laboratory.

Anesthetic management

The anesthetic management goals are summarized in Table 6.8.

Induction and maintenance

As discussed previously, control of ventilation is the most reliable way to manipulate PVR. For infants and children without congestive heart failure (CHF), an inhalational induction is well tolerated. For neonates and patients with CHF, an IV induction with fentanyl or sufentanil will provide better hemodynamic stability. In particular, for patients with reactive pulmonary vasculature, high doses of fentanyl and sufentanil will be useful in blunting increases in PVR associated with surgical stimulation. In the absence of IV access, IM ketamine and atropine may be used for induction, followed by placement of an IV catheter.

Table 6.8 Anesthetic management goals in patients with atrial septal defect (ASD), ventricular septal defect (VSD), atrioventricular canal defect (AVC), and patent ductus arteriosus (PDA).

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1 Maintain heart rate, contractility, and preload to maintain cardiac output. A reduction in cardiac output will compromise systemic perfusion, despite a relatively high pulmonary blood flow
2 Avoid decreases in the PVR:SVR ratio. The increase in pulmonary blood flow that accompanies a reduced PVR:SVR ratio necessitates an increase in cardiac output to maintain systemic blood flow
3 Avoid large increases in the PVR:SVR ratio. An increase may result in production of a right-to-left shunt
4 In instances in which a right-to-left shunt exists, ventilatory measures to decrease PVR should be used. In addition, SVR must be maintained or increased. These measures will reduce the magnitude of the right-to-left shunt

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PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

Post-CPB management

The post-CPB management goals are summarized in Table 6.9.

Closure of the VSD will prevent further exposure of the pulmonary vasculature to high flows and pressures. This usually will result in some immediate decrease in PA pressures. For patients with small defects and patients with large VSDs in whom PVOD has not yet developed, near-normal PA pressures may result. In these patients, inotropic support post-CPB is rarely necessary. In fact, reduction in the large volume load on the LV usually results in post-CPB hypertension. Direct vasodilators such as sodium nitroprusside (0.5–1.0 µg/kg/min) or inodilators such as milrinone (0.5–1.0 µg/kg/min) may be necessary.

Pulmonary artery pressures and PVR will remain elevated in patients with underlying PVOD. In addition, the pulmonary vasculature of these patients will remain hyper-responsive to vasoconstricting stimuli due to medial hypertrophy that accompanies PVOD. Therapy to reduce PVR in the post-CPB period may be necessary for these patients to avoid RV afterload mismatch.

Separation from CPB may be complicated by a variety of surgical problems. Inadequate closure of the VSD or the presence of an unrecognized VSD may prevent separation from CPB. Assessment of the presence and location of such defects in the operating room can be accomplished with TEE. In addition, tricuspid valve damage due to a difficult transatrial approach may produce tricuspid regurgitation (TR). Patch closure of the VSD may create subaortic or subpulmonic obstruction. Because the AV node and His bundle are often near the area where the surgeon is working, transient heart block may occur. Temporary epicardial A–V sequential pacing may be necessary to terminate CPB.

Atrial septal defect

Anatomy

Strictly speaking an atrial septal defect (ASD) is a communication between the LA and RA due to a defect in the intra-atrial septum (IAS). The IAS consists of a central membranous portion and a thicker inferior and superior fatty limbus. The central membranous portion is formed by tissue of the septum primum ultimately forming the fossa ovalis. This membrane lies posterior to the superior aspect of the fatty limbus.

ASDs, like VSDs, are classified by their location. Figure 6.11 illustrates the anatomy of ASDs. There are four morphological types of ASDs: (i) ostium secundum defects; (ii) ostium primum defects; (iii) inferior and superior sinus venosus defects; and (iv) coronary sinus (CS) defects. Although they are classified as ASDs, sinus venosus and CS defects are not truly defects in the IAS.

Ostium secundum ASD
These defects comprise 80% of ASDs. While a PFO results from incomplete fusion of an intact fossa ovalis membrane with the superior aspect of the fatty limbus, an ostium secundum ASD is the result of actual deficiencies in the membrane (septum primum) of the fossa ovalis.

Table 6.9 Post-cardiopulmonary bypass (CPB) management goals in patients with atrial septal defect (ASD), ventricular septal defect (VSD), and atrioventricular canal defect (AVC).

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1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart rate dependent in the post-CPB period
2 Reduce PVR through ventilatory interventions. This is particularly important if PVOD is present
3 Inotropic support of the right ventricle may be necessary, particularly if PVR is high. In VSD and AVC patients the left ventricle will no longer contribute to ejection of blood via the pulmonary artery and the right ventricle will face a high afterload. Dobutamine (5–10 µg/kg/min) or dopamine (5–10 µg/kg/min) is useful in this instance because both agents provide inotropic support without increasing PVR. Milrinone (0.5–1.0 µg/kg/min following a loading dose of 50 µg/kg) may also be considered. Milrinone has more direct PVR reducing effects in addition to inotropic, lusitrophic, and SVR reducing effects

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AVC, atrioventricular canal defect; PVOD, pulmonary vascular occlusive disease; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; VSD, ventricular septal defect.
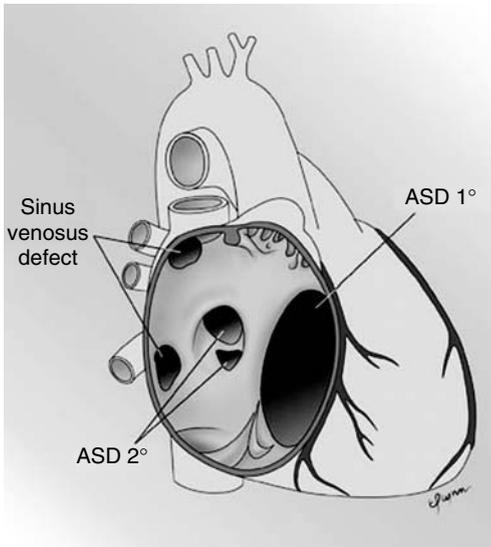
Fig. 6.11 Location of atrial septal defects (ASDs). ASD 1 = primum ASD; ASD 2 = secundum ASD. Superior and inferior sinus venous defects are shown.

Ostium primum ASD
Isolated ostium primum ASDs, also know as partial AV canal defects develop when partial fusion of the endocardial cushions separates the two AV valves and closes the ventricular septal communication, but fails to close the ostium primum. This defect occurs outside the confines of the fossa ovalis inferiorly at the level of the AV valves. The isolated ostium primum defect extends from the inferior IAS fatty limbus, to the crest of the IVS. A characteristic finding of this lesion is insertion of the septal portions of both AV valves on the IVS at the same level. Normally insertion of the TV to the IVS is inferior to the mitral valve (MV), producing the ventriculoatrial septum (VAS) that separates the RA from the LV. Isolated ostium primum defects are commonly associated with a cleft anterior MV leaflet and mitral regurgitation (MR) resulting from partial fusion of the leftward portions of the antero-superior and infero-posterior bridging leaflets that normally fuse to form the anterior MV leaflet.

Sinus venous defects
These defects are located either superiorly at the junction of the RA and the SVC, or inferiorly at the junction of the RA and the IVC. Both defects are located posterior to the fossa ovalis. Superior defects comprise the majority and inferior defects are rare. These defects are believed to result from a deficiency in the common wall that normally separates the right upper pulmonary vein/LA junction from the RA/SVC junction and the right lower pulmonary vein/LA junction from the RA/IVC junction, rather than a defect in the IAS or a change in the position of the pulmonary veins per se. Unroofing of the pulmonary vein (located posteriorly) permits drainage of the LA directly in the SVC or IVC (located anteriorly). Intra-atrial communication occurs at the level of the pulmonary vein/LA junction rather than through an IAS defect.

Both types are associated with partially anomalous pulmonary venous return (PAPVR). In the case of the superior defect, anomalous drainage of the right upper pulmonary vein into the SVC/RA junction is the most common finding. In the case of the inferior defect Scimitar syndrome (anomalous drainage of the right upper and lower pulmonary veins to the IVC/RA junction, aortopulmonary collaterals to the right lower lobe, and hypoplasia of the right lung) can be seen.

CS defect
Unroofing of the CS (posterior) allows direct communication with the LA (anterior). At its entry in the RA, the CS orifice becomes the connection between the LA and RA. CS defects are commonly associated with a persistent left superior vena cava (LSVC) draining to a large dilated CS.

Physiology
An ASD is a simple shunt. A small, restrictive defect will allow minimal shunt flow. A large defect (at least 1 mm in diameter), is unrestrictive and the atria act like a single chamber with shunt magnitude and direction dependent on the relative resistances of the pulmonary and systemic vascular beds. After the high PVR present after birth declines, a L–R shunt occurs because:
- PVR is 1/10–1/20 that of SVR.
- Increased pulmonary blood flow increases LAP. This favors flow of blood from the LA into the RA.

• RV compliance is greater than LV compliance. This also favors flow of blood from the left to the RA.

A large defect will greatly increase pulmonary blood flow however, unlike a VSD, systemic pressures are not transmitted to the pulmonary vasculature. In fact, PAP may remain normal for many years due to the distensibility of the pulmonary arteries. In contrast to a patient with VSD, the onset of PVOD may not occur until the third or fourth decade of life for a patient with ASD. Finally, a large ASD imposes a large volume load on the LA, RA, and RV. RV volume overload (RVVO) is typically reported on echocardiograms in patients with ASD.

Surgical therapy

Some small ostium secundum ASDs can be primarily closed; whereas larger defects are patched, usually with pericardium. An alternative is non-operative device closure of secundum ASDs in the cardiac catheterization laboratory. Primum ASDs generally require patch closure and suture closure of the anterior leaflet mitral cleft. Sinus venous defects without PAPVR can be closed primarily with a patch.

An alternative procedure is performed when the pulmonary vein(s) anomalously enter the SVC. The SVC is transected above the origin of the anomalous vein(s). The proximal end of the SVC is over sewn, and the SVC orifice is directed across the defect into the LA with a pericardial patch. The distal end of the SVC is then anastomosed end-to-end to the roof of the RA appendage recreating SVC to RA continuity.

CS defects are treated as follows:

• In the absence of a persistent LSVC draining to the CS, a CS defect is treated by oversewing the orifice of the CS and allowing CS blood to drain to the LA (a very small physiologic right-to left shunt).

• In the presence of a persistent LSVC draining to the CS in which the LSVC is connected to the right SVC by the innominate vein the LSVC can be ligated below the innominate vein and the CS over sewn.

• In the presence of a persistent LSVC draining to the CS in which the LSVC is not connected to the right SVC by the innominate vein the CS defect must be closed with a patch from the LA. This isolates the LA from the LSVC blood and directs LSVC blood thru through the orifice of the CS into the RA.

Anesthetic management

The anesthetic management goals are summarized in Table 6.8.

Induction and maintenance

Most children with ASDs have excellent cardiac reserve and will tolerate an inhalation induction without problems. Good airway management is necessary to allow manipulation of PVR and prevent reversal of L–R shunting. The presence of an enlarged atrium may predispose atrial dysrhythmias; these usually are well tolerated.

For children with an isolated ASD and no PVOD early extubation in the ICU or extubation in the operating room after repair is possible. An inhalational induction with sevoflurane followed by placement of an IV and administration of pancuronium 0.1 mg/kg and fentanyl 10–15 µg/kg can be used. An alternative following IV placement is thiopental, propofol, or etomidate in conjunction with pancuronium and a remifentanil infusion (0.3–1.0 µg/kg/min). In either case, anesthesia is maintained with isoflurane (0.5–1.0%) or sevoflurane (1.0–2.0%) supplementation. Caudal morphine (70 µg/kg in 5–10 mL of preservative-free saline) can be administered after induction. A vaporizer on the CPB circuit can provide anesthesia during CPB.

Post-CPB management

The post-CPB management goals are summarized in Table 6.9.

Separation from CPB usually is not problematic. In primum defects, there is the possibility of heart block, as the patch must be sutured to the crest of the IVS. In addition, the possibility of residual mitral regurgitation exists. If partial anomalous pulmonary venous drainage is unrecognized during sinus venous defect closure, a residual L–R shunt may exist after repair. Intraoperative TEE can be used to detect this defect. In the rare patient with PVOD, the pulmonary vasculature is likely to be hyper-reactive in the post-CPB period. Therefore, it is necessary to use ventilatory measures to reduce post-CPB PVR. These manipulations will prevent

right ventricular dysfunction secondary to increased afterload.

Atrioventricular canal defects

Anatomy

Embryologically, there are four endocardial cushions that contribute to the development of the lower ostium primum portion of the atrial septum and the upper, posterior inlet portion of the IVS where the AV valves insert. The cushions also contribute to the tissue that forms the septal leaflets of the mitral and tricuspid valves. Therefore, cushion defects, or atrioventricular canal (AVC) defects, include abnormalities in all these structures. The terminology of these lesions can be confusing and is summarized (Figs 6.12 and 6.13a–c) as follows:

• *Partial AVC.* This is an ostium primum ASD in association with a cleft mitral valve. There are two separate AV valve (mitral and tricuspid) annuli. No inlet VSD is present.

• *Transitional AVC.* This is an ostium primum ASD, common AV valve orifice, common antero-superior and postero-inferior bridging leaflets with dense chordal attachments to the crest of the IVS creating functionally separate mitral and tricuspid valves. There is a very small or absent inlet VSD.
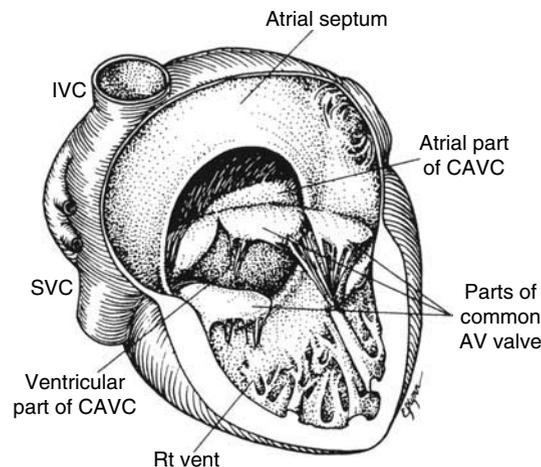
Fig. 6.12 Right ventricle opened to reveal components of a common atrioventricular canal defect. AV, atrioventricular; CAVC, common atrioventricular canal; IVC, inferior vena cava; Rt vent, right ventricle; SVC, superior vena cava.

• *Complete AVC (CAVC).* This is an ostium primum ASD, common AV valve orifice, common anterio-superior and posterio-inferior bridging leaflets with varying chordal attachments to the crest of the IVS. There is a moderate to large inlet VSD. The type of chordal attachments are summarized as follows:

• *Rastelli A.* The anterio-superior bridging leaflet is effectively divided into left (mitral) and right (tricuspid) anterio-superior leaflets by choral attachments to the crest of IVS. There is usually attachment of the postero-inferior leaflets to the crest of the IVS as well. The majority (70%) of CAVC are of this type.

• *Rastelli B.* There are chordal attachments from the right side of the IVS (RV septal papillary muscle) to left side of the anterio-superior bridging leaflet.
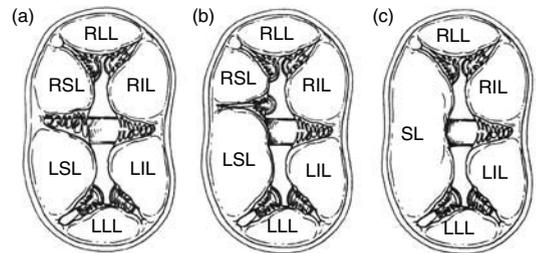
Fig. 6.13 Types of complete atrioventricular canal seen from above. (a) Rastelli type A – the most frequent form of common atrioventricular canal (CAVC). The superior (anterior) bridging leaflet is effectively divided into mitral (LSL) and tricuspid (RSL) portions, both of which are attached to the crest of the ventricular septum. The tricuspid portion represents the true anterior tricuspid valve leaflet. (b) Rastelli type B – the least frequent form of CAVC. The superior (anterior) bridging leaflet is effectively undivided but there are choral attachments from a right ventricle (RV) septal papillary muscle to the left side of the leaflet. (c) Rastelli type C – the form of CAVC most commonly associated with other major cardiac anomalies (such as tetralogy of Fallot). The superior (anterior) bridging leaflet is clearly undivided with no chordal attachments to the ventricular septum. LIL and RIL, left and right inferior (posterior) leaflets; LLL and RLL, left and right lateral leaflets; LSL and RSL, left and right superior (anterior) leaflets; SL, superior (anterior) bridging leaflet. (From Jacobs JP, *et al.* Congenital heart surgery nomenclature and database project; atrioventricular canal defect. *Ann Thorac Surg* 2000;**69**:S37, with permission.)

There are no choral attachments to the crest of the IVS.

- *Rastelli C.* There are no chordal attachments of the anterio-superior bridging leaflet to any portion of the IVS; there is usually an attachment to a RV free wall papillary muscle. This creates what appears to be a free-floating common AV valve. This type is seen most commonly in conjunction with other lesion such as TOF.

Physiology

These defects can result in communication between all four heart chambers as well as in abnormalities of the mitral and tricuspid valves. Because the orifice between the four chambers is large, these lesions tend to produce dependent simple shunts. As with large VSDs, this results in: (i) production of a large L–R shunt; (ii) increased pulmonary blood flow; (iii) transmission of systemic pressures to the RV and pulmonary arteries; and (iv) volume overloading of the RV and LV.

As with large VSDs, CAVC defects predispose the early development of PVOD. Advanced PVOD may increase the PVR:SVR ratio such that a bidirectional or R–L shunt develops. This is a particular concern for patients with trisomy 21. CAVC defects are common in these patients, who are particularly prone to early development of PVOD. In some CAVC defects, the presence of severe mitral insufficiency results in regurgitation of left ventricular blood directly into the RA (LV–RA shunt). This increases the L–R shunt. In addition, mitral regurgitation increases the volume work of the LV.

Surgical therapy

Repair of these defects involves:

- Septation of the common AV valve tissue into two separate competent, nonstenotic tricuspid and mitral valves.
- Closure of the ostium primum ASD.
- Closure of the inlet VSD.

This can usually be accomplished using a one-patch technique wherein a single patch is used to close both the VSD and ASD and the reconstructed AV valves are re-suspended by sutures to the patch. When the VSD is large and extends to other areas of the septum (as in TOF) two patches (atrial and ventricular) may be necessary. When the inlet VSD component is small the AV valve tissue can be sutured down to the crest of the ventricular septum essentially closing the VSD. A patch is then sutured to the crest of the ventricular septum and is used to close the ASD.

Anesthetic management

The anesthetic management goals are summarized in Table 6.8.

Induction and maintenance

Anesthetic management is similar to that for large VSDs. However, the child with CAVC also may have severe mitral regurgitation and a highly reactive pulmonary vasculature. Because control of ventilation is the most reliable way to manipulate PVR, prompt and reliable control of the airway at induction is important. The goal should be to use a reduced Fio_2 and to maintain $Paco_2$ at 35–40 mmHg. Inhalational induction should be reserved for infants and children with small defects, no mitral regurgitation, and no PVOD. Cardiac reserve often is limited or exhausted in patients with large shunts and high pulmonary blood flow. Moreover, the additional volume load imposed on the LV by mitral regurgitation will further limit cardiac reserve.

An IV induction and maintenance with fentanyl or sufentanil will provide better hemodynamic stability. In particular, for patients with reactive pulmonary vasculature, high doses of fentanyl and sufentanil will be useful in blunting increases in PVR associated with surgical stimulation. In addition, high doses of fentanyl or sufentanil will blunt stimulation-induced increases in SVR, which will increase the mitral regurgitant fraction.

Post-CPB management

The post-CPB management goals are summarized in Table 6.9.

Closure of the defects will prevent further exposure of the pulmonary vasculature to high blood flows and pressures. This usually will result in some immediate decrease in PA pressures. In patients with small defects and patients with large defects in whom PVOD has not yet developed, near-normal

PA pressures may result. However, PA pressures and PVR will remain elevated in patients with underlying PVOD. In addition, the pulmonary vasculature of these patients (especially patients with trisomy 21) will remain hyper-responsive to vasoconstricting stimuli due to medial hypertrophy that accompanies PVOD. Therapy to reduce PVR in the post-CPB period may be necessary for these patients to avoid RV afterload mismatch.

Separation from CPB may be complicated by a variety of surgical problems. Inadequate closure of the defects or persistent mitral regurgitation may prevent separation from CPB. Assessment of the presence and location of such defects in the OR can be accomplished with TEE. The presence of large V waves on the pressure trace obtained from a left atrial catheter may be helpful in assessing the degree of mitral regurgitation, whereas TEE will provide definite information. Occasionally, patch placement reduces the left ventricular chamber size and limits stroke volume. Because the AV node is near the area of patch placement, heart block may occur. Temporary epicardial AV sequential pacing may be necessary to terminate CPB.

Patent ductus arteriosus

Anatomy
A patent ductus arteriosus (PDA) connects the main pulmonary trunk near the origin of the left PA with the proximal descending aorta just distal to the origin of the left subclavian artery (Fig. 6.14).

Physiology
A PDA is a simple shunt. When the PDA is large, there is little or no pressure gradient across the duct and shunting becomes dependent on the ratio of PVR to SVR. Initially, the high PVR present after birth tends to limit the shunt magnitude of even the largest PDAs until PVR begins to decrease. As PVR decreases a L–R shunt with increased pulmonary blood flow develops. In order for systemic blood flow to be maintained left ventricular output must increase and a volume load must be imposed on the LV. The increased pulmonary blood flow increases pulmonary venous return and LAP. These factors may, in turn, increase PVR and the work of
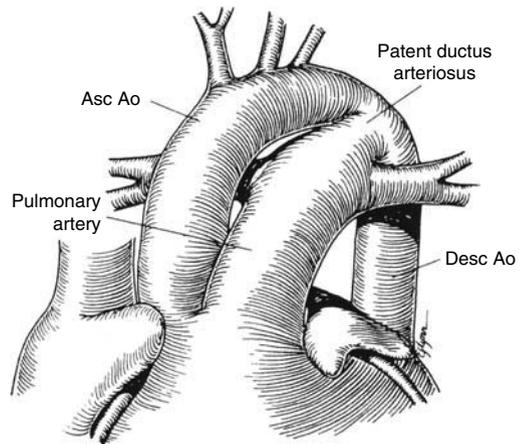
Fig. 6.14 Patent ductus arteriosus. Asc Ao, ascending aorta; Desc Ao, descending aorta.

breathing. Finally, runoff of blood from the proximal aorta into the PA tends to compromise distal organ perfusion and decreases aortic diastolic blood pressure reducing CPP.

Surgical therapy
Closure of the PDA was the first "cardiac" operation, successfully performed by Robert Gross at Children's Hospital Boston in 1938. The usual surgical approach is via a left thoracotomy or via video-assisted thoracoscopic surgery (VATS). CPB is not used. The ductus is either ligated or ligated and transected. The left PA, left main stem bronchus, or descending aorta is at risk to be inadvertently ligated if the PDA is misidentified. Injury to the recurrent laryngeal nerve is also possible.

Closure of a PDA currently is being accomplished in some cardiac catheterization laboratories using occlusion devices. An anesthetic often is necessary for this procedure, because catheter insertion is painful and placement of the device is impossible in a moving child. Dislodgement of the device downstream into the PA or aorta may occur and require surgical intervention.

Anesthetic management
The anesthetic management goals are summarized in Table 6.8. There are a few additional considerations. Surgical retraction of the left lung may

necessitate high inspired oxygen concentrations to prevent hypoxemia. Blood pressure should be monitored in an upper and lower extremity. The right arm is preferable to the left arm because the surgeon may have to place a clamp on the aorta if control of the aortic end of the PDA is lost during dissection or ligation. In patients with a large L–R shunt there will be an increase in aortic diastolic blood pressure following ligation due to cessation of runoff of blood into the pulmonary circulation. An upper and lower extremity blood pressure should be compared following ligation to assure that a coarctation has not been created.

Induction and maintenance

Most patients presenting for PDA ligation are premature infants with respiratory distress syndrome. Age and the likelihood that CHF exists make these patients poor candidates for inhalational anesthesia. A technique using high-dose fentanyl or sufentanil in combination with a benzodiazepine or low inspired concentration of inhalation agent is well tolerated.

For older children with an isolated PDA and no PVOD, early extubation or extubation in the operating room after ligation is possible. In this age group thoracotomy can be avoided using VATS. An inhalational induction with halothane or sevoflurane followed by placement of an IV and administration of pancuronium 0.1 mg/kg and fentanyl 10–15 μg/kg. Alternatively a remifentanil infusion (0.5–1.0 g/kg/min) can be utilized. Anesthesia is supplemented with isoflurane (0.5–1.0%) or sevoflurane (1.0–2.0%) supplementation. Caudal morphine (70 μg/kg in 5–10 mL of preservative-free saline) can be administered after induction for postoperative analgesia if a thoractomy is used.

Coarctation of the aorta

Anatomy

Coarctation of the aorta is a focal narrowing of the aorta and represents 6–8% of all congenital cardiac defects. Coarctation of the aorta is more commonly found in males and is the most common lesion in patients with Turner syndrome. Almost half of all cases have associated cardiac and noncardiac anomalies. The anatomic pathology is remarkably consistent with a discrete posterior shelf or invagination in the aortic wall just opposite of the insertion of the DA (juxta-ductal) and distal to the left subclavian artery. In some instances this shelf may be circumferential. Longer segment coarctation and coarctation of the abdominal aorta are also seen.

It has been postulated that coarctation develops as the result of fetal blood flow patterns which reduce antegrade aortic blood flow with a proportionate increase in PA and DA blood flow. It is not surprising then that coarctation is associated with aortic valve stenosis (most commonly bicuspid aortic valve), with hypoplasia of other left heart structures such as the mitral valve and LV, and with hypoplasia of the aortic arch. Hypoplasia of the aortic isthmus (the region of the aortic arch from the left subclavian to the DA) is the isolated aortic arch lesion most commonly associated with coarctation. VSDs, particularly posterior malalignment VSDs that cause left ventricular outflow tract (LVOT) obstruction and divert flow from the ascending aorta into the PA, are also associated with coarctation. In contrast, coarctation is virtually never found in association with obstructive right heart lesions.

Physiology

Despite remarkably consistent anatomic pathology, the pathophysiology of coarctation is varied and depends on the severity of the coarctation and the location of associated lesions (Fig. 6.15a,b). These variations in pathophysiology have led to the use of confusing terms such as infantile and adult coarctation or pre- and post-ductal coarctation, which are of little practical significance. Coarctation of the aorta produces LV pressure overload and a reduction in lower body perfusion. The physiologic consequences of a coarctation will depend on several factors:

- The severity of the coarctation.
- The extent of bypass afforded by the patent or partially PDA.
- The extent of collateralization to the distal aorta.
- The type and severity of associated heart lesions.
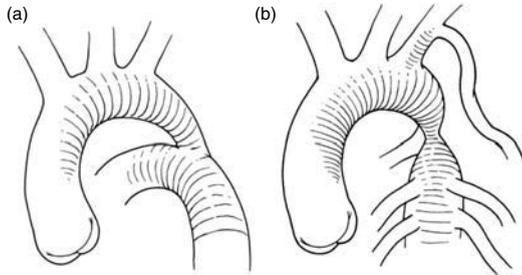
Fig. 6.15 Typical appearances of coarctation of the aorta. (a) Coarctation associated with hypoplasia of the aortic isthmus and ductal dependent perfusion of the descending aorta present at birth. Closure of the ductus arteriosus will likely result in left ventricle (LV) afterload mismatch with compromise of perfusion and oxygen delivery, and presentation in infancy. (b) Coarctation of the aorta in a patient who has tolerated ductal closure and developed extensive collateralization. Extensive fibrosis in the juxta-ductal region in association with growth of the native aorta has produced a discrete hourglass constriction. Presentation will be as a child or young adult.

The DA plays a critical role in pathophysiology. Closure of the DA after birth initially occurs at the pulmonary end with constriction of the aortic orifice normally delayed for several weeks or months. Closure of the aortic end of the DA may abruptly impede flow of blood around the aortic shelf lesion and increase the severity of the lesion (Fig. 6.16a–c). Ductal closure may also be associated with constriction of the aorta at the level of the DA presumably due to the presence of ductal tissue in this area. When coarctation is severe, distal aortic perfusion will, in part, be supplied with blood from the PA via a PDA (Fig. 6.17a–c). This will result in differential cyanosis with a higher arterial saturation proximal to the coarctation as compared to distal to the coarctation. When the development of aortic obstruction is gradual, collateral flow to the distal aorta will be established via the intercostal, internal thoracic, subclavian, and scapular arteries.

Presentation will be in infancy for all patients except those capable of tolerating ductal closure without overt hemodynamic compromise. In general, presentation beyond infancy is limited to patients with an isolated coarctation of mild to moderate severity or to those with rapid compensatory collateral formation. In these patients there is a secondary phase of fibrosis that occurs in the first 2–3 months of life. As the child grows, the ligamentum arteriosum develops a thick fibrous shelf within the lumen of the aorta.

In the presence of severe coarctation, particularly in association with left heart and aortic arch hypoplasia, patency of the DA is necessary to provide blood flow to the aorta distal to the coarctation (R–L physiologic shunt). In this ductal dependent physiology, RV pressures are systemic and femoral pulses are present.

Ductal closure in patients with a severe coarctation will result in near loss of distal perfusion. LV dilation from the acute afterload increase, left atrial hypertension, and pulmonary edema may ensue. The reduction in LV output may be so severe that proximal hypertension will not be present. The infant may present in a profound low cardiac output state or following cardiopulmonary arrest. In the case of a less severe coarctation, ductal closure will result in a diminution of distal perfusion and evidence of left atrial hypertension.

If an anatomic intracardiac shunt lesion (such as ASD or VSD) is also present the increased impedance to aortic ejection induced by the coarctation will enhance physiologic L–R shunting. Reductions in PVR will increase pulmonary blood flow thereby diverting flow from the distal aorta. Left atrial hypertension will be exacerbated by the increase in pulmonary blood flow.

In all these instances institution of PGE_1 (0.05–0.1 μg/kg/min) to re-establish ductal and aortic patency can be lifesaving. Mechanical ventilatory support, inotropic support, and diuretic therapy are usually necessary to stabilize the sickest infants following administration of PGE_1. These patients often present with a profound metabolic acidosis and suffer transient renal and hepatic dysfunction following initial resuscitation.

Patients presenting in childhood with coarctation will not be ductus dependent and will have well developed collaterals. In addition, they will have developed the concentric LV hypertrophy that accompanies chronic LV pressure overload lesions. These patients will have proximal aortic hypertension.
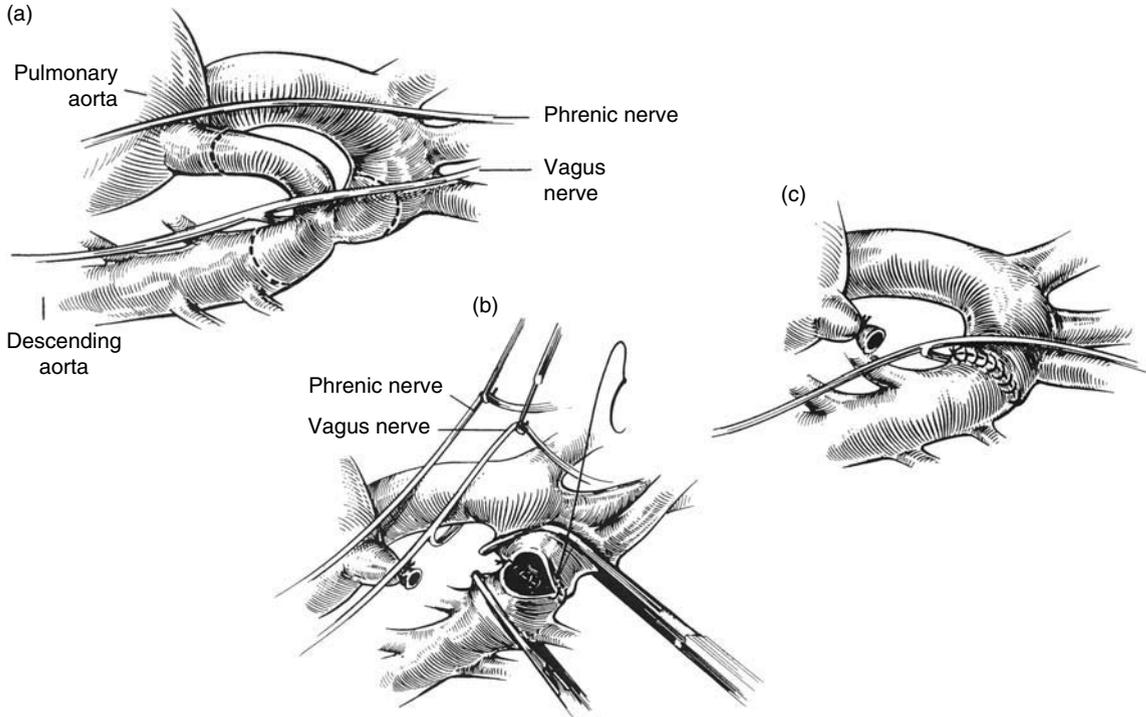
Fig. 6.16 Anatomy of coarctation of the aorta involving a small patent ductus arteriosus (PDA). Closure of this PDA will create a shelf-like invagination of the posterior aortic wall and increase the severity of the coarctation. The repair shown here (a–c) is resection of the coarcted segment, ligation of the PDA, and primary end-to-end reanastomosis of the aorta. Clamp placement has compromised flow to the left subclavian artery.

Surgical therapy

Three basic types of repair are used for correction of coarctation of the aorta: reverse subclavian patch angioplasty, synthetic patch angioplasty, and end-to-end anastomosis of the aorta after resection of the coarcted segment (see Figs 6.16 and 6.17). These procedures are performed via a left thoracotomy. It is necessary to cross-clamp the aorta to perform these procedures. For older children, partial CPB or a shunt from proximal to distal aorta may be used if the adequacy of the collateral circulation is in question.

Presentation as an infant generally leads to medical stabilization followed by surgical intervention. Complete excision of the area of coarctation and surrounding ductal tissue with end-to-end anastomosis is indicated. In the case of coarctation associated with a hypoplastic aortic isthmus complete excision in conjunction with an extended end-to-end or end-to-side anastomosis is recommended. The descending aorta is anastomosed to the underside of the aortic arch in an end-to-end or end-to-side fashion.

Dacron patch aortoplasty following resection of the posterior coarctation ridge is associated with late development of hypertension and aneurysm formation as compared to end-to-end anastomosis. Reverse subclavian patch angioplasty is rarely utilized, as the rate of re-coarctation is high. In adult patients placement of an interposition graft is usually necessary as there is insufficient mobility of the aorta to allow resection and end-to-end anastomosis.

Endovascular stent placement may prove to be an alternative therapy for treatment of coarctation in older children and adults with results superior
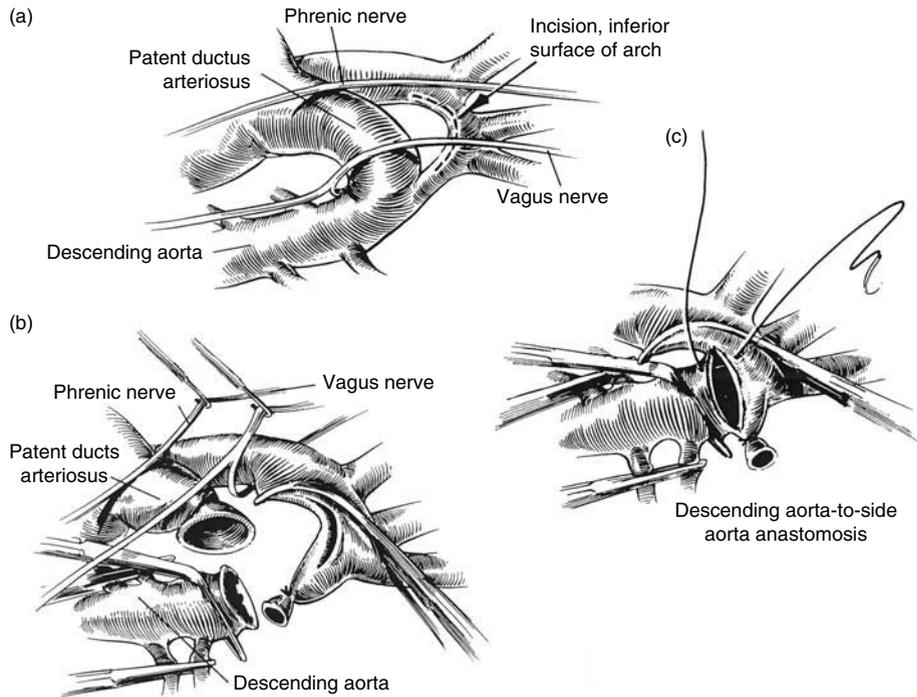
Fig. 6.17 Anatomy of coarctation of the aorta involving a large patent ductus arteriosus (PDA) and severe tubular hypoplasia of the aortic isthmus (arch). A good portion of the flow to the distal aorta is supplied from right-to-left (R–L) shunting through the PDA. The repair shown here is resection of ductal tissue and mobilization of the descending aorta and aortic arch to perform a primary reanastomosis. This increases the caliber of the aortic arch. Clamp placement has compromised flow to the left carotid artery.

to balloon dilation alone. This technique allows for subsequent percutaneous stent dilations over time as necessary.

The most devastating complication associated with coarctation repair is the development of paraplegia secondary to spinal cord ischemia. The incidence of paraplegia is quite low (0.14–0.40%). Several factors are associated with an increased risk of developing paraplegia: hyperthermia, prolonged aortic cross-clamp time, elevated cerebral spinal fluid (CSF) pressures, low proximal and distal aortic blood pressures, and poorly developed collaterals to the descending aorta.

Anesthetic management

Goals

1 Maintain heart rate, contractility, and preload to maintain cardiac output. The high afterload faced by the LV makes it particularly vulnerable to reductions in contractility.

2 For neonates and infants with coarctation, continuation of PGE_1 (0.01–0.05 μg/kg/min) to maintain ductal patency may be necessary to prevent cardiovascular collapse.

3 If there is an associated ASD or VSD, reduction in the PVR:SVR ratio should be avoided. Such reductions will increase pulmonary blood flow and will necessitate an increase in cardiac output to maintain systemic blood flow.

4 Avoid increases in SVR. Increased SVR will worsen LV pressure overload, which may cause large reductions in LV output.

5 Cross-clamping of the aorta may produce impressive proximal hypertension or LV dysfunction. This is less likely in the presence of well-developed collaterals.

The arterial line should be in the right arm. No blood pressure will be obtainable in the lower extremities during cross-clamping. The left arm is an unreliable blood pressure source during clamping because the proximal clamp may occlude or compromise the origin of the left subclavian artery. This is particularly true if the left subclavian patch technique is utilized.

Induction and maintenance

Neonates and infants presenting for coarctation repair generally are PGE_1 dependent with compromised distal perfusion and pulmonary congestion. They are not candidates for inhalational anesthesia. Ketamine may worsen hemodynamics by increasing SVR and probably should be avoided. A technique using high-dose fentanyl or sufentanil in combination with a benzodiazepine or low inspired concentration of an inhalation agent is well tolerated by these patients. In older children with only proximal systemic hypertension, IV or inhalational techniques are well tolerated. Regardless of the technique chosen, it should be appreciated that proximal blood pressure response to stimulation will be exaggerated.

Management after cross-clamp removal

Cross-clamping of the thoracic aorta has been shown to produce increases in both proximal aortic blood pressure and CSF pressure and decreases in distal aortic blood pressure. Use of sodium nitroprusside to normalize proximal aortic blood pressure results in further increases in CSF pressure and further decreases in distal aortic blood pressure. This combination of increased CSF pressure and reduced aortic blood pressure reduces spinal cord blood perfusion pressure and may place the spinal cord at greater risk for ischemia. Therefore, vasodilators should be used cautiously to control extreme proximal hypertension and LV dysfunction.

TEE is useful during cross-clamping, particularly for infants with coexisting cardiac lesions. LV function and the extent of intracardiac shunting can be monitored. In some instances of severe coarctation in infants, particularly those with proximal tubular hypoplasia, vasodilator therapy may be insufficient to prevent LV dilatation and inotropic support may be necessary. Inotropic therapy for patients with intracardiac shunts may only serve to increase L–R shunting. Ventilatory control of PVR will be complicated by the fact that the left lung must be retracted for exposure. It is important to know which arch vessels are clamped during the surgical procedure. At least one of the carotid arteries must be patent for cerebral perfusion (see Figs 6.16 and 6.17). The use of NIRS may be helpful in assessing the adequacy of cerebral blood flow.

Removal of the cross-clamp will result in reactive hyperemia in distal tissues with subsequent vasodilation and transient hypotension. Release of lactic acid will increase $Paco_2$. Volume expansion and hyperventilation just before clamp removal diminishes these effects. Cross-clamp times for these repairs are relatively short (<15 minutes), which reduces the hemodynamic consequences of clamp removal.

Postoperatively, rebound hypertension may occur and persist for up to 1 week. Initially this is likely due an altered baroreceptor response resulting in very high circulating levels of catecholamines play a role. Later, there may be involvement of the renin–angiotensin–aldosterone system. Beta-blockers and vasodilators are used to control this hypertension.

Older children without coexisting diseases are candidates for early extubation using the technique described for PDA ligation.

Tetralogy of Fallot (TOF)

Anatomy

TOF (Figs 6.18 and 6.19a,b) is actually more accurately described as TOF with pulmonary stenosis (TOF/PS) to distinguish it from TOF with pulmonary atresia (TOF/PA) and TOF with absent pulmonary valve (TOF/APV). TOF is characterized by a VSD, overriding of the aorta, right ventricular hypertrophy, and pulmonic stenosis (infundibular or subvalvular, valvular, supravalvular, or a combination). The key malformation is underdevelopment of the right ventricular infundibulum and displacement of the infundibular septum resulting in right ventricular outflow tract stenosis. Patients with TOF have displacement of the infundibular septum in an anterior, superior, and leftward direction. The posterior wall of the right ventricular outflow tract is formed by the infundibular septum and this
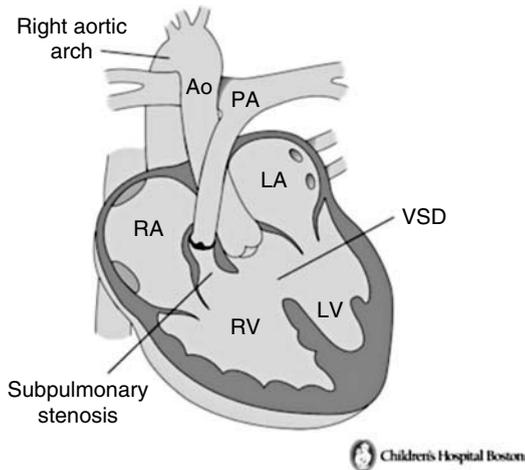
Fig. 6.18 Anatomy in tetralogy of Fallot (TOF). The following features are notable: malalignment ventricular septal defect (VSD), overriding aorta (Ao), infundibular pulmonic stenosis, and small pulmonary arteries. There is a right aortic arch with mirror image arch vessel branching as occurs in 25% of patients with TOF. LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.
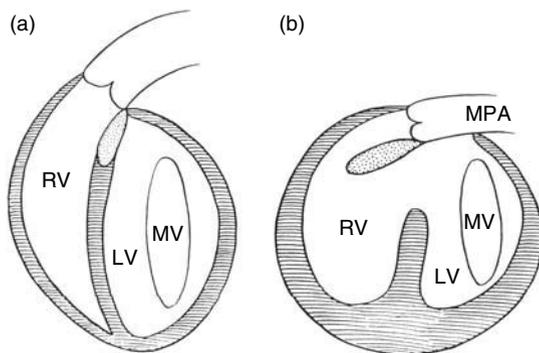
Fig. 6.19 (a) Long-axis view of heart illustrating the normal relationship of the infundibular septum (stippled) and the trabecular septum (striped). (b) Long axis view of heart in tetralogy of Fallot. Lack of connection between infundibular and trabecular septum results in malalignment ventricular septal defect. Right ventricular outflow tract is narrowed by upward, anterior tilt of infundibular septum. LV, left ventricle; MPA, main pulmonary artery; MV, mitral valve; RV, right ventricle.

abnormal displacement results in narrowing of the right ventricular outflow tract. In addition, this displacement of the infundibular septum creates a large malalignment VSD with the aorta overriding the intraventricular septum. Abnormalities in the septal and parietal attachments of the outflow tract further exacerbate the infundibular stenosis (Fig. 6.20a–c). Seventy-five percent of TOF patients will have both infundibular and valvular stenosis. A small proportion of patients will have multiple muscular VSDs.

The pulmonary valve is almost always bileaflet. At one end of the spectrum of TOF the pulmonary valve may be mildly hypoplastic (reduced annulus size) with minimal fusion of the pulmonary valve leaflets. At the other end of the spectrum the pulmonary annulus may be very small with near fusion of the valve leaflets. In addition, there are varying degrees of main PA and branch PA hypoplasia.

The most common associated lesion, present in 25% of patients is a right aortic arch with mirror image arch vessel branching (innominate artery gives rise to left carotid and left subclavian, right carotid and right subclavian arise separately).

Physiology

TOF is a complex shunt in which a communication (VSD) and a partial obstruction to RV outflow are present. In most patients with TOF, there is a fixed and a dynamic component to RV outflow obstruction. The fixed component is produced by the infundibular, valvular, and supra valvular pulmonary stenoses (SVAS). The dynamic component (subvalvular PS) is produced by variations in the caliber of the RV infundibulum.

In patients with TOF, the arterial saturation is a direct reflection of pulmonary blood flow. The typical TOF patient has fixed and variable components that create severe right ventricular outflow obstruction. This produces a right-to left shunt and cyanosis. A small subset of TOF patients ("pink tet") have minimal obstruction to pulmonary blood flow at the right ventricular outflow and PA level and may have normal oxygen saturation. Some of these patients have a L–R shunt with increased pulmonary blood flow and symptoms of CHF.
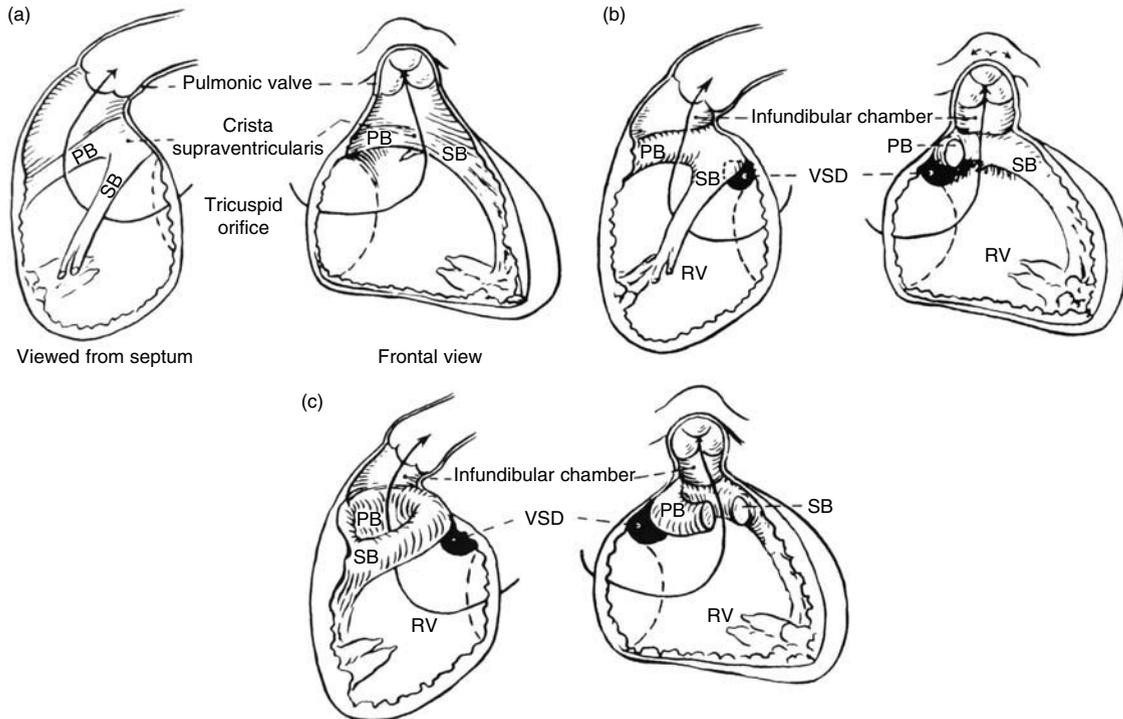
Fig. 6.20 Spectrum of infundibular stenosis produced by abnormalities in septal and parietal bands of crista supraventricularis. (a) Normal anatomy of crista supraventricularis. (b) Moderate infundibular stenosis and creation of an infundibular chamber secondary to hypertrophy and anterior, superior displacement of parietal band. (c) Severe infundibular stenosis with creation of infundibular chamber secondary to hypertrophy and anterior, superior displacement of both septal and parietal bands. PB, parietal band; RV, right ventricle; SB, septal band; VSD, ventricular septal defect.

Hypoxic or hypercyanotic episodes ("Tet spells")

The occurrence of hypoxic episodes in TOF patients may be life-threatening and should be anticipated in every patient, even those who are not normally cyanotic. Spells occur more frequently in cyanotic patients with the peak frequency of spells between 2 and 3 months of age. The onset of spells usually prompts urgent surgical intervention, so it is not unusual for the anesthesiologist to care for an infant who is at great risk for spells during the preoperative period.

The etiology of spells is not completely understood, but infundibular spasm or constriction may play a role. Crying, defecation, feeding, fever, and awakening all can be precipitating events. Paroxysmal hyperpnea is the initial finding. There is an increase in rate and depth of respiration, leading to increasing cyanosis and potential syncope, convulsions, or death. During a spell, the infant will appear pale and limp secondary to poor cardiac output. Hyperpnea has several deleterious effects in maintaining and worsening a hypoxic spell. Hyperpnea increases oxygen consumption through the increased work of breathing. Hypoxia induces a decrease in SVR, which further increases the R–L shunt. Hyperpnea also lowers intrathoracic pressure and leads to an increase in systemic venous return. In the face of infundibular obstruction, this results in an increased RV preload and an increase in the R–L shunt. Thus, episodes seem to be associated with events that increase oxygen demand

while simultaneous decreases in Pao_2 and pH and an increase in $Paco_2$ are occurring. Treatment of a "Tet spell" includes the following:

• Administration of 100% oxygen.

• Compression of the femoral arteries or placing the patient in a knee–chest position transiently increases SVR and reduces the R–L shunt. Manual compression of the abdominal aorta is particularly effective for the anesthetized patient. After the chest is open, the surgeon can manually compress the ascending aorta to increase impedance to ejection through the LV.

• Administration of morphine sulfate (0.05–0.10 mg/kg), which sedates the patient and may have a depressant effect on respiratory drive and hyperpnea.

• Administration of 15–30 mL/kg of a crystalloid solution. Enhancing preload will increase heart size, which may increase the diameter of the RV outflow tract.

• Administration of sodium bicarbonate to treat the severe metabolic acidosis that occur during a spell. Correction of the metabolic acidosis will normalize SVR and reduce hyperpnea. Bicarbonate administration (1–2 mEq/kg) in the absence of a blood gas determination is warranted during a spell.

• Phenylephrine in relatively large doses (5–10 μg/kg IV as a bolus or 2–5 μg/kg/min as an infusion) increases SVR and reduces R–L shunting. In the presence of severe RV outflow obstruction, phenylephrine-induced increases of PVR will have little or no effect in increasing RV outflow resistance. It is important to point out that treatment with α-adrenergic agents to increase SVR does nothing to treat the underlying cause of the spell although the decrease in unstressed venous volume induced by these agents may augment preload.

• Beta-adrenergic agonists are absolutely contraindicated. Increasing contractility will further narrow the stenotic infundibulum.

• Administration of propranolol (0.1 mg/kg) or esmolol (0.5 mg/kg followed by an infusion of 50–300 μg/kg/min) may reduce infundibular spasm by depressing contractility. In addition, slowing of heart rate may allow for improved diastolic filling (increased preload), increased heart size, and an increase in the diameter of the RV outflow tract.

• Extracorporeal membrane oxygenation (ECMO) resuscitation in refractory episodes when immediate operative intervention is not possible.

Surgical therapy

Palliative shunts

Palliative shunt procedures to increase pulmonary blood flow can be used for patients with TOF in whom complicated surgical anatomy precludes definitive repair at the time of presentation. In addition, some institutions delay elective complete repair until 12–18 months of age with placement of a palliative shunt if cyanosis occurs prior to that time interval. The disadvantages of a palliative shunt in TOF patients can be summarized as follows:

• The volume load imposed on the LV by these shunts parallels the increases in pulmonary flow produced. There will be progressive hypertrophy of the body and infundibulum of the RV during the interval from shunt placement to definitive repair as right ventricular outflow tract (RVOT) obstruction will not be relieved.

• Shunt placement may distort PA anatomy and impair subsequent growth making definitive repair more difficult.

• A large shunt with high pulmonary blood flow puts the patient at risk for development of PVOD.

The palliative shunt procedures involve creation of a systemic-to-pulmonary arterial shunt, essentially a surgically created PDA. Ideally, these surgical shunts should be mildly restrictive simple shunts. In the presence of a proximal obstruction to pulmonary blood flow, these shunts produce a L–R shunt and an increase in pulmonary blood flow. The shunts can be summarized as follows (Fig. 6.21a–d):

• *Waterston and Potts shunts.* The Waterson shunt is a side-to-side anastomosis between the ascending aorta and the right PA. This procedure is performed via a right thoracotomy without CPB. The Potts shunt results is a side-to-side anastomosis between the descending aorta and the left PA. This procedure is performed via a left thoracotomy without CPB. Waterston and Potts shunts are of historic interest only. It is difficult to size the orifice of these shunts correctly. Too small an orifice will limit pulmonary
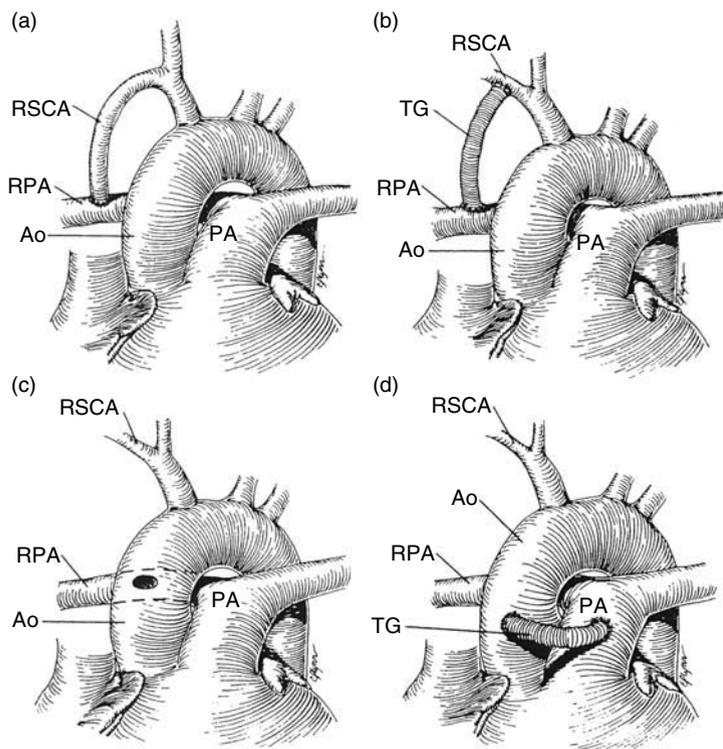
Fig. 6.21 Surgically created systemic to pulmonary artery shunts. (a) Blalock–Taussig shunt. (b) Modified Blalock–Taussig shunt. (c) Waterston shunt. (d) Central shunt. Ao, aorta; PA, pulmonary artery; RPA, right pulmonary artery; RSCA, right subclavian artery; TG, tube graft.

blood flow, whereas too large an orifice will create pulmonary overperfusion and congestion and predispose to development of unilateral PVOD. These shunts may produce distortion of the PA, making subsequent definitive repair difficult. In addition, they are difficult to take down at the time of the definitive procedure.

• *Central shunt.* This shunt places a synthetic tube graft between the ascending aorta and the main or branch PA. It often is used when prior shunt procedures have failed.

• *Blalock–Taussig shunt (BTS).* As originally described, this involves creation of an end to-side anastomosis of the right or left subclavian artery to the ipsilateral branch PA. Currently, a modification of this procedure known as the modified Blalock–Taussig shunt (MBTS) is used. It involves interposing a length of Gore-Tex tube graft (3.5–4.0 mm in infants) between the subclavian or innominate artery and the branch PA. These shunts are performed on the side opposite the aortic arch. This shunt can be performed with or without CPB via a thoracotomy or median sternotomy (see Fig. 6.18).

Definitive repair
Currently, most patients with TOF have an elective full correction between the ages of 2–10 months of age. In some centers surgery is delayed as long as possible within this time interval with the precise timing of repair dictated by the onset of cyanotic episodes. Definitive repair for TOF is being accomplished in neonates in some centers if favorable anatomy is present. Surgery is aimed at relieving the outflow obstruction by resection of hypertrophied, obstructing muscle bundles and augmentation and enlargement of the outflow tract with a pericardial patch. Unless the pulmonic annulus is near normal size, and the pulmonary valve is only mildly stenotic, enlargement of the outflow tract involves extension of the patch across the pulmonary valve annulus and into the main PA. Because a transannular patch creates pulmonic insufficiency it is best avoided when possible. If stenosis of the PA extends

to the bifurcation, the pericardial patch can be extended beyond the bifurcation of the pulmonary arteries. Finally, the VSD is closed. In neonates this is usually done through the right ventriculotomy created for resection of RVOT obstruction and placement of the transannular patch. In infants and older children the VSD can be closed via a trans-tricuspid valve approach.

An important surgical consideration for patients with TOF/PS is the occurrence of coronary artery abnormalities. Approximately 8% of patients have either the left main coronary artery or the left anterior descending artery as a branch of the right coronary artery. In these cases, a right ventriculotomy to enlarge the right ventricular outflow tract will endanger the left coronary artery. In such cases, an extracardiac conduit (RV to main PA) may be necessary to bypass the outflow tract obstruction and avoid injury to the coronary artery.

Anesthetic management

Goals
1 Maintain heart rate, contractility, and preload to maintain cardiac output. Euvolemia is important to prevent exacerbation of dynamic RVOT obstruction from hypovolemia and reflex increases in heart rate and contractility.
2 Avoid increases in the PVR:SVR ratio. The less severe the RV outflow obstructive lesions, the more important this becomes. Increases in PVR relative to SVR, and decreases in SVR relative to PVR, will increase R–L shunting, reduce pulmonary blood flow, and produce or worsen cyanosis.
3 Use ventilatory measures to reduce PVR. Care must be taken to minimize mean airway pressure so as to avoid mechanical obstruction of pulmonary blood flow.
4 Maintain or increase SVR. This is particularly important when RV outflow obstruction is severe and changes in PVR will have little or no effect on shunt magnitude and direction.
5 Aggressively treat episodes of hypercyanosis.
6 Maintain contractility. Depression of contractility, particularly in the face of severe RV outflow obstruction, may produce RV afterload mismatch (see Chapter 2) and drastically reduce pulmonary

blood flow. The exception to this is patient in whom the dynamic component of infundibular obstruction is active. Reducing contractility in these patients may reduce RV outflow obstruction via relaxation of the infundibulum.

Creation of surgical shunts to increase pulmonary blood flow presents the anesthesiologist with several additional management problems:
1 When a thoracotomy approach is used, unilateral lung retraction will be required for surgical exposure. The resulting atelectasis may severely compromise oxygenation and carbon dioxide removal. Intermittent reinflation of the lung may be necessary during the operative procedure. These reinflations should be coordinated with the surgeon. For all the shunts described, the main or branch PA will have to be partially occluded by a clamp to allow creation of the distal anastomosis. The resulting increase in physiological dead space may compromise oxygenation and carbon dioxide removal and will increase the arterial–ET_{CO_2} gradient.
2 Efforts to increase pulmonary blood flow by reducing PVR with ventilatory interventions and by increasing L–R shunting should be initiated before PA occlusion.
3 Partial occlusion of the aorta with a clamp will be necessary during creation of Waterston, Potts, and central shunts. The resulting increase in LV afterload may compromise systolic function.
4 All of the palliative shunts impose a volume load on the LV. Inotropic support may be necessary to ensure systemic and shunt perfusion after shunt creation.
5 Palliative shunts are mildly restrictive simple shunts. It is important to maintain SVR and reduce PVR to maintain pulmonary blood flow in patients with surgical shunts.
6 Be prepared to treat an episode of hypercyanosis.

Induction and maintenance
Regardless of the mode of induction, aggressive volume expansion with 10–15 mL/kg of 5% albumen or normal saline should be initiated once IV access is obtained. This is particularly true in patients who have been NPO for a long interval prior to induction. This is the most effective first line

therapy in preventing and treating dynamic RVOT obstruction.

An IV induction is desirable but most infants and children will tolerate a mask induction with either sevoflurane or halothane as there is a parallel decrease in PVR and SVR. Halothane may be better at attenuating the dynamic component of RVOT obstruction than sevoflurane given halothane's more potent negative inotropic effect. Systemic hypotension should be avoided or treated promptly. Systemic hypotension is particularly likely to cause or increase R–L shunting when RV outflow obstruction is severe as anesthesia-induced decreases in PVR have little effect on decreasing RV outflow resistance. Reduced SVR can be normalized with phenylephrine (0.5–1.0 μg/kg).

Ketamine is a useful induction agent in patients with TOF. Ketamine has been shown to cause no significant alteration in Q_P:Q_S in these patients. Fentanyl or sufentanil will provide very stable induction and maintenance hemodynamics and will blunt stimulation induced increases in PVR. Maintenance of anesthesia with fentanyl or sufentanil, a muscle relaxant, and a benzodiazepine or inhalation agent is appropriate.

Post-CPB management

Goals

1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart-rate-dependent during the post-CPB period. Atrial pacing may be necessary in the presence of junctional ectopic tachycardia (JET).

2 Reduce PVR through ventilatory interventions.

3 Inotropic support of the RV may be necessary. Dobutamine (5–10 μg/kg/min) or dopamine (5–10 μg/kg/min) is useful in this instance because they provide potent inotropic support without increasing PVR. Milrinone (0.5–1.0 μg/kg/min following a loading dose of 50 μg/kg) should be considered for its inotropic and lusitrophic effects and its effect on PVR.

4 In patients with RV systolic or diastolic function and an atrial fenestration a PaO$_2$ of 40–50 mmHg is acceptable in the presence of adequate cardiac output.

After definite repair for TOF, several factors may contribute to impaired RV systolic and diastolic function:

• Creation of a right ventriculotomy and placement of the RV outflow patch produces a segment of dyskinetic RV free wall.

• Protection of the RV from ischemia during aortic cross-clamping is difficult in patients with a hypertrophied RV as occurs in TOF.

• Enlargement of the RV outflow tract with a transannular patch will create pulmonary regurgitation, which imposes a volume load on the RV.

• Stenosis or hypoplasia of the distal pulmonary arteries or residual RV outflow obstruction will impose a pressure load on the RV.

• A residual VSD will impose a volume load on the RV.

A residual VSD is likely to very poorly tolerated in the patient with TOF with the most likely manifestation being low cardiac output syndrome associated with elevated CVP, LAP, and PAP. RVOT obstruction will be completely or nearly completely eliminated post-repair. PVR is likely to be low and the pulmonary vasculature very compliant. As a result, there will be potential for a large L–R intracardiac shunt with a residual VSD. This will place a large volume load on the LV and RV. An acute volume load will not be well tolerated by the RV that is likely to be concentrically hypertrophied and poorly compliant in response to the chronic pressure overload that existed preoperatively. The presence of pulmonary insufficiency will further exacerbate RV dysfunction by imposing an additional volume load. Any distal PA stenoses, high mean airway pressures, and elevated PVR will all increase the regurgitant volume and subsequent RV volume load.

Following complete repair of TOF with no residual lesions and minimal intrapulmonary shunt the SaO$_2$ should be 100%. In infants and small children, particularly those left with pulmonary insufficiency as the result of a transannular patch and those expected to have restrictive RV diastolic function as a result of a ventriculotomy and/or extensive RV hypertrophy the surgeon may choose to leave a "pop-off" valve by leaving the PFO open or by

creating a small (3–4 mm) atrial level fenestration. This will allow physiologic intracardiac R–L shunting with the ability to augment systemic cardiac output at the expense of systemic oxygen saturation in the setting of RV dysfunction. There will be direct delivery of some desaturated venous blood to the LA. In these patients, a PaO$_2$ of 40–50 mmHg and a SaO$_2$ of 70–80% is acceptable until RV function improves over the course of days.

TEE is invaluable in assessing for residual lesions, ventricular function and the direction of shunting across the atrial fenestration. As described in Chapter 2, hemodynamic and saturation data can be used to identify and quantify residual intracardiac shunts.

Postoperative JET is a transient tachyarrhythmia that occurs immediately following congenital heart surgery. The incidence of JET following TOF repair may be as high as 20%. JET is likely secondary to surgical trauma in the area of the AV node secondary to the retraction necessary to expose the VSD and RVOT from across the tricuspid valve.

JET typically manifests with a junctional rate only slightly faster than the sinus node rate and is the only narrow complex tachycardia in which the atrial rate is less than the ventricular rate (A:V ratio <1:1). Much less commonly (10%), there may be retrograde activation of the atrium with inverted p waves noted and an A:V ratio of 1:1. In either case, there is loss of AV synchrony (loss of atrial kick). At a heart rate <160–170 b/min this arrhythmia may be well tolerated. It is unlikely to be tolerated in the presence of restrictive diastolic function at any rate. JET with heart rate >170 b/min is associated with hemodynamic instability and increased postoperative mortality.

Neither cardioversion nor adenosine is effective. Treatment of JET is atrial pacing at a rate slightly faster than the junctional rate reinitiating A–V synchrony. This therapy is effective unless the junctional rate is very fast (>160–170 b/min) at which point atrial pacing at a faster rate is unlikely to improve hemodynamics because the reinitiation of A–V synchrony is offset by the reduction in diastolic filling time present at these rates.

Transposition of the great arteries

Anatomy

In transposition of the great arteries (TGA) there is concordance of the atrioventricular connections associated with discordance of the ventriculoarterial connections. The most common manifestation of this anatomy occurs in patients with [S, D, D] segmental anatomy (Fig. 6.22). That is, there is atrial situs solitus, D-loop ventricles, and D-loop great arteries. A right-sided RA connects via a right-sided tricuspid valve and RV to a right sided and anterior aorta. A left sided LA connects via a left sided mitral valve and LV to a left sided and posterior PA. As a result, there is fibrous continuity between the mitral and pulmonic valves with a lack of fibrous continuity between the tricuspid and aortic valves (conus). This anatomy is most commonly referred to as D-TGA.

The coronary arteries in D-TGA arise from the aortic sinuses that face the PA. In normally related vessels, these sinuses are located on the anterior portion of the aorta while in D-TGA they are located posteriorly. In the majority of D-TGA patients (70%), the right sinus is the origin of the right coronary artery, whereas the left sinus is the origin of the left main coronary artery. In the remainder of cases, there is considerable variability (Fig. 6.23).
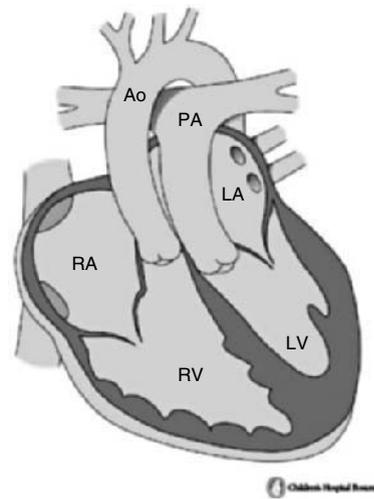
Fig. 6.22 Anatomy of dextro-transposition of the great arteries (D-TGA). Ao, aorta; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.
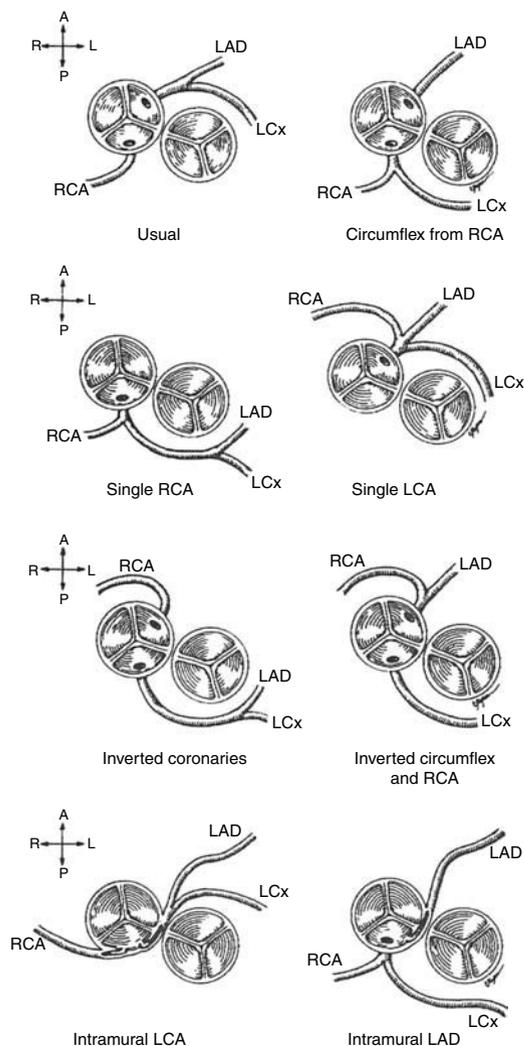
Fig. 6.23 Most common coronary artery patterns in transposition of the great arteries (TGA). The aorta is anterior and rightward of the pulmonary artery. LAD, left anterior descending; LSA, left coronary artery; LCx, left circumflex; RCA, right coronary artery. (From Mayer JE, *et al.* Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries. *Circulation* 1990;**82** (suppl IV):144, with permission.)

In patients with D-TGA, the most commonly associated cardiac anomalies are a VSD, and subpulmonic stenosis. In D-TGA subpulmonic stenosis is left ventricular outflow tract obstruction (LVOTO). Approximately 50% of patients with D-TGA will present with a PDA. The FO is almost always patent, but a true secundum ASD exists in only about 5% of patients. Although angiographically detectable VSDs may occur in 30–40% of patients, only about one third of these defects are hemodynamically significant. Thus, for practical purposes, 75% of patients have an intact ventricular septum (IVS). LVOTO is present in about 30% of patients with VSD and is most often due to an extensive subpulmonary fibromuscular ring or posterior malposition of the outlet portion of the ventricular septum. Only 5% of patients with IVS have significant LVOTO. In these patients, there is a dynamic obstruction of the LVOT during systole due to the leftward bulging of the ventricular septum and the anterior movement of the anterior mitral valve leaflet. The septal shift necessary to produce this obstruction is uncommon in neonates due to the presence of elevated PVR. Valvular PS is rare in patients with TGA. Other less commonly seen lesions are tricuspid or mitral regurgitation (4% of each) and a coarctation of the aorta (5%).

Bronchopulmonary collateral vessels (aorta to PA proximal to the pulmonary capillaries) are visible angiographically in 30% of patients with D-TGA. The larger and more extensive collaterals generally involve the right lung. These collaterals provide a site for intercirculatory mixing and have been implicated in the accelerated development of PVOD.

Physiology

D-TGA produces two parallel circulations with recirculation of systemic and pulmonary venous blood. Survival depends on one or more communications between the two circuits to allow intercirculatory mixing (see Fig. 6.4). The sites available for intercirculatory mixing in D-TGA can be intracardiac (PFO, ASD, VSD) or extracardiac (PDA, bronchopulmonary collaterals). Several factors affect the amount of intercirculatory mixing. The number, size, and position of anatomic communications are important. One large, nonrestrictive communication will provide better mixing than two or three restrictive communications. Reduced ventricular compliance and elevated systemic and PVR tend to reduce intercirculatory mixing by

impeding flow across the anatomic communications. The position of the communication is also important. Poor mixing occurs even with large anterior muscular VSDs due to their unfavorable position.

Patients with PS will have low pulmonary blood flow and may be hypoxemic despite a relatively large intercirculatory communication. Patients with high pulmonary blood flow, particularly those with a VSD in whom systemic pressures are transmitted to the pulmonary vasculature, are at risk of developing PVOD. In the presence of a good-sized intercirculatory communication, these patients will initially not be hypoxemic. However, the progressive development of PVOD will eventually reduce pulmonary blood flow and produce hypoxemia. Finally, all patients with TGA and increased pulmonary blood flow will have a large volume load imposed on the LA and LV.

In TGA with VSD some intercirculatory mixing occurs at the ventricular level but there is predominantly anatomic R–L shunting (effective pulmonary blood flow) at the VSD (RV to LV to PA) and PDA (RV to AO to PA) and anatomic L–R shunting (effective systemic blood flow) at the PFO or ASD (LA to RA to RV to AO). Obviously, the more severe the LVOTO the more dependent effective pulmonary blood flow will be on the presence of a PDA.

In TGA with IVS the anatomic mixing sites are usually a PDA and a PFO. The dynamics of intercirculatory mixing in TGA/IVS are complex. Anatomic shunting at the atrial level is ultimately determined by the size of the atrial communication and the cyclical pressure variations between the left and right atria. The volume and compliance of the atria, ventricles, and vascular beds in each circuit, as well as heart rate and phase of respiration all influence this relationship. Shunting is from the RA to the LA during diastole as the result of the reduced ventricular and vascular compliance of the systemic circuit. In systole, shunt is from the LA to the RA primarily because of the large volume of blood returning to the LA as a result of the high volume of recirculated pulmonary blood flow.

The direction of shunting across the PDA largely depends on the PVR and the size of the intra-atrial communication. When the PVR is low and the intra-atrial communication is nonrestrictive, shunting is predominantly from the aorta to the PA via the PDA (effective pulmonary blood flow) and predominantly from the L–R atrium across the atrial septum (effective systemic blood flow). When PVR is elevated, shunting across the PDA is likely to be bidirectional, which would in turn encourage bidirectional shunting across the atrial septum. When PVR is high and PA pressure exceeds aortic pressure, shunting at the PDA will be predominantly from the PA to the aorta. This will create reverse differential cyanosis. In this physiology the preductal arterial saturation is lower than the postductal arterial saturation. This is usually the result of a restrictive atrial communication producing left atrial hypertension and is associated with low effective blood flows (poor mixing) and hypoxemia. A balloon atrial septostomy (BAS) can be lifesaving in this setting. Decompression of the LA promotes mixing at the atrial level and also reduces PVR and PA pressure promoting mixing at the PDA.

The majority of neonates with D-TGA and IVS will be hypoxemic (arterial saturation $\leq 60\%$) within the first day of life. A proportion of these patients will have severely reduced effective pulmonary and systemic blood flow resulting in a $PaO_2 < 20$ mmHg, hypercarbia, and an evolving metabolic acidosis secondary to the poor tissue oxygen delivery. PGE_1 (maintenance 0.01–0.05 µg/kg/min) is administered to dilate and maintain the patency of the DA. This will be effective in increasing effective pulmonary and systemic blood flow, and in improving PaO_2 and tissue oxygen delivery if PVR < SVR and there is a nonrestrictive or minimally restrictive atrial septal communication. In some centers, all neonates stabilized on PGE_1 alone have a BAS to enlarge the atrial septal communication so that PGE_1 can be stopped and surgery scheduled on a semi-elective basis. PGE_1 infusion is associated with apnea, pyrexia, fluid retention, and platelet dysfunction. Recent investigations linking BAS to subsequent embolic neurologic injury must be considered in the risk-benefit analysis of nonemergent BAS.

If PGE_1 does not improve tissue oxygen delivery then an emergent BAS is performed in the catheterization laboratory utilizing angiography or in the ICU

utilizing echocardiography. These patients require tracheal intubation and mechanical ventilation. This allows reduction of PVR via induction of a respiratory alkalosis and elimination of pulmonary V/Q mismatch. Sedation and muscle relaxation reduce oxygen consumption thereby increasing mixed venous oxygen saturation. For a given amount of intercirculatory mixing and total systemic blood flow, an increase in systemic venous or pulmonary venous saturation will result in an increase in arterial saturation.

In rare instances the combination of PGE_1, a BAS, and mechanical ventilation with sedation and muscle relaxation may be ineffective. In this circumstance, ECMO (either veno–arterial or veno–veno) support to improve tissue oxygenation and to reverse end-organ insult and lactic acidosis prior to surgery is indicated.

Surgical therapy

Intra-atrial physiologic repair: Mustard and Senning procedures

Both the Mustard and the Senning procedures are atrial switch procedures that surgically create discordant atrioventricular (AV) connections in the presence of the preexisting discordant ventriculoarterial connections. Therefore, after repair, systemic venous blood is routed to the LV, which is in continuity with the PA. Likewise, pulmonary venous blood is routed to the RV, which is in continuity with the aorta. This arrangement results in physiologic but not anatomic correction of D-TGA. Following these procedures the RV remains the systemic ventricle and the tricuspid valve remains the systemic AV valve.

The Mustard procedure redirects pulmonary and systemic venous return via an intra-atrial baffle after excision of the interatrial septum. The baffle is made from pericardium or synthetic material to preserve atrial contractility and optimize atrial growth potential. In the Senning procedure, autologous tissue from the right atrial wall and IAS is used in place of pericardium or synthetic material to preserve atrial contractility and optimize atrial growth potential. Following both procedures, pulmonary venous blood is directed over the top of
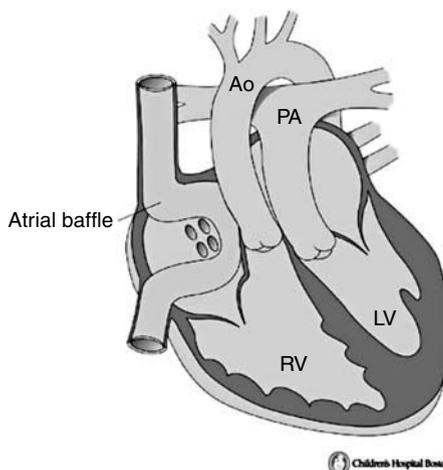
Fig. 6.24 Schematic of completed Mustard operation. There has been creation of an atriotomy, enlargement of atrial septal defect, and creation of an intra-atrial baffle. Orifices of superior and inferior vena cavae are encircled by distal ends of the baffle such that systemic venous blood is directed under the baffle, across the enlarged atrial septal defect into mitral valve, left ventricle, and pulmonary artery. Pulmonary venous blood remains above the baffle to be directed across the tricuspid valve into the right ventricle and aorta. Ao, aorta; LV, left ventricle; PA, pulmonary artery; RV, right ventricle.

the baffle to cross the tricuspid valve while systemic venous blood is directed beneath the baffle to cross the mitral valve (Fig. 6.24).

Long-term exposure of the RV and tricuspid valve to systemic pressure results in progressive right ventricular dysfunction. Both systemic and pulmonary venous obstruction may occur as the result of both procedures. The incidence of dysrhythmias after these procedures is high: 64% of patients have dysrhythmias, 28% of which are serious (bradycardia, sick-sinus syndrome, atrial flutter).

Anatomic repair or the arterial (Jatene) switch procedure

The arterial switch operation (ASO) anatomically corrects the discordant ventriculoarterial connections. After repair, the RV is connected to the PA and the LV is connected to the aorta. Clinical success with the ASO, summarized in Fig. 6.25(a–f), was achieved in 1975. In brief, the PA and the aorta are transected distal to their respective valves.
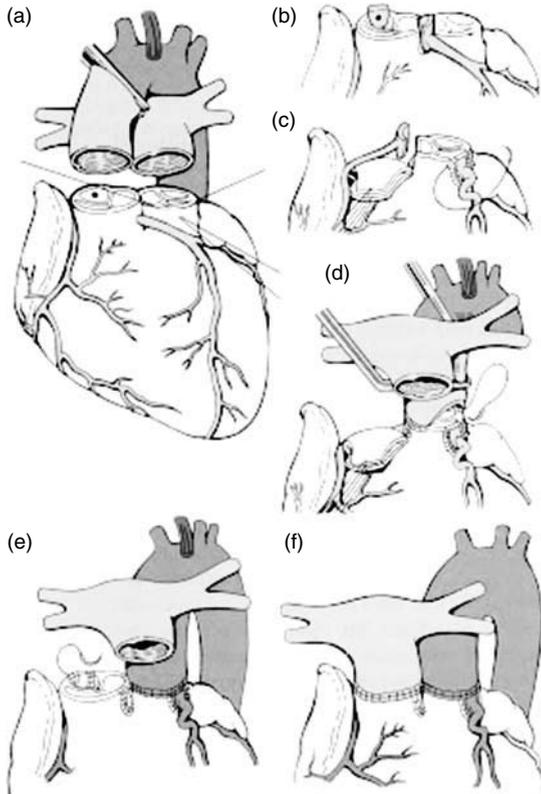
Fig. 6.25 Arterial switch operation (ASO). (a) Aorta is cross-clamped and the aorta and pulmonary artery are transected. (b) Left and right main coronary arteries are excised from the anterior aorta using a segment of aortic wall extending from rim of aorta. (c) Equivalent segments of pulmonary arterial wall are excised and coronary arteries are translocated posteriorly to the pulmonary artery (neoaorta). (d) Distal pulmonary artery is brought anterior to ascending aorta (Lecompte maneuver), and proximal pulmonary artery (neoaorta) is anastomosed to distal aorta. (e) Sites of coronary explantation are repaired using pericardium. (f) Proximal aorta is sutured to distal pulmonary artery.

The coronary arteries are initially explanted from the ascending aorta with 3–4 mm of surrounding tissue. The explant sites are repaired either with pericardium or synthetic material. The coronary arteries are reimplanted into the proximal PA (neoaorta). The great arteries are then switched with the distal PA brought anterior (LeCompte maneuver) to be reanastomosed to the old proximal

aorta (right ventricular outflow) and the distal aorta reanastomosed to the old proximal PA (LV outflow).

Most patients with D-TGA have coronary anatomy that is suitable for coronary reimplantation. Patients with certain types of coronary anatomy (inverted coronaries, single right coronary artery) are at risk for postoperative myocardial ischemia and death because reimplantation can result in distortion of the coronary ostia or narrowing of the artery itself. The emergence of two parallel coronary arteries above but in contact with the posterior valve commissure or the intramural origin of the coronaries also presents a technical challenge. These patients may require resuspension of the neopulmonary valve after the coronaries and a surrounding tissue cuff have been excised.

In order for the ASO to be successful, the original pulmonary ventricle (LV) must have sufficient mass to be capable of becoming the systemic ventricle. Patient selection and the timing of the surgical procedure are important variables in determining the success of this procedure. Two-dimensional echocardiography is used to noninvasively assess the LV:RV pressure ratio and to determine the extent to which LV mass has regressed.

The ASO was originally described in patients with D-TGA and a large VSD or a large PDA. In these patients, the pulmonary ventricle (LV) remains exposed to systemic pressures and the LV mass remains sufficient to support the systemic circulation. For such patients, the ASO must be performed within the first 2–3 months of life to prevent intractable CHF or irreversible PVOD. In these patients, the ASO is generally performed within the first few weeks of life. Closure of the VSD is preferentially performed transatrially through the tricuspid valve. It is desirable to avoid approaching a VSD through the RV because an incision in the RV may contribute substantially to postoperative RV dysfunction.

In patients with D-TGA and IVS, there is progressive reduction in LV mass as the physiologic pulmonary hypertension present at birth resolves progressively over the first days after birth. Adequate LV mass to support the systemic circulation exists in these patients for only the first 2–3 months after birth. In patients with D-TGA and

IVS, the ASO can be performed primarily or as the second phase of a staged procedure. A primary ASO is generally suitable for D-TGA and IVS patients within the first 2 months of life and is usually performed within the first week of life.

The two-stage repair for D-TGA with IVS is used for neonates in whom there has been significant regression of LV mass. These are generally neonates in whom surgery cannot be performed during the first several weeks of life secondary to prematurity, sepsis, low birth weight (<1.5 kg), or late referral. The LV is prepared to accept the systemic workload by placement of a PA band. In addition, an aortopulmonary shunt with entry to the PA distal to the band is necessary to prevent hypoxemia. The band must be tight enough to increase pressure in the pulmonary ventricle (LV) to approximately one-half to two-thirds that in the systemic ventricle (RV). This will increase afterload sufficiently to prevent regression of LV mass. However, if the band is too tight, there may be LV decompensation secondary to afterload mismatch.

Generally a rapid two-stage repair is performed. The ASO is performed as early as 1 week after preparatory PA banding, often during the same hospitalization. This approach is based on the fact that a doubling of LV mass is seen after 1 week of PA banding. The staged procedure is complicated by the fact that placement of the PA band to the proper tightness is not an easy task and that the PA band and systemic to PA shunt may result in distortion of the PA, making the definite ASO difficult.

The ASO is generally not performed on patients in whom mechanical LVOTO (subpulmonic stenosis) exists. Correction of the LVOTO is difficult, and without complete correction of the LVOTO, these patients will be left with aortic or subaortic stenosis. On the other hand, patients with dynamic LVOTO have been shown to have no gradient across the LV outflow tract after the ASO.

Rastelli procedure

For patients with D-TGA, VSD, and severe LVOTO (subpulmonary stenosis), a Rastelli procedure is performed. Closure of the VSD is performed through a right ventriculotomy. The VSD is closed so that LV blood is directed through the aorta.
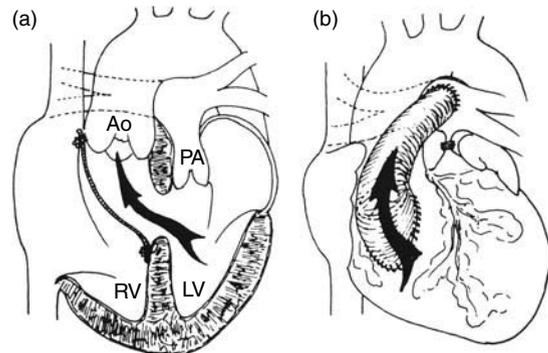
Fig. 6.26 Schematic of Rastelli procedure for repair of transposition of the great vessels associated with pulmonic stenosis and ventricular septal defect (VSD). (a) VSD is closed with patch such that left ventricular output is directed across the aortic valve. (b) Proximal main pulmonary artery is ligated and valved conduit is placed from right ventricle to main pulmonary artery. Ao, aorta; LV, left ventricle; PA, pulmonary artery; RV, right ventricle.

The proximal PA is ligated and a valved conduit is placed from the right ventriculotomy to the PA, thereby bypassing the subpulmonic stenosis (Fig. 6.26a,b). Subaortic stenosis may result from placement of the VSD patch. Replacement of the valved conduit may be necessary in later years secondary to calcification.

Anesthetic management

Goals

1 Maintain heart rate, contractility, and preload to maintain cardiac output. Decreases in cardiac output decrease systemic venous saturation with a resultant decrease in arterial saturation.

2 Maintain ductal patency with PGE_1 (0.01–0.05 µg/kg/min) in ductal-dependent patients.

3 Avoid increases in PVR relative to SVR. Increases in PVR will decrease pulmonary blood flow and reduce intercirculatory mixing. For patients with PVOD, ventilatory interventions should be used to reduce PVR. For patients with LVOTO that is not severe, ventilatory interventions to reduce PVR increase pulmonary blood flow and intercirculatory mixing.

4 Reductions in SVR relative to PVR should be avoided. Decreased SVR increases recirculation of systemic venous blood and decreases arterial saturation.

Induction and maintenance

In prostaglandin dependent neonates the PGE_1 infusion should be continued until CPB to assure an adequate intercirculatory mixing. The increased pulmonary blood flow will limit the cardiac reserve of these patients and the immature myocardium will be sensitive to anesthetic-induced myocardial depression. Anesthesia is generally induced and maintained using a synthetic opioid (fentanyl or sufentanil) based technique. A high-dose fentanyl or sufentanil technique will provide hemodynamic stability without adversely affecting intercirculatory mixing.

In infants older than 6–8 months, premedication may be necessary to facilitate the separation from the parents. In the absence of IV access oral midazolam (0.5–1.0 mg/kg) is useful. Older, better-compensated children, such as those presenting for a Rastelli repair with a functioning systemic to PA shunt, may require a more substantial oral premedication.

In patients with reduced pulmonary blood flow or poor intercirculatory mixing, efforts to reduce PVR should be made to increase pulmonary blood flow and intercirculatory mixing. In patients with PVOD, ventilatory measures to reduce PVR are useful if PVR is not fixed. An inhalational induction or an IM ketamine induction followed by placement of an IV and conversion to a high-dose fentanyl or sufentanil technique may be suitable for these patients. A similar approach may be taken for older children with subpulmonic stenosis. A high-dose fentanyl or sufentanil technique is useful in blunting the stress-induced increases in PVR that are so detrimental to these patients.

Hypercarbia, acidosis, and hypoxemia further increase PVR and should be avoided because of the limited myocardial reserve of neonates and infants. This is particularly true in neonates with TGV and IVS, where systemic oxygen delivery is tenuous, and in infants with TGV and VSD, in whom left ventricular volume overload is present. In addition, reactive increases in PVR are commonly seen in the immature pulmonary vasculature and may severely compromise pulmonary blood flow.

Post-CPB management

Goals

1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart-rate-dependent during the post-CPB period. For patients having undergone atrial baffle procedures, anti-dysrhythmic therapy or pacing may be necessary.

2 Myocardial ischemia after coronary reimplantation should be treated aggressively and prompt immediate re-evaluation of the anastomoses and the possibility of external compression.

3 Reductions in aortic and PA pressures may be necessary to help prevent suture line bleeding after the ASO.

4 Systemic ventricular (RV after atrial baffle procedures and LV after arterial switch procedures) dysfunction may necessitate inotropic and vasodilator therapy to terminate CPB. Dobutamine (5–10 μg/kg/min) or dopamine (5–10 μg/kg/min) is useful. Milrinone (0.5–1.0 μg/kg/min following a loading dose of 50 μg/kg) may be a better choice if SVR is high. Milrinone has direct SVR reducing effects in addition to inotropic, lusitrophic, and PVR reducing effects.

After atrial baffle repairs, there may be pulmonary and systemic venous obstruction. Systemic venous obstruction will produce systemic venous congestion and a low RA pressure. Pulmonary venous obstruction may result in pulmonary venous and pulmonary arterial hypertension, pulmonary edema, and hypoxemia. Efforts to reduce SVR will reduce the RV afterload and help prevent tricuspid regurgitation. Therapy for atrial dysrhythmias also may be necessary. TEE will prove useful in ruling out pulmonary and systemic venous obstruction. In addition, large baffle leaks that may require surgical revision will be detected.

After the arterial switch procedure, there may be extensive bleeding from the aortic and pulmonary suture lines. Myocardial ischemia following reimplantation of the coronary arteries is a potential

problem following the ASO. In some circumstances, the ischemia is transient secondary to coronary air emboli. Transesophageal echocardiography is very useful to assure adequate removal of air from the LA and ventricle prior to the termination of CPB. It is also useful in assessing the potency of the reimplanted coronary arteries. Maintenance of high perfusion pressures on CPB after aortic cross-clamp removal will facilitate the distal migration of air emboli. In other instances, kinking of the reimplanted artery or compromise of the implanted coronary ostia may require immediate surgical intervention. External compression of the coronaries by clot or surgical hemostatic packing material should also be considered. Pharmacologic intervention with traditional therapies to improve the balance of myocardial oxygen demand and delivery such as nitroglycerin and beta-blockade are never a long-term alternative to prompt surgical revision of the appropriate anastomosis.

Despite comprehensive preoperative evaluation, the LV of patients undergoing an ASO may be marginal in its ability to support the systemic circulation in the post CPB period. This may occur as the result of myocardial ischemia, inadequate LV mass, poor protection of the LV during aortic cross-clamping, or a combination of these variables. Transesophageal echocardiography is useful in identifying and continuously evaluating both global and regional LV systolic dysfunction. It also detects mitral regurgitation, which may occur secondary to papillary muscle dysfunction or to dilation of the mitral valve annulus. Inotropic support of the LV and afterload reduction may be necessary to terminate CPB. Initial inotropic support is accomplished with dopamine (3–10 μg/kg/min). In rare instances where LV failure is severe, epinephrine (0.05–0.50 μg/kg/min) may have to be added in combination with nitroprusside (starting at 0.15–0.50 μg/kg/min).

Milrinone (0.5–1.0 μg/kg/min following a 50 μg/kg loading dose) is a useful agent in these patients as it is an inodilator. These patients are at particular risk for LV dysfunction in the immediate postoperative period secondary to afterload mismatch (insufficient contractility for the degree of systemic afterload). While the vasodilation that accompanies milrinone administration in infants is substantially less than that seen in adult patients it is nonetheless advisable to administer the loading dose of milrinone over 10–15 minutes.

A unique cycle of LV dilation initiating and exacerbating myocardial ischemia exists in patients having undergone the arterial switch. Myocardial ischemia, afterload mismatch, or overzealous volume infusion can result in LV distension and LA hypertension. This will be particularly likely if there is mitral insufficiency from either papillary muscle dysfunction or dilation of the mitral valve annulus. LV distension may result in tension on and kinking of the coronary re-anastomosis sites. LA hypertension produces elevations in PA pressure and distension of the PA. Since the LeCompte maneuver (see Fig. 6.25) brings the distal PA anterior to the ascending aorta distension of the PA may actually compress or place tension on the coronary ostia. The resulting myocardial ischemia produces further LV dilation, progressive elevations in LA and PA pressures, and continuing compromise of coronary blood flow.

TEE usually allows visualization of the reimplanted coronary arteries and allows patency to be assessed. In addition, TEE will provide online assessment of LV function, which may allow early detection of a kinked or compromised coronary anastomosis. Inotropic support of the LV also can be guided by the use of TEE.

Total anomalous pulmonary venous return

Anatomy

Total anomalous pulmonary venous return (TAPVR) is characterized by drainage of all of the pulmonary veins into the systemic venous system rather than directly into the left atrium. In this lesion there is usually a single common pulmonary venous confluence with no direct connection to the LA. The pulmonary vein confluence then drains into the systemic venous circulation via one of four of the following drainage patterns (Fig. 6.27a–d):

- *Supracardiac (type 1)*. In 46% of patients, drainage of the pulmonary vein confluence is into a supracardiac structure. Most commonly drainage is to the
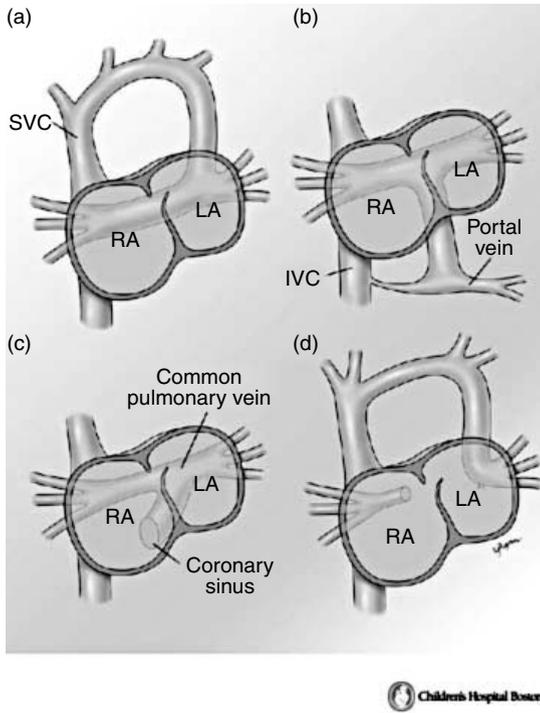
Fig. 6.27 Types of totally anomalous pulmonary venous return (TAPVR). (a) Supracardiac. A vertical vein connects the confluence of pulmonary veins to the innominate vein. (b) Infracardiac. A vertical vein, which transverses the diaphragm, connects the confluence of pulmonary veins to the portal vein which here has a stenotic connection to the IVC. Pulmonary venous return will be obstructed. (c) Cardiac. The confluence of pulmonary veins drains directly into the coronary sinus. (d) Mixed. The left pulmonary veins drain via a vertical vein into the innominate vein while the right pulmonary veins drain directly into the right atrium.

SVC via a vertical vein that connects the pulmonary vein confluence with the innominate vein, which then empties into the SVC.

• *Intracardiac (type 2).* In 24% of patients, drainage of the pulmonary vein confluence is directly into the RA via the CS.

• *Infracardiac (type 3).* In 22% of patients, drainage is into an infracardiac structure such as the IVC, portal vein, or hepatic vein. A vertical pulmonary vein passes through the esophageal hiatus of the diaphragm to connect the pulmonary vein confluence to one of these infracardiac vessels.

• *Mixed (type 4).* In 8% of patients, pulmonary venous drainage is some combination of types 1, 2, and 3.

In general, the greater the distance the vertical vein travels the greater the likelihood that this pathway will be stenotic or compressed and that there will be pulmonary venous obstruction. For this reason infracardiac drainage is most commonly associated with pulmonary venous obstruction. Some patients with supracardiac TAPVR have compression of the vertical vein between the left main stem bronchus and left PA. As PA pressure rises due to obstruction of pulmonary venous return the connecting vein may become further compressed between the left main stem bronchus and left PA leading to near complete compression of the connecting vein.

Physiology

The delivery of all pulmonary venous blood to the RA results in a large physiologic L–R shunt. There is complete mixing of systemic and pulmonary venous blood in the RA. There must be an anatomic R–L shunt and delivery of effective systemic blood flow if there is to be filling of the left heart and survival outside the uterus. Normally, an ASD or patent FO exists as the communication with the left heart. The magnitude and direction of shunting across the ASD or FO is determined by the principles of simple shunting. Normally a non or mildly restrictive atrial level communication exists in these patients. Delivery of blood across the atrial septum can be impeded by the poor compliance of the LA and LV, as these structures tend to be small due to reduced blood flow to the left side of the heart *in utero*. As a result, in the absence of obstruction neonates will have a $Q_P{:}Q_S$ close to 1:1. As PVR falls following birth there will preferential delivery of the mixed systemic and pulmonary venous blood to the pulmonary circuit. Pulmonary artery pressures will be near systemic because although PVR is near normal the $Q_P{:}Q_S$ will be high (>2–3:1).

Compression or stenoses along the vertical vein pathway will produce obstructed TAPVR leading to pulmonary venous hypertension, elevated PVR, and systemic or suprasystemic RV and PA pressures.

Some of these patients may develop PVOD *in utero* as well. In addition, pulmonary venous obstruction will produce pulmonary edema further elevating PVR, much as it does with mitral stenosis. These patients have a small heart and congested lung fields on chest radiograph.

Cardiac output can be severely compromised in these patients. Systemic or suprasystemic RV pressures will result in a leftward septal shift that "pancakes" the LV thereby further reducing the compliance of the small LV. This will impede delivery of blood across the atrial septum. There is likely to be RV afterload mismatch with RV distension and TR. Systemic cardiac output will be largely dependant on a physiologic R–L shunt across the DA supplied by a failing RV.

These patients will be hypoxemic because all the determinates of Sao_2 with complete mixing will be reduced:

• Pulmonary edema will induce intrapulmonary shunt and V/Q mismatch leading to low $Spvo_2$.
• $Q_P:Q_S$ will be reduced by the presence of high PVR.
• Low cardiac output will reduce Svo_2.

Efforts to increase pulmonary blood flow in these patients will only worsen the pulmonary edema and NO (as well as other inhaled pulmonary vasodilators) is clearly contraindicated. In patients with severe pulmonary venous obstruction leading to suprasystemic RV and PA pressures and R–L shunting across the DA ductal patency is necessary to maintain cardiac output. In patients with less severe obstruction and subsystemic RV and PA pressures ductal flow will be bidirectional or L–R. In these patients ductal patency may exacerbate pulmonary edema. Patients with obstructed TAPVR present at birth with hypoxemia and poor systemic perfusion. In many there is an ongoing metabolic acidosis and evidence of end-organ (hepatic and renal) dysfunction. Obstructed TAPVR is a surgical emergency, one of the few remaining in the era of PGE_1 therapy.

Surgical therapy

Definitive repair involves anastomosis of the pulmonary venous confluence to the posterior LA, ligation of the vertical vein, and closure of the ASD.

Anesthetic management

Goals

1 Maintain heart rate, contractility, and preload to maintain cardiac output. Decreases in cardiac output will reduce systemic venous saturation. In a complete mixing lesion, this will reduce arterial saturation.

2 For patients with TAPVR and pulmonary venous obstruction, emergency surgery is necessary. Efforts to increase pulmonary blood flow through ventilatory interventions and pulmonary vasodilators will worsen pulmonary edema.

3 For patients with increased pulmonary blood flow, decreases in the PVR:SVR ratio should be avoided. The increase in pulmonary blood flow that accompanies a reduced PVR:SVR ratio necessitates an increase in cardiac output to maintain systemic blood flow.

4 For patients with increased pulmonary blood flow and right ventricular volume overload, ventilatory interventions should be used to increase PVR, reduce pulmonary blood flow, and decrease the volume load on the RV.

Induction and maintenance

Neonates with pulmonary venous obstruction generally arrive in the operating room intubated, ventilated, and on inotropic support. These patients are best anesthetized with a high-dose narcotic technique using fentanyl or sufentanil. Older patients without obstruction and compensated RV volume overload may be candidates for an inhalational induction. Patients with TAPVR, particularly those with venous obstruction, have a highly reactive pulmonary vasculature. High doses of fentanyl and sufentanil will be useful for blunting increases in PVR associated with surgical stimulation.

Post-CPB management

Goals

1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart-rate-dependent in the post-CPB period.

2 In the presence of postoperative pulmonary venous obstruction, efforts to increase pulmonary

blood flow may worsen pulmonary edema. Surgical revision may be necessary.

3 For patients with PVOD and reactive pulmonary vasculature, blunting of stress-induced increases in PVR with narcotics is warranted.

4 For patients with PVOD and reactive pulmonary vasculature ventilatory interventions to reduce PVR and use of selective pulmonary vasodilators such as NO are warranted.

5 Inotropic support of the RV may be necessary, even in the face of aggressive therapy to reduce PVR. Dobutamine (5–10 μg/kg/min) or dopamine (5–10 μg/kg/min) is useful in this instance because both agents provide potent inotropic support without increasing PVR. In the absence of systemic hypotension milrinone (0.5–1.0 μg/kg/min following a 50 μg/kg loading dose) can be considered.

RV and PA hypertension are the most common problems encountered post-CPB. This may be the result of one or more of the following:

• Residual pulmonary venous obstruction may exist due the technical difficulty of constructing a nonrestrictive surgical anastomosis.

• In the presence of a nonrestrictive surgical anastomosis an appropriate cardiac output may produce LA hypertension due to the presence of a small, noncompliant LA and LV or LV dysfunction.

• Reactive pulmonary vasoconstriction (capillary and pre-capillary) may cause labile increases in PVR.

• Pre-existing PVOD.

The use of TEE and of surgically placed PA and LA lines is helpful in sorting out these etiologies. The presence of high PA pressures, an elevated LAP, and a PA diastolic pressure < 5 mmHg above the LAP suggests that LA hypertension is the cause of PA hypertension. The presence of high PA pressures, a low or normal LAP, and a PA diastolic pressure > 15–20 mmHg above the LAP suggests that reactive pulmonary vasoconstriction, PVOD, or pulmonary venous obstruction exists. In the presence of reactive pulmonary vasoconstriction or PVOD the PAOP (wedge pressure) should not exceed the LAP by >3–5 mmHg. A PAOP that exceeds the LAP by more than 5–10 mmHg suggests that pulmonary venous obstruction exists. TEE is valuable in assessing the patency of the pulmonary venous to LA anastomosis and in assessing ventricular function.

Obstruction to LV filling

Anatomy

Several congenital causes of obstruction to LV filling exist:

• *Valvular mitral stenosis.* Isolated congenital mitral stenosis is very rare and usually is caused by short, fused chordae tendineae.

• *Parachute mitral valve.* In this lesion, two mitral valve leaflets are attached to shortened chordae that insert on the same papillary muscle.

• *Supravalvular mitral stenosis.* In this lesion, an obstructive ring of thickened endocardium is found above the mitral valve downstream from the atrial appendage.

• *Cor triatriatum.* In this lesion, an obstructive membrane is located upstream of the atrial appendage.

Physiology

All of these lesions have the same physiologic consequences as valvular mitral stenosis: obstruction to LV diastolic filling and pulmonary venous congestion. The physiology of mitral stenosis is discussed in detail in Chapter 5.

Surgical therapy

Resection of a supravalvular ring or of the membrane in cor triatriatum normally suffices. Repair of the mitral valve is a superior alternative to mitral valve replacement in infants and children. If a valve replacement is done a low-profile valve must be used to prevent LV outflow tract obstruction. A mechanical valve generally is chosen over a porcine or homograft valve because of the short *in situ* half-life of these valves. Mechanical valves require long-term anticoagulation, which may be problematic for growing, active children.

The anesthetic and post-CPB management of patients with mitral stenosis is discussed in detail in Chapter 5.

Left ventricle outflow tract obstruction

Anatomy

Several categories of congenital LV outflow tract obstruction exist:

• *Valvular aortic stenosis.* This is most commonly caused by a bicuspid aortic valve. Most of these patients will remain asymptomatic until the fourth or fifth decade of life. In infants presenting with valvular aortic stenosis, the LV may be small. These patients may represent a milder form of HLHS.

• *Subaortic stenosis.* This may occur secondary to a discrete membranous ring located 1–2 cm below the aortic valve or to a fibromuscular overgrowth of the LV outflow tract that produces a tunnel-like stenosis.

• *Congenital SVAS.* This is most commonly caused by Williams–Beurin syndrome as the result of a microdeletion in the q11.23 region of chromosome 7. This deletion involves several genes, including the elastin gene. As a result there develops a characteristic hourglass narrowing of the aorta at the sinotubular junction; in a smaller percentage of cases (approximately 30%) there is diffuse tubular narrowing of the ascending aorta often extending to the arch and the origin of the brachiocephalic vessels. In approximately 40% of SVAS patients severe pulmonary stenoses and right ventricular pressure overload exist in conjunction with SVAS.

Physiology

Infants with aortic stenosis tend to have a small LV and varying degrees of endocardial fibroelastosis secondary to prolonged subendocardial ischemia. When aortic stenosis is severe in the neonatal period, systemic blood flow and survival may be dependent on R–L shunting across a PDA. This will result in perfusion of the periphery with systemic venous blood producing cyanosis. When the stenosis is severe and there is little antegrade aortic blood flow, the coronary arteries will be perfused retrograde down the aortic arch with desaturated blood. This, combined with the high left ventricular end-diastolic pressure (LVEDP) that accompanies aortic stenosis, will exacerbate myocardial ischemia.

In Williams–Beurin syndrome, adhesion of the right or left aortic leaflet edge to the narrowed sinotubular junction can restrict coronary blood flow into the sinus of Valsalva. The thickened aortic wall may narrow the coronary artery orifice itself. Coronary artery dilation and tortuosity due to exposure of the coronary arteries to high pre-stenotic pressures and coronary artery structural changes consistent with elastin arteriopathy may further directly compromise coronary flow. Finally, the SVAS impairs coronary diastolic flow, as the pressure in the pre-stenotic region is lower than in the post-stenotic region during diastole.

Surgical therapy

These lesions usually are approached by transecting or opening the ascending aorta. Subaortic lesions are then approached across the aortic valve. Resection of discrete subvalvular or supravalvular membranes is relatively straightforward. Treatment of fibromuscular tunnel-like stenosis is difficult. Resection of the fibromuscular tissue is limited by potential damage to surrounding structures such as the conduction system, mitral valve and the septum. In some instances, repair of a tunnel-like stenosis may require widening of the LV outflow tract with a patch and an aortic valve replacement. SVAS is best repaired by symmetrical reconstruction of the aortic root using two or three patches to widen the aortic sinuses. In instances where diffuse tubular hypoplasia of the aorta and arch exists, symmetrical reconstruction of the ascending aorta with extension of the patch to the underside of the aortic arch is necessary. In some circumstances surgical relief of coronary ostial stenosis may be necessary.

Post-repair TEE can be used to detect residual gradients and to rule out damage to the mitral valve and ventricular septum. In particular, the presence of a small VSD should be ruled out.

The anesthetic and post-CPB management of patients with aortic stenosis is discussed in detail in Chapter 5.

Single ventricle lesions

As previously discussed, some single ventricle lesions are amenable to a two-ventricle repair
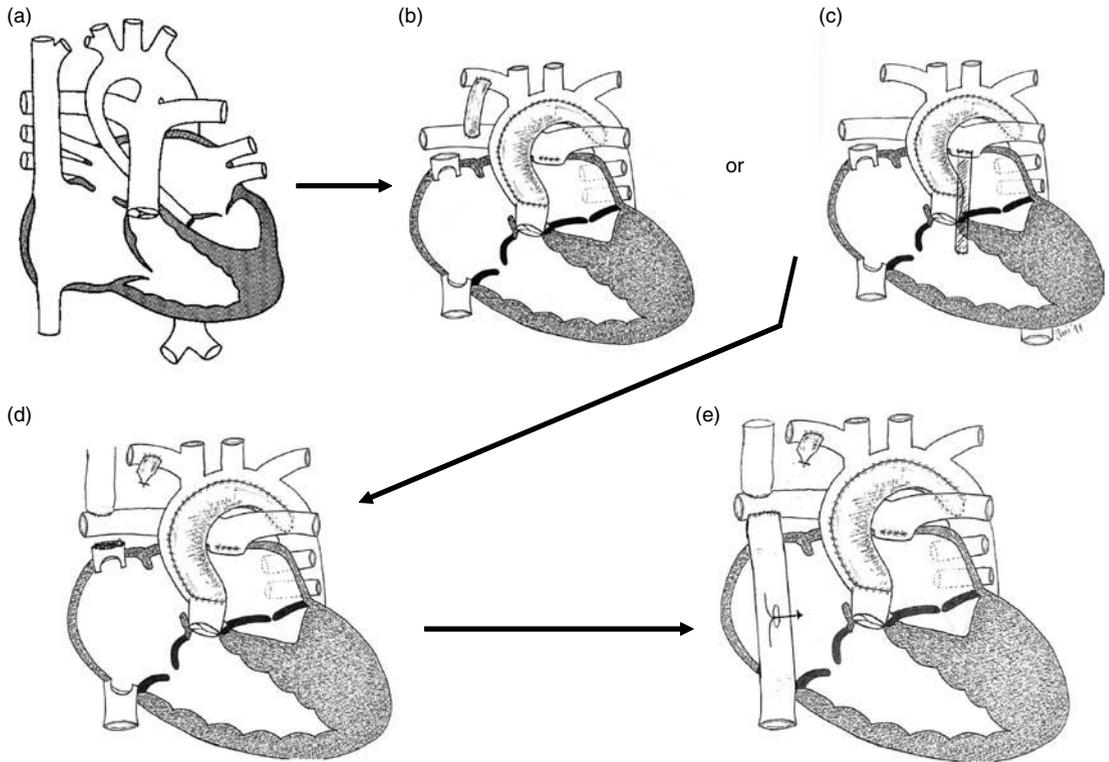
Fig. 6.28 Diagram illustrating the sequence of repairs in the surgical staging of hypoplastic left heart syndrome (HLHS) to a fenestrated lateral tunnel Fontan.
(a) Hypoplastic left heart syndrome (HLHS). (b) Initial repair involving atrial septectomy, Damus–Kaye–Stansel (DKS) anastomosis of main pulmonary artery to ascending aorta, homograft augmentation of the aortic arch, and a right modified Blalock–Taussig shunt (BTS) to supply pulmonary blood flow. (c) Initial repair involving atrial septectomy, DKS anastomosis of main pulmonary artery to ascending aorta, homograft augmentation of the aortic arch, and a right ventricle to pulmonary artery conduit to supply pulmonary blood flow. (d) Superior cavopulmonary shunt or bidirectional Glenn (BDG). The right modified BTS has been taken down and ligated. (e) The completed total cavopulmonary connection or Fontan procedure. A lateral tunnel Fontan with a fenestration is shown. The small arrows indicate flow from the systemic venous baffle to the common pulmonary venous atrium causing a small right-to-left (R–L) physiologic shunt.

while other require a staged approach to a Fontan procedure (Fig. 6.28a–e). Single ventricle lesions amenable to two-ventricle repair include truncus arteriosus, severe neonatal aortic stenosis, interrupted aortic arch and TOF with PA. Other single ventricle lesions such as TA and HLHS require a staged approach to the Fontan procedure. PA/IVS is an example of a single ventricle lesion that is occasionally amenable to a two-ventricle repair.

There are three phases in the single ventricle pathway: the initial physiology, the superior cavopulmonary shunt (generally a bidirectional Glenn (BDG) shunt), and the completed Fontan procedure that creates a total cavopulmonary connection (TCPC). During each of these phases three physiologic goals must be achieved:
• There must be a reliable source of an appropriate quantity of pulmonary blood flow. The appropriate quantity is the quantity that is sufficient to

prevent hypoxemia but not so large as to cause PVOD. The presence of PVOD is a contra-indication to completion of the Fontan procedure.

• There must be unobstructed delivery of pulmonary venous blood to the systemic ventricle.

• There must be an unobstructed pathway from the systemic ventricle to all segments of the aorta.

Single ventricle pathway, initial procedures

The initial palliative procedures described here are applicable to any patient with single ventricle physiology. Most patients require multiple initial procedures; rarely a patient may not require any initial procedure before proceeding to a superior cavopulmonary shunt.

Initial procedures to optimize pulmonary blood flow

The following describes the initial approach to optimizing pulmonary blood in patients with single ventricle physiology:

• Patients with ductal dependant pulmonary blood flow will require stabilization on PGE_1 followed by placement of a surgical aortopulmonary shunt as described in the section on TOF. In most cases a MBTS will be placed and the PDA ligated. A superior cavopulmonary shunt (BDG) cannot be used in the neonatal period as PVR is elevated to point where a supraphysiologic SVC pressure would be necessary to provide adequate pulmonary blood flow. More than 70% of patients with tricuspid atresia (TA) have ductal dependant pulmonary blood flow and require a shunt in the newborn period (Fig. 6.29a,b and Table 6.10).

• Patients with unrestricted pulmonary blood flow are at risk for compromise of systemic oxygen delivery due to high pulmonary blood flow in the setting of fixed cardiac output and ultimately for development of PVOD. These patients need restriction of pulmonary blood flow:

a In patients with high pulmonary blood flow and significant intracardiac sources of pulmonary blood flow (type 1C or 2C TA; see Fig. 6.29 and Table 6.10) the PDA can be allowed to close. In some instances this will appropriately limit pulmonary blood flow. More commonly it will be necessary to mechanically restrict pulmonary blood flow and reduce $Q_P:Q_S$ and the volume load on the systemic ventricle by banding the PA. The main PA is constricted with a circumferential band. This reduces pulmonary blood flow and distal PA pressure by creation of a restrictive lesion. Banding is most effective when PA pressure distal to the band is reduced to one-third to one-half of systemic blood pressure. Pulmonary artery banding may cause distortion of the main PA. In addition, distortion of branch pulmonary arteries may be caused by migration of the band distally. This distortion may complicate or preclude definite repair. Pulmonary artery banding is accomplished via a thoracotomy or a median sternotomy without CPB. An excessively tight PA band will severely reduce pulmonary blood flow and expose the ventricle to high afterload. Pulse oximetry has proved useful during PA banding because arterial desaturation precedes hypotension and bradycardia when banding is excessive. TEE is valuable in assessing ventricular function during PA banding. Ventricular distension may require loosening of the band or initiation of inotropic support. TEE also allows the pressure gradient across the band to be determined. This will help in determining the tightness of the band. PA banding is contraindicated in patients where aortic blood flow is derived from a restrictive intracardiac pathway from the systemic ventricle or where this pathway is likely to become restrictive once the ventricular volume load is reduced by a PA band. These patients require a Damus–Kaye–Stansel (DKS) procedure (see below) to provide an unobstructed pathway to the aorta from the systemic ventricle.

b The treatment of patients with high pulmonary blood flow due to major aorto-pulmonary collateral arteries (MAPCAs) is discussed in the section on TOF/PA.

• Rarely the combination of a restrictive VSD and mild PS (type 2B TA; see Fig. 6.29 and Table 6.10) can result in the appropriate quantity of pulmonary blood flow without intervention.

Initial procedures to optimize pulmonary venous blood flow

In instances where pulmonary venous blood must cross the atrial septum to reach the systemic
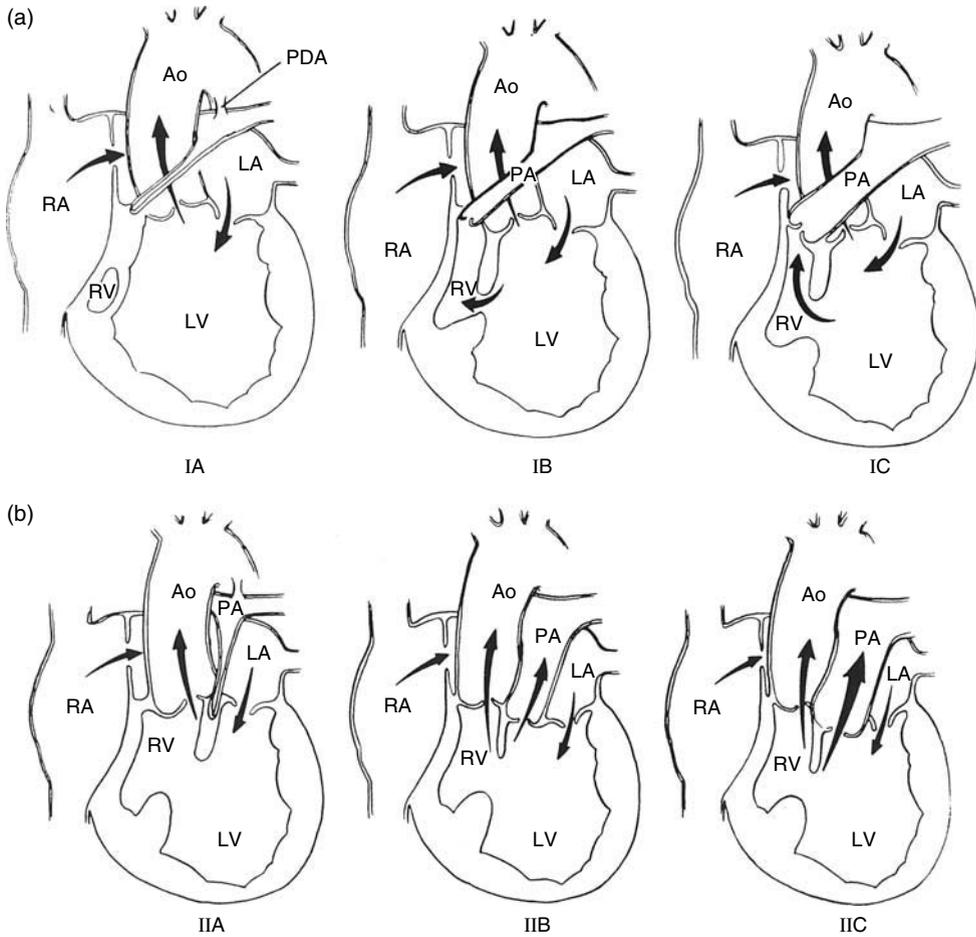
Fig. 6.29 Classification of tricuspid atresia. (a) Type 1: tricuspid atresia without transposition of great vessels. Type 1A: pulmonary atresia with pulmonary blood flow via patent ductus arteriosus or major aortopulmonary collateral arteries (MAPCAs). Type 1B: small ventricular septal defect and pulmonary stenosis. Type 1C: large ventricular septal defect and no pulmonary stenosis.

(b) Type 2: tricuspid atresia with dextro-transposition of the great vessels. Type 2A: pulmonary atresia with pulmonary blood flow via patent ductus arteriosus or MAPCAs. Type 2B: pulmonary stenosis. Type 2C: no pulmonary stenosis. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

ventricle the atrial septum must be nonrestrictive. Creating a nonrestrictive atrial septum may occur in the cardiac catheterization laboratory using a Rashkind–Miller balloon atrial septostomy. In some cases the septum may be so thick as to require placement of a stent. A surgical atrial septectomy to create a nonrestrictive atrial septum (common atrium) can also be performed at the time of initial palliation in procedures that require CPB.

Initial procedures to optimize systemic blood flow
When the pathway to the aorta from the systemic ventricle is obstructed (type 2C or 3B TA; see Fig. 6.29 and Table 6.10) or when the LV and proximal/transverse aorta are hypoplastic (as with HLHS) a DKS procedure alone or in conjunction with an aortic arch reconstruction (as with HLHS), can be used. The PA is transected just proximal to its bifurcation, and the proximal end of the PA is

Table 6.10 Classification of tricuspid atresia.

Type	Pulmonary blood flow	Frequency (%)
Type 1: NRGA		**70**
A No VSD, pulmonary atresia	↓	10
B Small VSD, pulmonary stenosis	↓	50
C Large VSD, no pulmonary stenosis	↔↑	10
Type 2: D-TGA		**30**
A VSD, pulmonary atresia	↓	2
B VSD, pulmonary stenosis	↔↓	8
C VSD, no pulmonary stenosis	↑↑	20
Type 3: L-TGA		**<1**
A VSD, D-loop ventricles, pulmonary or subpulmonary stenosis	↓	
B VSD, L-loop ventricles, sub-aortic stenosis	↑	

D-loop ventricles, right ventricle anterior and rightward; D-TGA, dextro transposition of the great arteries; L-loop ventricles, right ventricle anterior and leftward; L-TGA, levo transposition of the great arteries; NRGA, normally related great arteries; VSD, ventricular septal defect.

Fig. 6.30 Graph of systemic oxygen (O_2) delivery (mL/kg/min) versus Q_P:Q_S for two different systemic ventricular outputs (300 mL/kg/min and 450 mL/kg/min) in single ventricle physiology. In this example oxygen consumption is assumed to be 9 mL/kg/min and $Spv_{O_2} = 95\%$. It is clear that systemic oxygen delivery peaks just below a Q_P:Q_S of 1:1 (line across graph) and declines rapidly above or below this narrow peak.

re-anastomosed end to side or side to side to the ascending aorta. This provides systemic ventricle to aortic continuity (LV to proximal PA to aorta in type 3B TA; RV to proximal PA to aorta in HLHS). In the neonatal period, pulmonary blood flow is then supplied to the oversewn end of the main PA by a MBTS in patients with type 3B TA or a MBTS or RV to PA conduit in patients with HLHS (see Fig. 6.28).

Management of single ventricle physiology

The primary goal in the management of patients with single ventricle physiology is optimization of systemic oxygen delivery and perfusion pressure. This is necessary if end-organ (myocardial, renal, hepatic, splanchnic) dysfunction and failure are to be prevented. This goal is achieved by balancing the systemic and pulmonary circulations. The term "balanced circulation" is used because both laboratory and clinical investigations have demonstrated that maximal systemic oxygen delivery (the product of systemic oxygen content and systemic blood flow) is achieved for a given single ventricle output when Q_P:Q_S is at or just below 1:1. This relationship is illustrated in Fig. 6.30. Increases in Q_P:Q_S in excess of 1:1 are associated with a progressive decrease in systemic oxygen delivery because the subsequent increase in systemic oxygen content is more than offset by the progressive decrease in systemic blood flow. Decreases in Q_P:Q_S just below 1:1 are associated with a precipitous decrease in systemic oxygen delivery because the subsequent increase in systemic blood flow is more than offset by the dramatic decrease in systemic oxygen content.

Since Q_P:Q_S is not readily measurable parameter in a clinical setting Sa_{O_2} is commonly used as surrogate method of assessing the extent to which

a balanced circulation exists. An arterial saturation of 75–80% is felt to be indicative of a balanced circulation. It is important to point out however that an arterial saturation of 75–80% is indicative of a $Q_P:Q_S$ at or near 1:1 only if the pulmonary venous saturation is 95–100% and the mixed venous saturation is 50–55%. In fact, based on these assumptions the equation used to calculate $Q_P:Q_S$ in patients with univentricular physiology: $(Sao_2–Smvo_2)/(Spvo_2–Sao_2)$ can be simplified to: $25/(95–Sao_2)$. In this simplified equation $Spvo_2$ is assumed to be 95% and the A–V oxygen saturation difference is assumed to be 25%. Use of this simplified equation requires that the Fio_2 be at or near 0.21 in order that the dissolved oxygen content of the pulmonary venous blood can be ignored and an $Spvo_2$ of 95% used. Unfortunately, an arterial saturation of 75–80% can exist at the extremes of $Q_P:Q_S$ depending on pulmonary and systemic venous saturation. Specifically, in the presence of a high $Q_P:Q_S$ it is possible for there to be inadequate systemic oxygen delivery (systemic venous desaturation, a wide $Sa–vo_2$ difference, metabolic acidosis) in the presence of what is considered to be an adequate arterial saturation of 75–80%. In addition, clinically unrecognized episodes of pulmonary venous desaturation ($Spvo_2 < 90\%$) further confound assessment of $Q_P:Q_S$ based on Sao_2.

Mathematic modeling of univentricular physiology reveals that systemic oxygen delivery ($Cao_2 \times Q_P$) is a complex function of cardiac output (CO), pulmonary venous oxygen content ($Cpvo_2$), systemic oxygen consumption (CVo_2), and $Q_P:Q_S$ described by the equation:

$$Cao_2 \times Q_S = \frac{CO \times Cpvo_2}{1 + (Q_P/Q_S)} - \frac{CVo_2}{Q_P/Q_S}$$

Given the complex relationships of the multiple variables that determine $Q_P:Q_S$ and oxygen delivery in patients with univentricular physiology, it is not surprising that neither Sao_2 nor the equation $25/(95–Sao_2)$ reliably predicts $Q_P:Q_S$.

In fact, Sao_2 correlates poorly with $Q_P:Q_S$ and the measurement of $Spvo_2$ and $Ssvco_2$ substantially improves estimation of $Q_P:Q_S$. Regression analysis demonstrates that Sao_2 accounts for 8% of the error in estimating $Q_P:Q_S$ while $Ssvco_2$
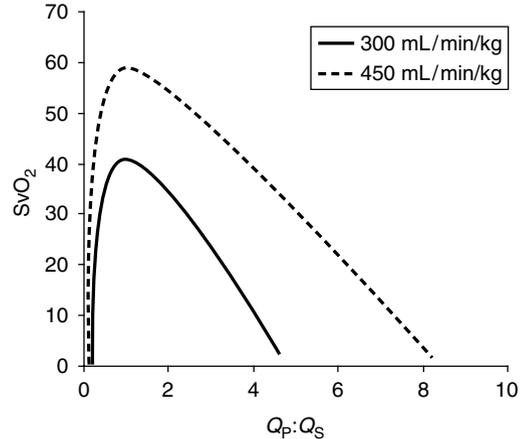
Fig. 6.31 Graph of systemic Svo_2 versus $Q_P:Q_S$ for two different systemic ventricular outputs (300 mL/kg/min and 450 mL/kg/min) in single ventricle physiology. In this example oxygen (O_2) consumption is assumed to be 9 mL/kg/min and $Spvo_2 = 95\%$. It is clear that Svo_2 peaks at a $Q_P:Q_S$ of 1:1 and declines rapidly above or below this narrow peak. $Svo_2 < 30$ is not compatible with mitochondrial oxygen delivery making the clinically relevant range even narrower.

and $Spvo_2$ contribute 48% and 44% respectively. Figures 6.30 and 6.31 illustrate the effect of cardiac output (450 vs. 300 mL/kg/min) on oxygen delivery and Svo_2 as $Q_P:Q_S$ varies with $Spvo_2 = 95\%$ and oxygen consumption = 9 mL/min/kg. Figure 6.32 illustrates the relationship between systemic oxygen delivery and Sao_2. It is clear that while Sao_2 remains satisfactory over a wide range of $Q_P:Q_S$, Svo_2 decreases precipitously outside a narrow range of $Q_P:Q_S$ near 1.0. Furthermore, $Sa–vo_2$ increases dramatically once $Q_P:Q_S > 1.0$. It is also clear that a higher cardiac output allows maintenance of satisfactory oxygen delivery and $Ssvco_2$ over a wider range of $Q_P:Q_S$.

Any combination of variables which produces a $Ssvco_2 < 30\%$ is likely to result in the development of anaerobic metabolism. A modification of the oxygen delivery equation can be used to take this into account where a threshold level of capillary saturation (Sat_{Thresh}) is defined. Any contributions to oxygen delivery by saturations below this threshold are ignored, as they do not provide physiologically useful oxygen delivery. As a result a new term
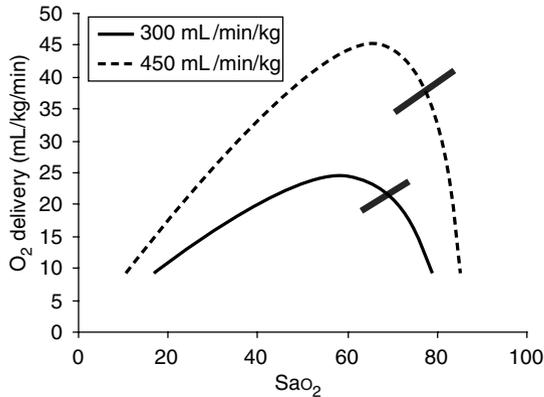
Fig. 6.32 Graph of systemic oxygen (O_2) delivery versus SaO_2 for two different systemic ventricular outputs (300 mL/kg/min and 450 mL/kg/min) in single ventricle physiology. In this example oxygen consumption is assumed to be 9 mL/kg/min and $Spv_{O_2} = 95\%$. Solid line on curve is $Q_P:Q_S$ of 1:1. It is clear that systemic oxygen delivery is maximal at or near a Sa_{O_2} of 75–80%. However systemic oxygen delivery falls off precipitously as Sa_{O_2} increases by imperceptible increments above this level as $Q_P:Q_S$ increases. It is clear that Sa_{O_2} alone can never serve as a surrogate measure of systemic oxygen delivery. Figure 6.5 illustrates the miniscule increases in Sa_{O_2} that occur as $Q_P:Q_S$ exceeds 1:1 in single ventricle physiology.

"useful oxygen delivery to the body" defined as $D(u)_{O_2} = [(Ca_{O_2})(1 - Sat_{Thresh})](Q_S)$ is utilized rather than the tradition oxygen delivery $D_{O_2} = (Ca_{O_2})(Q_S)$. A realistic Sat_{Thresh} would be 30–35%.

The oxygen excess factor (Ω) is calculated as $Sa_{O_2}/(Sa-v_{O_2})$; it is the inverse of the oxygen extraction ratio. A direct linear relationship between Ω and oxygen delivery exists. This direct linear relationship is independent of Spv_{O_2} and cardiac output; however the slope of this relationship increases as oxygen consumption increases. Nonetheless, interventions to improve systemic oxygen delivery will be associated with an increase in measured Ω. This is a clinically useful parameter as it can be obtained with a systemic saturation from an arterial blood gas or a pulse oximeter and an SVC saturation obtained from a venous blood gas drawn from a central venous catheter positioned just at or above the SVC/RA junction.

These patients are at risk for subendocardial ischemia because volume overload increases ventricular end diastolic volume and pressure and because run-off of blood into the lower resistance pulmonary circuit reduces aortic diastolic blood pressure. Under these conditions a small increase in heart rate may reduce subendocardial perfusion enough to induce ischemia and ventricular fibrillation.

Anesthetic management, pre-initial repair

Goals

1 A continuous infusion of PGE_1 is used to maintain ductal patency in patients with ductal dependent blood flow (either systemic or pulmonary). PGE_1 can be discontinued in any patient determined by echocardiogram to have a reliable nonductal source of systemic or pulmonary blood flow. Ductal patency generally produces unrestrictive pulmonary blood flow.

2 A target Pa_{O_2} of 40–45 mmHg and a Sa_{O_2} of 70–80% is reasonable and is likely to be associated with adequate systemic oxygen delivery.

3 In single ventricle (SV) patients with unrestricted pulmonary blood flow control and manipulation of PVR and subsequently of $Q_P:Q_S$ is accomplished most reliably through ventilatory interventions. Clinically, both hypercarbia in combination with a 21% Fi_{O_2} to achieve a pH of 7.30–7.35 and normocarbia in combination with a 17% Fi_{O_2} (inspired N_2) can be utilized to increase PVR and reduce $Q_P:Q_S$. Both strategies reduce $Q_P:Q_S$ to a comparable degree versus baseline (21% Fi_{O_2} and normocarbia) but hypercarbia results in better systemic oxygen delivery (as determined by a narrower A–V oxygen saturation difference and a higher $Sa_{O_2}/(Sa-v_{O_2})$), a higher mean arterial pressure, and a higher cerebral oxygen saturation (as determined by NIRS).

4 Hypercarbia (Pa_{CO_2} of 45–55 mmHg) can be reliably obtained via alveolar hypoventilation or via increased inspired carbon dioxide (3% Fi_{CO_2}). Hypercarbia can be obtained utilizing hypoventilation without use of inspired carbon dioxide. Care is taken to assure adequate tidal volumes with maintenance of FRC and avoidance of atelectasis so as not to induce intrapulmonary shunting and V/Q mismatch resulting in inadvertent hypoxemia. An appropriate degree of hypercarbia can be obtained

with a tidal volume of 8–12 mL/kg, PEEP of 3–5 cm H_2O and a respiratory rate of 4–8 breaths/min. Additional PEEP and larger tidal volumes can be used to mechanically limit excessive pulmonary blood flow. The lower rates are required as the infant cools and metabolic rate decreases.

5 Avoid a high FiO_2 unless the $PaO_2 < 35$–40 mmHg and intrapulmonary V/Q mismatch is suspected.

6 Because ventilatory interventions are incapable of reducing $Q_P{:}Q_S$ much below 2:1 increased cardiac output is often necessary to ensure adequate systemic oxygen delivery and CPP in the these patients. The ability to recruit stroke volume with preload augmentation in very limited in these patients with volume overloaded ventricles. Increasing heart rate $>$140–150 b/min has the potential of initiating myocardial ischemia in patients with aortic diastolic blood pressures in the 20–30 mmHg range. This is a particular risk in patients with HLHS. Inotropic support may be necessary; dopamine in doses of 3–5 μg/kg/min is usually sufficient to accomplish these goals.

7 Once the chest is open the surgeon can mechanically limit pulmonary blood flow and reduce $Q_P{:}Q_S$ by placing a vessel loop around a PA (usually the right). This will often dramatically improve hemodynamics. $ETCO_2$ will fall as the $ETCO_2$–$PaCO_2$ gradient increases. It is not appropriate to decrease minute ventilation at this time; in fact it may need to be increased slightly because of the increase in alveolar deadspace. A small increase in FiO_2 may also be necessary.

8 Infants with single ventricle physiology who arrive in the operating room un-intubated from the ICU require special attention. These patients may clinically have a balanced circulation but this occurs in the setting of several factors that increase PVR including low lung volumes, increased interstitial lung water, and hypoxia pulmonary vasoconstriction. Following induction, intubation and mechanical lung expansion these patients may have a precipitous drop in PVR and immediate compromise of systemic circulation. Despite this, denitrogenation with 100% oxygen is recommended prior to laryngoscopy and tracheal intubation so as to prevent hypoxemia during this interval. Once the airway is secured the FiO_2 can be reduced.

Induction and maintenance

These patients have tenuous cardiovascular status with limited cardiovascular reserve. Ventricular fibrillation can be seen in association with light anesthesia or during routine maneuvers, such as opening the pericardium. Many of them arrive in the operating room intubated receiving inotropic support and PGE_1. In the absence of an accurate prenatal diagnosis many undergo one or more days of medical stabilization following an episode of shock or cardiopulmonary arrest.

An IV induction using a high-dose synthetic narcotic technique in combination with a muscle relaxant is recommended. A benzodiazepine (usually midazolam) can be added as tolerated. Inhalation agents are generally poorly tolerated. Pancuronium is normally utilized. However, in patients with a low aortic diastolic blood pressure and a high baseline heart rate consideration should be given to use of one of the muscle relaxants that do not affect heart rate such as vecuronium or cisatracurium so as to avoid iatrogenic subendocardial ischemia.

Post-CPB management, post-initial repair

Goals

After the initial repair single ventricle physiology persists and the same principles described for pre-CPB management hold true with a few notable exceptions:

1 After CPB, it is not uncommon for a high PVR to result in reduced pulmonary blood flow and hypoxemia.

2 The MBTS or RV to PA conduit may be too large or too small for prevailing physiologic conditions.

3 Ventricular dysfunction may exist due to the long CPB and DHCA or regional low flow perfusion intervals that are necessary to complete these complicated repairs.

4 Myocardial and tissue edema may be significant precluding chest closure.

5 Bleeding from long arterial suture lines may be significant.

6 Inhaled pulmonary vasodilators such as NO may be necessary to improve SaO_2 or reduce the transpulmonary gradient in this patient population.

This is particularly true in the subgroup of patients who have repair of partially obstructed pulmonary venous drainage at the time of their initial repair.

Management of the four clinical scenarios present after initial repair and the appropriate interventions necessary are summarized in Table 6.11.

Single ventricle pathway; superior cavopulmonary shunt, or bidirectional Glenn (BDG)

The BDG (Figs 6.28, 6.33a,b–6.35) directs systemic venous blood from the SVC directly to the pulmonary circulation. The BDG is normally undertaken at 3–6 months of age at which point the PVR has decreased to point where pulmonary blood flow can be provided with systemic venous pressure as the driving pressure. Patients who have outgrown their PA band, RV to PA conduit, or MBTS and have a low SaO_2 and patients who are not tolerating the additional volume on their ventricle with a loose PA band or large MBTS will be staged to a BDG earlier in this interval.

The original Glenn shunt involved an end-to-side anastomosis of the cranial end of the transected SVC to the distal end of the transected right pulmonary artery (RPA). Both the proximal SVC and RPA were over sewn. This procedure was performed through a right thoracotomy without CPB. Currently the bidirectional Glenn is used in which the cranial end of the transected SVC is anatomosed end-to-side to the RPA (which is in continuity with the main and left PAs) and the cardiac end of the SVC is over sewn. This creates SVC continuity with both the left and right pulmonary arteries and bidirectional pulmonary blood flow. The main PA is over sewn if it is not atretic. Unless the IVC is interrupted with azygous continuation the azygous vein is ligated so that the SVC does not decompress retrograde to the IVC thereby reducing the quantity of blood delivered to the PAs. This procedure is performed on CPB through a median sternotomy. The previous aortopulmonary shunt is ligated or the PA band taken down.

Normally all upper extremity and cerebral venous drainage reaches the SVC. In some patients with CHD (particularly those with heterotaxy syndrome)

there may be bilateral SVCs that are not in continuity via a connecting vein. In this case a bilateral BDG must be done with one SVC anatomosed end-to-side to the RPA and the other SVC anatomosed end-to-side to the LPA. LPA to RPA continuity is maintained.

The differences between an aortopulmonary shunt and a BDG are summarized in Fig. 6.33. The most obvious difference between the two is that for a given cardiac output, SaO_2, $SpvO_2$, and SvO_2 the volume load on the systemic ventricle will be twice as large with an aortopulmonary shunt as it is with a BDG. Effective pulmonary blood flow in the aortopulmonary shunt and BDG circulations are equal. However, in the aortopulmonary shunt circulation there is recirculated pulmonary blood (physiologic L–R shunt) while in the BDG circulation there is no recirculated pulmonary blood flow. As a result, a child with a BDG will have the same SaO_2 as a child with an aortopulmonary shunt but with a significant reduction in the volume load on the systemic ventricle.

Modifications of the BDG have been devised to potentially simplify the conversion to a Fontan. The hemi-Fontan refers specifically to a procedure in which atriopulmonary anastomosis is constructed between the dome of the RA at the RA/SVC junction and the inferior surface of the RPA. A Gore-Tex baffle or dam is used to supplement the central PA area and to isolate the cavopulmonary connection from the RA. Another modification (incorrectly called a hemi-Fontan) involves creation of a double cavopulmonary anastomosis. The cranial end of the divided SVC is anastomosed to the superior surface of the RPA. The cardiac end of the divided SVC is anastomosed to the inferior surface of the RPA. The internal orifice of the SVC is closed with a Gore-Tex patch (see Fig. 6.35).

Anesthetic management, pre-superior cavopulmonary shunt

Goals

The principles outlined in section on management of single ventricle physiology before and after the initial repair apply here (see Table 6.11). By the age of 3–6 months when these infants present for their

Table 6.11 Management of single ventricle physiology.

Clinical presentation	Physiology	Management
Sao_2 75–80% Sa-vo_2 25–30% BP > 60/30	**Balanced flow** $Q_P:Q_S = 0.7$–1.5:1	No intervention
Sao_2 > 85–90% Sa-vo_2 35–40% BP < 60/30 Diastolic BP < 15–25 with MBTS; likely higher with RV–PA conduit	**Overcirculated** $Q_P:Q_S$ > 2–3:1 *Causes:* Low PVR Large MBTS or RV–PA conduit Residual arch obstruction	*Raise PVR:* Controlled hypoventilation Mild acidosis Low Fio_2 (0.17–0.19) *Increase systemic O_2 delivery:* Afterload reduction Inotropic support Hematocrit >40% *Surgical intervention:* Clip MBTS or RV–PA conduit Revise arch
Sao_2 < 65–75% Sa–vo_2 25–30%; but Svo_2 likely less than critical value of 30% BP > 70/40 Diastolic BP > 40	**Undercirculated** $Q_P:Q_S$ < 0.7:1 *Causes:* High PVR Small MBTS or RV–PA conduit Pulmonary venous desaturation with underestimation of actual $Q_P:Q_S$	*Lower PVR:* Controlled hyperventilation Alkalosis Sedation/paralysis Aggressively treat atelectasis (pulmonary venous desaturation) Consider NO *Increase systemic O_2 delivery:* Inotropic support *Surgical intervention:* Revise MBTS or RV–PA conduit
Sao_2 < 70–75% Sa-vo_2 35–40% and Svo_2 likely less than critical value of 30% BP < 60/30	**Low cardiac output** *Causes:* Ventricular dysfunction • Myocardial ischemia • Depressed contractility • Afterload mismatch (residual arch obstruction) • AV valve regurgitation	*Minimize O_2 consumption:* Sedation/paralysis Inotropic support/afterload reduction *Surgical intervention:* Repair AV valve Revise arch *Consider mechanical support:* • Post-cardiotomy support • Bridge-to-transplantation

AV, atrioventriculat; BP, blood pressure; MBTS, modified Blalock–Taussig shunt; PVR, pulmonary vascular resistance; RV–PA, right ventricle–pulmonary artery.

(a)

(b)
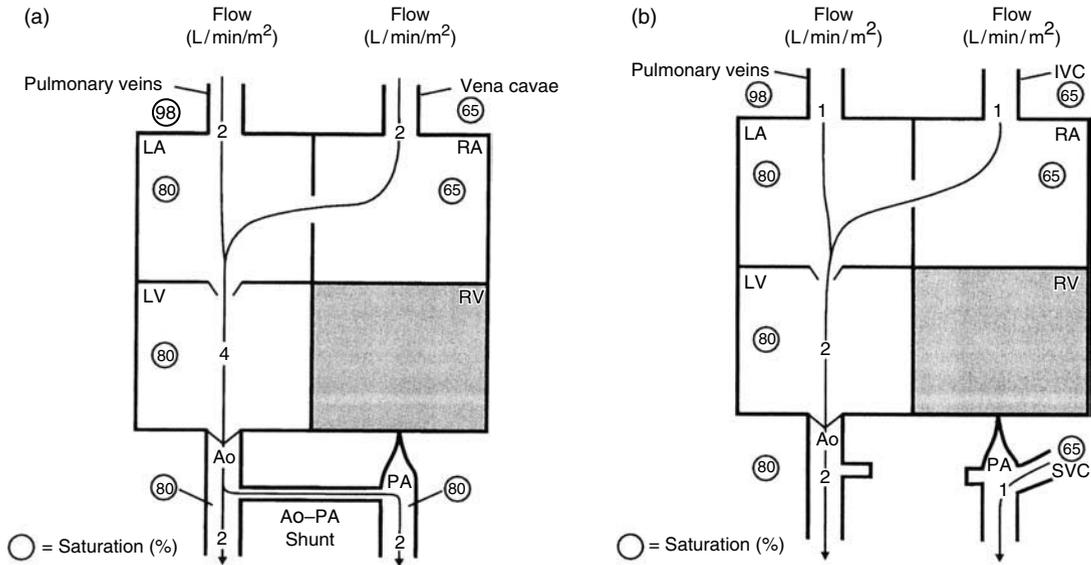
Fig. 6.33 (a) Depiction of saturations and blood flows in tricuspid atresia with a nonrestrictive atrial septal defect (ASD), a hypoplastic right ventricle (RV), and pulmonary atresia palliated with an aortopulmonary shunt. Complete mixing occurs at the atrial level. The left ventricle (LV) is volume overloaded in this parallel circulation to provide pulmonary blood flow. Q_S and Q_P are 2 L/min/m^2 and the arterial saturation is 80% ($Q_P{:}Q_S = 1{:}1$.) (b) Depiction of saturations and blood flows in tricuspid atresia with a nonrestrictive ASD, a hypoplastic RV, and pulmonary atresia palliated with a bidirectional superior cavopulmonary shunt. Complete mixing occurs at the atrial level. The LV is not volume overloaded in this series circulation. Q_S is 2 L/min/m^2,

and Q_P is 1 L/min/m^2; $Q_P{:}Q_S = 0.5{:}1.0$. Nonetheless, cardiac output and arterial saturation are identical to the patient palliated with the aortopulmonary shunt. This is because arterial saturation in complete mixing is determined by the relative volumes and saturations of systemic and pulmonary venous blood. In this instance, Q_S and the volume of systemic venous blood reaching the right atrium (RA) are not equal because half of Q_S has been diverted to become pulmonary venous blood. As a result, $Q_P{:}Q_S$ is deceptive here. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

cavopulmonary shunt they have generally grown and gained weight such that their $Q_P{:}Q_S$ is likely to be 1.0–1.5:1. As a result these patients are much less prone to compromise of systemic oxygen delivery by an excess of pulmonary blood flow.

Induction and maintenance
An IV induction is preferred in these patients. Vascular access may be difficult, as many of these patients have prolonged ICU stays after their initial repair. In addition, many of these patients are tolerant to opioids and benzodiazepines following their ICU stay. This should be considered if premedication is planned prior to IV placement.

Post-CPB management, post-superior cavopulmonary shunt

Goals
1 Maintain heart rate, contractility, and preload to maintain cardiac output. Decreases in cardiac output will reduce IVC saturation. In BDG physiology where there is mixing of IVC and pulmonary venous blood in a common atrium this will reduce arterial saturation.
2 Low $P_{PV}O_2$ saturation will produce a low S_{aO_2}. Maneuvers to reduce V/Q mismatch and intrapulmonary shunt should be undertaken. A high F_{iO_2} may be necessary in the presence of significant V/Q mismatch.
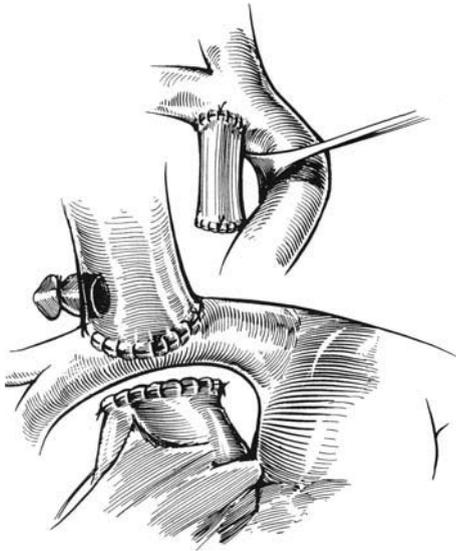
Fig. 6.34 The anatomy of a completed bidirectional superior cavopulmonary shunt. The cephalad portion of the superior vena cava (SVC) is anastomosed end-to-side to the right pulmonary artery. The right pulmonary artery is in continuity with the left pulmonary artery. A previously modified Blalock–Taussig shunt (right subclavian to right pulmonary artery with interposed Gore-Tex graft) is ligated and the subclavian artery is being retracted. The azygous vein is also ligated. The cardiac portion of the SVC is over sewn.

3 Normocarbia should be maintained. Mean airway pressure should be kept at the minimal compatible with delivery of an adequate tidal volume and lung expansion. High mean airway pressure will mechanically limit the nonpulsatile pulmonary blood flow. This can usually be accomplished with a relatively large tidal volume (10–12 mL/kg), slow respiratory rates (10–15 breaths/min), and short inspiratory times (I:E of 1:3–1:4). PEEP should be used with caution.

4 A central line placed in the internal jugular (IJ) will measure SVC pressure, which equals mean pulmonary artery pressure (mPAP) following a BDG. A surgically placed atrial line will measure common atrial pressure. The transpulmonary pressure gradient (TPG) (mPAP – common atrial pressure) is usually <10 mmHg with appropriate ventilation. A mPAP of 12–18 mmHg is usually seen in presence of good systemic ventricular function.
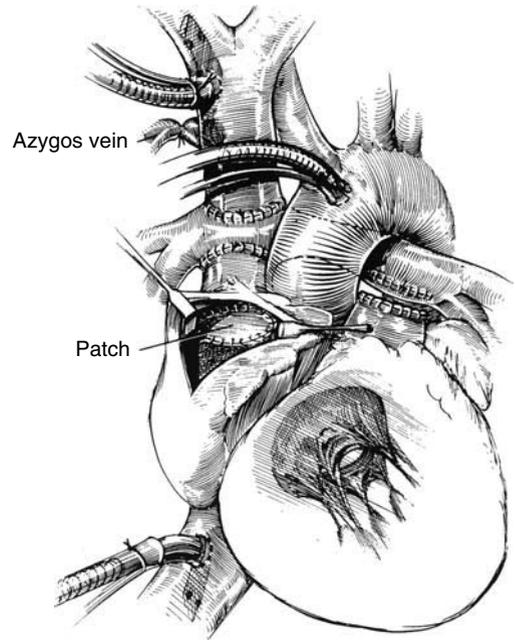
Fig. 6.35 The anatomy of a double cavopulmonary anastomosis with internal patch closure of the cardiac anastomosis. Both the cardiac and cephalic portions of the superior vena cava (SVC) are in continuity with the right pulmonary artery. The right pulmonary artery is in continuity with the left pulmonary artery, and the main pulmonary artery is divided and over sewn. Inferior vena cava (IVC) blood is prevented from reaching the pulmonary arteries due to a patch occluding the right atrium (RA)–SVC junction. The physiology is identical to that in Figs 6.31 and 6.32.

5 Inotropic support of the systemic ventricle may be necessary due to ventricular dysfunction induced by chronic volume overload and CPB. Dopamine (3–5 µg/kg/min) is useful. Milrinone (0.5–1.0 µg/kg/min) is useful for those patients who have high SVR and hypertension.

6 Inhaled pulmonary vasodilators such as NO generally do not improve SaO_2 or reduce the transpulmonary gradient in this patient population. The exception to this may be the subgroup of patients who have repair of partially obstructed pulmonary venous drainage at the time of their BDG.

7 The most likely cause of a low SaO_2 following a BDG is low cardiac output with a low

IVC saturation. TEE will help delineate the cause (ventricular dysfunction, hypovolemia, AV valve dysfunction). If a low Sao_2 persists despite optimization of ventricular function, consideration should be given to causes of reduced pulmonary blood flow such as a stenotic anastomosis or the presence of decompressing venous collaterals from the SVC to the IVC.

These patients will have a Sao_2 of 75–80%, similar to that prior to their BDG. The $Q_P{:}Q_S$ ranges from 0.5–0.7:1 and as a result there will be the acute reduction in volume load on the systemic ventricle as shown in Fig. 6.33. There is an acute increase in SVC pressure and presumably in intracranial pressure (ICP). The volume load reduction and elevated SVC pressure are believed to contribute to the initial systemic hypertension and postoperative irritability that is commonly seen in these patients. The majority of pulmonary blood flow will be supplied via venous blood from the brain; the largest contributor to venous drainage from the upper body. Hyperventilation and hypocarbia, while beneficial in reducing PVR will also reduce cerebral blood flow and cerebral venous drainage. Maintaining normocarbia following BDG has been demonstrated to provide maximal $Q_P{:}Q_S$ and Sao_2. These patients tend to have a large $ETco_2$–$Paco_2$ gradient due to increased physiologic dead space. An increased portion of the lung in these patients is ventilated but not perfused due to the low PA driving pressure (SVC pressure).

Attention is focused on the TPG that, in normal patients, is defined as the mPAP–LAP. In BDG patients, the mPAP = SVC pressure. In BDG patients the equivalent of a LAP or pulmonary venous atrial pressure is the common atrial pressure. A common atrium exists in these patients because the atrial septectomy creates a nonrestrictive communication between the LA and RA.

Definitive repair: the Fontan procedure or total cavopulmonary connection (TCPC)

Fontan physiology

The Fontan procedure is generally performed in staged patients at 2–3 years of age. Fontan physiology is a series ("normal") circulation that can be described as follows:
- There is one ventricle with sufficient diastolic, systolic, and AV valve function to support systemic circulation. This ventricle must in turn:

a Be in unobstructed continuity with the aorta.

b Be in unobstructed continuity with pulmonary venous blood.

- There is unobstructed delivery of systemic venous blood to the pulmonary circulation (total cavopulmonary continuity).

In the absence of any residual physiologic intracardiac or intrapulmonary R–L shunting these patients should have a normal Sao_2. It is often stated that pulmonary blood flow is passive and gradient driven (systemic venous pressure > mean PA pressure > pulmonary venous atrial pressure). In fact, the systemic ventricle generates the energy necessary to provide flow through the pulmonary capillary bed because the systemic vascular bed and pulmonary vascular bed are in continuity without an intervening atria and ventricle to provide reservoir and pumping capacity. As a result, the single ventricle in a series Fontan circulation is faced with higher afterload then the systemic ventricle in a two-ventricle series circulation.

The Fontan procedure was first performed in 1968 and was applied to patients with TA. The original operation included a Glenn shunt, which drained the SVC directly into the distal right PA. The proximal end of the RPA was joined to the right atrial appendage via an aortic valve homograft and a pulmonary valve homograft valve was placed at the IVC–RA junction. The main PA was ligated and the ASD was closed. Subsequently, creation of the Glenn shunt and placement of homograft valves at the RA–PA and IVC–RA junctions were eliminated resulting in creation of a direct atriopulmonary connection.

Since then, many modifications have been described. Despite the modifications, the goal of the procedure remains the same: to provide delivery of all systemic venous blood directly to the pulmonary arteries without the benefit of the reservoir or pumping capability of a ventricle. This requires total cavopulmonary continuity either directly or
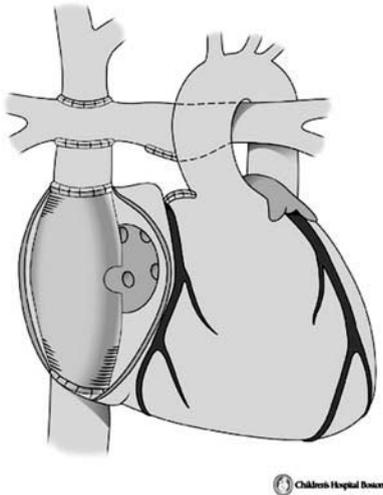
Fig. 6.36 Total cavopulmonary connection using an intra-atrial lateral tunnel or baffle. The tunnel is prosthetic graft material such as Gore-Tex. A fenestration has been placed in this prosthetic material allowing a physiologic right-to-left (R–L) shunt to exist when baffle pressure exceeds common (pulmonary venous) atrial pressure.

Fig. 6.37 Total cavopulmonary connection using an extracardiac conduit or baffle. The conduit is prosthetic graft material such as Gore-Tex. A small side-to-side anastomosis between a fenestration in the conduit and a fenestration in the atrial wall can be placed allowing a physiologic right-to-left (R–L) shunt to exist when baffle pressure exceeds common (pulmonary venous) atrial pressure.

via the system venous atrium. Currently, the most commonly performed procedures are the lateral tunnel and extracardiac Fontan (Figs 6.28, 6.36 and 6.37). The lateral tunnel procedure avoids incorporating any substantial volume of atrium in the cavopulmonary pathway while the extracardiac procedure does not incorporate any atrium. These procedures are referred to as TCPCs. Over time in atriopulmonary connections elevated systemic venous pressure leads to atrial dilatation. The atrium often expands to a volume as large as 300–500 mL. This is a source of stasis and a nidus for atrial arrhythmias. In theory, the extracardiac procedure may offer additional protection from development of atrial arrhythmias due to a lack of suture lines in atrium.

Contraindications to the Fontan procedure include: early infancy, PVR > 4 Wood units/m^2, severe PA hypoplasia, an ejection fraction (EF) < 25–30%, and a ventricular diastolic pressure > 25 mmHg. The majority of lesions felt in the past to be relative contraindications to the Fontan procedure such as AV valve regurgitation/stenosis or

focally narrowed or distorted pulmonary arteries can now be corrected at the time of the Fontan procedure.

Use of the staged single ventricle pathway results in reduced morbidity and mortality as compared to the acute transition from single ventricle to Fontan physiology. As previously described, the staged pathway makes use of a bidirectional cavopulmonary shunt procedure before the Fontan procedure. Use of the cavopulmonary shunt at 3–6 months of age allows early reduction in the volume overload that accompanies univentricular physiology. This allows systemic ventricular volume load to be reduced to normal and allows remodeling of the ventricle at lower end-diastolic volume.

Acute reduction of systemic ventricular volume in the univentricular heart results in impaired ventricular compliance because wall thickness does not regress as quickly as ventricular volume. The result is impaired ventricular diastolic function and elevated end-diastolic pressure. This will impede pulmonary venous return, which is a liability in the Fontan procedure, because this will subsequently

reduce pulmonary blood flow. A low cardiac output state will result because systemic ventricular output can only equal the quantity of blood that transverses the pulmonary vascular bed. The impaired ventricular diastolic function that accompanies acute ventricular volume reduction is better tolerated in BDG or hemi-Fontan physiology than in Fontan physiology. When there is impairment of pulmonary venous return after the BDG or hemi-Fontan, blood from the IVC will continue to provide systemic ventricular filling and cardiac output at a lower pressure than that required to traverse the pulmonary bed.

A risk of the staged procedures is the development of pulmonary arteriovenous malformations. These are the result of diversion of hepatic venous blood flow (IVC) blood to a systemic capillary bed before delivery to the pulmonary capillary bed as occurs in the bidirectional cavopulmonary shunts. This is generally not a problem when the BDG is eventually converted to a Fontan.

Fenestrated Fontan

With Fontan physiology, increased impedance to systemic venous blood flow across the pulmonary capillary bed will result in decreased delivery of blood to the pulmonary venous atrium, systemic ventricle, and aorta producing a low cardiac output state with a normal or near normal Sao_2. This increased impedance is not uncommon in the initial days and weeks following Fontan surgery. Attempts to increase cardiac output by increasing systemic venous pressure may result in development of refractory pleural effusions and ascites. In many institutions a 4 mm hole or fenestration is intentionally left in cavopulmonary pathway or baffle. This allows systemic venous blood to "pop-off" into the pulmonary venous atrium and ultimately into the systemic ventricle and aorta. This physiologic R–L shunt allows maintenance of systemic cardiac output at the expense of Sao_2. This fenestration can be easily closed in the cardiac catheterization laboratory with an occlusion device at later date following demonstration of adequate hemodynamics, gas exchange, and cardiac output with balloon occlusion of the fenestration.

Anesthetic management, pre-Fontan

Goals

The principles outlined in the section on management of BDG physiology after CPB generally apply here. At 2–3 years of age patients with a superior cavopulmonary shunt (BDG) generally have a stable cardiovascular system with a Sao_2 of 75–80% unless there are significant decompressing venous collateral vessels from the SVC to either the IVC or pulmonary venous system. These are usually addressed by coil occlusion in the cardiac catheterization laboratory prior to the Fontan. While these patients will tolerate an inhalation induction from a cardiovascular standpoint it should be recognized that several factors might make a pure inhalation induction difficult:

- Venous congestion of the head and tongue due to a relatively high SVC pressure.
- Coughing, breath holding, or any other cause of high intrathoracic pressure will cause almost complete cessation of pulmonary blood flow. Almost immediate arterial hypoxemia will occur.
- With a $Q_P:Q_S$ of 0.5–0.7:1.0 the speed of an inhalation induction will be slow.

Induction and maintenance

An IV induction is preferred. Consideration should be given to premedication as these patients and their families generally have had multiple hospital exposures for check-ups and procedures. In addition, many of these patients are tolerant to opioids and benzodiazepines following neonatal and subsequent exposure. This should be considered if premedication is planned prior to IV placement.

Post-CPB management, post-Fontan procedure

Goals

1 Maintain heart rate, contractility, and preload to maintain cardiac output. In Fontan patients with a fenestration or intrapulmonary shunt decreases in cardiac output will reduce Svo_2 and Sao_2. Svo_2 can be easily determined using a sample drawn from a central venous catheter.

2 Low pulmonary venous saturation will produce a low Sao_2. Maneuvers to reduce V/Q mismatch and intrapulmonary shunt should be undertaken. A high Fio_2 may be necessary in the presence of significant V/Q mismatch.

3 Ventilation and acid-base management should be optimized to keep PVR low. Mean airway pressure should be kept at the minimal compatible with delivery of an adequate minute ventilation and lung expansion. High mean airway pressure will mechanically limit the nonpulsatile pulmonary blood flow. This can usually be accomplished with a relatively large tidal volume (10–12 mL/kg), slow respiratory rates (10–15 breaths/min), and short inspiratory times (I:E of 1:3–1:4). PEEP should be used with caution.

4 A central line placed in the IJ will measure caval (baffle) pressure which equals mPAP following a Fontan. A surgically placed atrial line will measure common atrial pressure. The TPG (mPAP – common atrial pressure) is usually <10 mmHg with appropriate ventilation. A mPAP of 15–18 mmHg is usually seen in the presence of good systemic ventricular function.

5 Inotropic support of the systemic ventricle may be necessary due to ventricular dysfunction induced by chronic volume overload and CPB. Dopamine (3–5 μg/kg/min) is useful. Milrinone (0.5–1.0 μg/kg/min) is useful for those patients who have high SVR and afterload/contractility mismatch.

6 Inhaled pulmonary vasodilators such as NO generally do not improve Sao_2 or reduce the transpulmonary gradient in this patient population. The exception to this may be the subgroup of patients who have repair of partially obstructed pulmonary venous drainage at the time of their Fontan.

The management goals following the Fontan procedure are summarized in Table 6.12. As with a BDG patient, attention is focused on the transpulmonary gradient (TPG). In Fontan patients the mPAP = CVP. A CVP in a Fontan patient will measure pressure in the caval portion of the cavopulmonary connection and is commonly called a baffle pressure. As with a BDG patient in Fontan patients

the equivalent of a LAP is the common atrial pressure. In Fontan patients the pressure in the cavopulmonary connection can be obtained via a percutaneously placed central venous catheter or a surgically placed transthoracic baffle catheter. The common atrial pressure is obtained via a surgically placed transthoracic catheter. Thus in patients with a Fontan, the TPG = CVP – common atrial pressure.

Low pulmonary blood flow produces low cardiac output in this series circulation. The systemic ventricle can only pump the volume of blood that is delivered to it across the pulmonary vascular bed. This differs from the situation after superior cavopulmonary shunts because, in these patients, there is a source of blood supply (IVC blood) to the systemic ventricle that does not cross the pulmonary bed. It should be emphasized that in a Fontan patient, low cardiac output will not result in a low Sao_2 unless there are significant sources of intrapulmonary or intracardiac (fenestration, baffle leak) physiologic R–L shunting. When low cardiac output is due to ventricular dysfunction, common (pulmonary venous) atrial hypertension will lead to development of pulmonary edema and physiologic R–L intrapulmonary shunting. This situation is analogous to a normal patient with series circulation and no intracardiac lesions. Low cardiac output in a normal patient will result in a low Sao_2 only if a significant quantity of intrapulmonary R–L shunt exists and low cardiac output produces a low Svo_2. The presence of a fenestration or baffle leak will exacerbate this Sao_2 decrease in the Fontan patient.

It is commonly stated that early tracheal extubation and spontaneous ventilation enhance pulmonary gas exchange and hemodynamics in Fontan patients. It must be emphasized that low lung volumes, hypercarbia, and hypoxemia will negate any advantage obtained by spontaneous ventilation.

Tricuspid atresia

Anatomy

In Tricuspid atresia (TA), there is agenesis of the tricuspid valve and no communication between the RA and the hypoplastic RV (the tricuspid valve is embryologically part of the RV). Anatomic

Table 6.12 Management of Fontan physiology.

Physiology	Clinical presentation	Management
Low pulmonary blood flow and inadequate preload delivery to systemic (common) atrium TPG $\gg$ 10 mmHg *Causes:* Baffle obstruction Pulmonary artery obstruction Pulmonary vein obstruction Premature baffle fenestration closure	**No fenestration or premature fenestration closure** Sao_2 95–100% Sa-vo_2 > 35–40% Baffle pressure > 20 mmHg Common atrial pressure < 10 mmHg Hypotension Tachycardia Poor distal perfusion Metabolic acidosis **Fenestration patent or baffle leak present** Sao_2 75–80% Sa-vo_2 > 35–40% Baffle pressure > 20 mmHg Common atrial pressure < 10 mmHg Hypotension Tachycardia Poor distal perfusion Metabolic acidosis	Volume replacement to keep baffle pressure stable Reduce PVR Correct acidosis Inotropic support Afterload reduction Consider catheterization intervention to open or create baffle fenestration
Systemic ventricular dysfunction TPG = 5–10 mmHg *Causes:* Systolic dysfunction Diastolic dysfunction AV valve regurgitation/stenosis Loss of AV synchrony Afterload/contractility mismatch	**No fenestration or premature fenestration closure** Sao_2 85–90% Sa-vo_2 > 35–40% Baffle pressure > 20 mmHg Common atrial pressure > 15 mmHg Pulmonary edema Hypotension Tachycardia Poor distal perfusion Metabolic acidosis **Fenestration patent or baffle leak present** Sao_2 70–75% Sa-vo_2 > 35–40% Baffle pressure > 20 mmHg Common atrial presure > 15 mmHg Pulmonary edema Hypotension Tachycardia Poor distal perfusion Metabolic acidosis	Volume replacement to keep baffle pressure stable Correct acidosis PEEP may be necessary for pulmonary edema Inotropic support Afterload reduction Provide AV synchrony (antiarrhythmics/pacing) Mechanical support (post-cardiotomy support or bridge to transplantation) Surgical intervention (takedown to BDG)

AV, atrioventricular; BDG, bidirectional Glenn procedure; PVR, pulmonary vascular resistance; TPG, transpulmonary pressure gradient.

classification is based on the presence or absence of TGA, the extent of PS or atresia, and the size of the VSD. This classification and the frequency of the different lesion types are summarized in Fig. 6.29 and Table 6.10. Approximately 70% of patients with TA are type 1 and 30% are type 2. Type 3 lesions are very rare. Fifty percent of all TA patients are type 1B.

Physiology

TA is single ventricle physiology lesion. These patients are staged to a Fontan procedure. TA is a complex shunt with complete obstruction to RV inflow and variable obstruction to RV outflow. There is a communication (ASD or patent FO) which results in an obligatory R–L shunt at the atrial level with complete mixing of systemic and pulmonary venous blood in the LA. When the ASD or FO is restrictive, there will be a large right atrial to LAP gradient. This will result in poor decompression of the RA and systemic venous congestion. Pulmonary blood flow can be provided by a downstream shunt from one or both of the following sources:

- *Intracardiac.* The pathways are described in Table 6.1. This downstream shunt may be simple (VSD without PS), complex (VSD with PS), or complex with complete obstruction (pulmonary atresia with or without a VSD).
- *Extracardiac.* This is generally a PDA but in older patients MAPCAs may have developed. When pulmonary atresia exists (types 1A and 2A) these simple shunts are the sole source of pulmonary blood flow.

The quantity of pulmonary blood flow associated with each type of TA is summarized in Table 6.10.

In single ventricle lesions the degree of cyanosis will be determined largely by $Q_P{:}Q_S$. Therefore, patients with a $Q_P{:}Q_S < 1$ due to stenotic or atretic pulmonary outflow tracts, restrictive VSDs, or both will be more cyanotic than their counterparts with normal or increased pulmonary blood flow. TA imposes a volume load on the LV, and increased pulmonary blood flow produces an even larger LV volume load. Therefore, patients with TA and increased pulmonary blood flow are likely to present with CHF. Furthermore, patients with increased pulmonary blood flow are at risk to develop PVOD.

Surgical therapy

More than 70% of neonates with TA have ductal dependant pulmonary blood flow and require a MBTS in association with PDA ligation. This can often be done off-CPB through a median sternotomy. Following initial repair, TA patients proceed to a superior cavopulmonary connection or BDG at age 3–6 months and then on to the Fontan procedure at 1–2 years of age as previously described.

Anesthetic management

Goals

These patients are initially managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11). Subsequent management for the superior cavopulmonary shunt and Fontan procedure is described in later portions of the section on Management of single ventricle physiology.

Post-CPB management

These patients are managed according to the principles described in the section on Management of single ventricle physiology, post-CPB management (see Table 6.11). Subsequent management for the superior cavopulmonary shunt and Fontan procedure is described in later portions of the section on Management of single ventricle physiology.

Hypoplastic left heart syndrome

Anatomy

Patients with hypoplastic left heart syndrome (HLHS) have hypoplasia of all left heart structures. In the most severe form, mitral and aortic atresia with hypoplasia of the LA, LV, ascending aorta, and aortic arch (including coarctation) are present. Distal aortic blood flow occurs via the PDA. Proximal aortic blood flow and coronary blood flow occur by retrograde filling of a tiny ascending aorta via the PDA (Figs 6.28 and 6.38). This unique variation of single ventricle physiology in HLHS patients puts them at increased risk for development of myocardial ischemia.
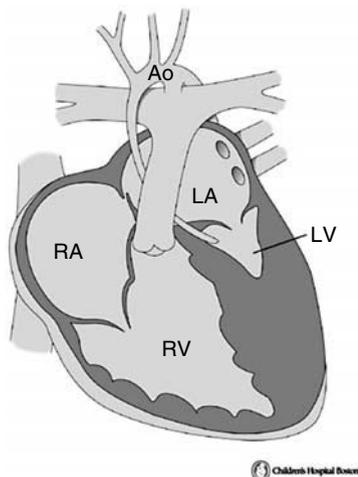
Fig. 6.38 Anatomy of hypoplastic left heart syndrome (HLHS). There is severe mitral stenosis/atresia, left ventricular hypoplasia, aortic valve atresia, and hypoplasia of the ascending aorta and transverse aortic arch. Pulmonary and systemic blood flows are both delivered via the right ventricle. Aortic blood flow is provided via a large ductus arteriosus. There is antegrade flow from the patent ductus arteriosus (PDA) to the descending aortic and retrograde flow to the proximal aortic arch and cerebral circulation. The coronary arteries are perfused retrograde via the tiny ascending aorta. The left ventricle (LV) is diminutive. Ao aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Physiology

The HLHS is a ductal dependant single ventricle physiology lesion. These patients are staged to a Fontan procedure. HLHS is a complex shunt with complete obstruction to outflow. There is a communication (ASD or patent FO) and a complete or near complete obstruction to LA outflow (mitral atresia or severe mitral stenosis) and LV outflow (aortic atresia or severe aortic stenosis). This results in an obligatory L–R shunt at the atrial level with complete mixing of systemic and pulmonary venous blood in the RA and ventricle. When the ASD or FO is restrictive, there will be a large left atrial to right atrial pressure gradient. This will result in poor decompression of the LA, pulmonary venous congestion and pulmonary hypertension. These patients need emergency decompression of the LA (pulmonary venous chamber) and medical

stabilization prior to surgery. This requires transatrial stent placement in the cardiac catheterization laboratory.

Systemic blood flow is provided by a simple downstream shunt (PDA). The shunt at the level of the PDA is a dependent shunt with net systemic and pulmonary blood flow determined by the ratio of systemic to PVR. Low PVR relative to SVR will allow run-off of blood into the pulmonary circuit compromising systemic perfusion. Flow to the ascending aorta, coronary arteries, and arch vessels are supplied entirely (aortic atresia) or almost entirely (severe mitral and aortic stenosis) retrograde from the PDA. Flow to the descending aorta is antegrade from the PDA. Closure of the PDA in infants with HLHS terminates coronary and systemic blood flow and results in immediate cardiovascular collapse. PGE_1 therapy is lifesaving for these patients.

Surgical therapy

Patients with HLHS are staged along the single ventricle pathway to a Fontan procedure (see Fig. 6.28). The initial procedure utilizing a MBTS is commonly referred to as a Norwood stage 1. The initial procedure utilizing an RV to PA conduit is commonly referred to as a modified Norwood stage 1 or a Sano procedure. As discussed previously it must incorporate procedures to meet the objective necessary at each stage in the single ventricle pathway:

- A DKS anastomosis in conjunction with an aortic arch reconstruction/coarctation repair utilizing homograft or pericardial tissue is necessary to provide an unobstructed systemic ventricle (RV) to aortic connection.
- An atrial septectomy is performed to allow unobstructed delivery of pulmonary venous blood from the LA to the systemic RV via the RA.
- A MBTS (usually 3.5 mm Gore-Tex conduit) or RV to PA conduit (usually a 5 or 6 mm valveless Gore-Tex conduit) is created to provide pulmonary blood flow.

The physiology of the MBTS and of the RV to PA conduit as a source of pulmonary blood flow differ in some important aspects:

- With a MBTS blood is distributed to the pulmonary circulation after it has entered the systemic

arterial tree (from the innominate artery to the PA) while with a Sano conduit blood is distributed to the pulmonary circulation before it has entered the systemic arterial tree (from the RV to the PA; much like a double outlet RV). As a result, for a given cardiac output and Q_P:Q_S, the pulse pressure is wider and the aortic diastolic blood pressure lower in patients with a MBTS. The higher diastolic blood pressure obtained with the Sano shunt may provide better cerebral, coronary and splanchnic perfusion.

• The Sano shunt requires creation of a small right ventriculotomy. The RV is the systemic ventricle and the long-term functional consequences of this ventriculotomy are unknown.

• The Sano conduit is valveless a resulting in some pulmonary insufficiency. The volume load on the RV induced by this is small and probably offset by the fact that Sano shunt patients have a slightly lower Q_P:Q_S and volume load than MBTS patients.

Following stage 1 repair, HLHS patients proceed to what is often called stage 2 – a superior cavopulmonary connection (BDG or hemi-Fontan) at age 3–6 months – and then on to the Fontan procedure at 1–2 years of age. Patients with an RV to PA conduit generally have their superior cavopulmonary connection at an earlier age than children with a MBTS as they have a lower Q_P:Q_S and tend to "outgrow" their shunt sooner.

Anesthetic management

Goals

These patients are managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11). These patients have ductal dependant systemic blood flow. Patients with HLHS are particularly vulnerable to myocardial ischemia because the coronary arteries are supplied retrograde from the PDA down a segment of hypoplastic ascending aorta (often 1–2 mm in diameter). Subsequent management for the superior cavopulmonary shunt and Fontan procedure is described in later portions of the section on Management of single ventricle physiology.

Post-CPB management

These patients are managed according to the principles described in the section on Management of single ventricle physiology, post-CPB management (see Table 6.11). Subsequent management for the superior cavopulmonary shunt and Fontan procedure is described in later portions of the section on Management of single ventricle physiology.

There are a few subtle differences in management of patients with a MBTS as opposed to a Sano RV to PA conduit in the initial postoperative period:

• In patients with a MBTS, high SVR tends to increase Q_P:Q_S, increase aortic diastolic runoff, and promote pulmonary overcirculation with compromise of systemic oxygen delivery. Afterload reduction with phenoxybenzamine is used in some institutions while in others a less aggressive approach utilizing milrinone is undertaken.

• High SVR is less disadvantageous to a patient with a Sano RV to PA conduit because pulmonary blood flow is derived from the RV prior to distribution to the arterial circulation and because of the inherent high resistance through the long RV to PA conduit. In these patients afterload reduction and reduced RV pressure may result in a low Q_P:Q_S and hypoxemia.

Tetralogy of Fallot with pulmonary atresia

Anatomy

Tetralogy of Fallot with pulmonary atresia (TOF/PA) involves the features of TOF and infundibular and pulmonary valvular atresia in conjunction with varying degrees of pulmonary arterial atresia. Four groups are said to exist. Group 1 patients have isolated infundibular and pulmonary valve atresia with a main PA and distal pulmonary arteries of near normal size and architecture. In some of these patients, the main PA may extend to the atretic infundibulum. In others, there is short segment atresia of the main PA (Fig. 6.39a,b). Patients in this group have pulmonary blood flow supplied from a PDA. Group 2 patients have absence of the main PA but the PAs are in continuity and supplied by a PDA. Group 3 patients have severely hypoplastic native PAs; the left and right PA may not be in continuity. There

(a)

(b)
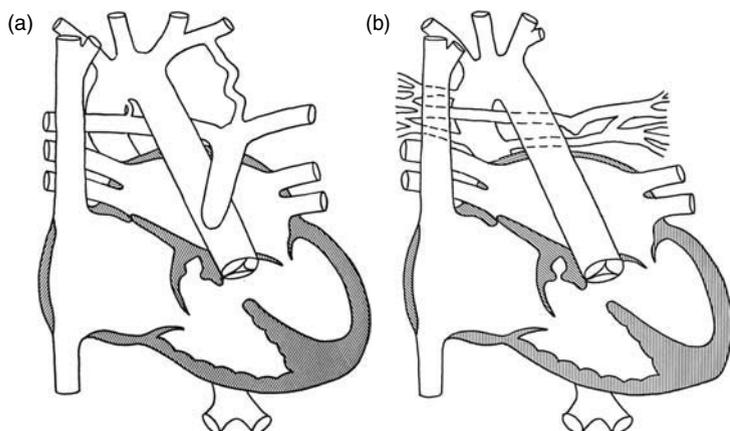
Fig. 6.39 (a) Anatomy of tetralogy of Fallot/pulmonary artery (TOF/PA) group 1 with short segment pulmonary atresia, good-sized PAs in continuity supplied by a right sided patent ductus arteriosus (PDA) and one large major aortopulmonary collateral artery (MAPCA) from the left subclavian artery. There is a right aortic arch with mirror image arch vessel branching. (b) Illustration of TOF/PA group 3 with no main PA, small branch PAs in continuity supplied by MAPCAs. Some lung segments are supplied by the native PAs while others are supplied directly by MAPCAs. There is a right aortic arch with mirror image arch vessel branching.

are major aortopulmonary collateral vessels (vessels from the aorta to the PA) known as MAPCAs. A PDA may be present as well. Some segments of lung may be supplied only by blood from MAPCAs, some only by the native PAs, and others by both sources (see Fig. 6.39). Group 4 patients have no native PAs and all pulmonary blood flow is derived from MAPCAs.

The anatomy of MAPCAs in TOF/PA can almost never be clearly delineated by two-dimensional echocardiography alone. Cardiac catheterization and/or MRI/MRA are necessary to delineate collateral anatomy and to determine $Q_P{:}Q_S$.

Physiology

TOF/PA is single ventricle physiology lesion. This lesion is generally amenable to a two-ventricle repair. TOF/PA is a complex shunt in which a communication (VSD) and total obstruction to RV outflow (PA) are present. This results in obligatory R–L shunting across the VSD with complete mixing of systemic and pulmonary venous blood in the LV. Pulmonary blood flow is provided by a downstream simple shunt (PDA or MAPCAs). For infants, in whom the PDA provides most of the pulmonary blood flow, PGE_1 infusion (0.01–0.05 μg/kg/min) will be necessary to ensure ductal patency.

Surgical therapy

Surgery in group 1 and 2 TOF/PA patients is aimed at establishing a reliable source of pulmonary blood flow in the neonatal period, as these patients are dependent on PGE_1 to maintain a PDA and pulmonary blood flow. These patients may undergo a palliative shunt procedure (usually a MBTS as described above) or a definite procedure. The definite procedure would be creation of continuity between the RV and the main PA via placement of a RV to PA conduit with VSD closure generally performed via the ventriculotomy used for the proximal end of the conduit. In cases where short segment atresia exists, it may be possible to obtain RV to PA continuity with a direct anastomosis augmented with homograft material or pericardium.

Patients in groups 3 and 4 present difficult management problems. As a rule these patients present with univentricular physiology with a tendency for pulmonary blood flow to become excessive ($Q_P{:}Q_S > 2$–3:1) as the PVR drops following birth. In group 3 patients neonatal repair with placement of a RV to PA conduit is undertaken to place the PAs in continuity with the RV in an effort to promote native PA growth. In this circumstance the VSD is left open as a source of R–L shunting and delivery of desaturated blood to the systemic circulation as it would be impossible for

the RV to deliver an adequate cardiac output to the LA across the hypoplastic pulmonary vascular bed. These infants then undergo multiple cardiac catheterization procedures in order to:

• Dilate and stent the hypoplastic native pulmonary arteries.

• Coil embolize MAPCAs which provide pulmonary blood flow which is competitive with blood flow supplied by native PAs. MAPCAs that provide pulmonary blood flow to segments of lung not supplied by native PAs must be unifocalized to the proximal pulmonary circulation.

Unifocalization involves removal of the collateral vessel from the aorta with subsequent reanastomosis to the RV to PA conduit or a proximal PA branch. Although the traditional approach has been through a thoracotomy more recently most groups have favored a central approach working through a median sternotomy. It is only when 80–90% of the pulmonary vascular bed is direct continuity with the RV that closure or fenestrated closure of the VSD can be considered. Usually this will mean that at least 10–12 bronchopulmonary segments are now in direct continuity with the RV.

In group 4 patients it may be necessary to unifocalize several large collaterals to the distal end of conduit from the RV as the initial intervention. Alternatively several large collaterals could be unifocalized to an MBTS or central shunt. These procedures serve to promote pulmonary vascular growth, prevent the development of PVOD, and control the Q_P:Q_S.

Anesthetic management

These patients are managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11).

Post-CPB management

The management issues in patients with types 1 and 2 TOF/PA having undergone definitive repair with RV to PA conduit and VSD closure are similar to those encountered in care of the patient having undergone repair for TOF/PS. A few differences merit discussion. These TOF/PA patients will not have pulmonary insufficiency due to the presence

of a competent valve in the conduit. The placement of a conduit will however require a larger right ventriculotomy and potential for significant RV free wall hypo- and dyskinesis.

The management issues in patients with types 3 and 4 TOF/PA having undergone palliative aortopulmonary shunt placement or RV to PA conduit placement without VSD closure will be similar to those described for patients with a large, nonrestrictive VSD and/or PDA. This will be particularly true for patients with a large number of residual MAPCAs. In these patients postoperative embolization of some MAPCAs in the cardiac catheterization laboratory may be necessary to control pulmonary blood flow.

Pulmonary atresia with intact ventricular septum

Anatomy

There is complete obstruction to RV outflow in pulmonary atresia with intact ventricular septum (PA/IVS) (Fig. 6.40). The complete outflow obstruction is at the level of the pulmonary valve due to fusion of the valve cusps. The main PA trunk and PA branches are generally of normal or near normal size. The normal RV is tripartite with an inflow region (tricuspid valve), a body (the trabeculated apical component), and an outflow region (infundibulum). In PA/IVS, the RV tends to be hypoplastic and tricuspid valve size generally parallels RV cavity size. In mild-to-moderate hypoplasia, the apical trabeculated component of the RV is poorly developed or even absent. With more severe degrees of hypoplasia the infundibulum may be absent as well. Occasionally the RV is miniscule. Approximately 25% of patients have mild hypoplasia, 40% have moderate hypoplasia, and 35% have severe hypoplasia. Finally, there is an ASD or patent FO and a PDA.

Physiology

PA/IVS is a single ventricle physiology lesion that may be amenable to a two-ventricle repair but in many instances patients are staged down the single ventricle pathway. PA/IVS is a complex shunt with complete obstruction to outflow. There is a
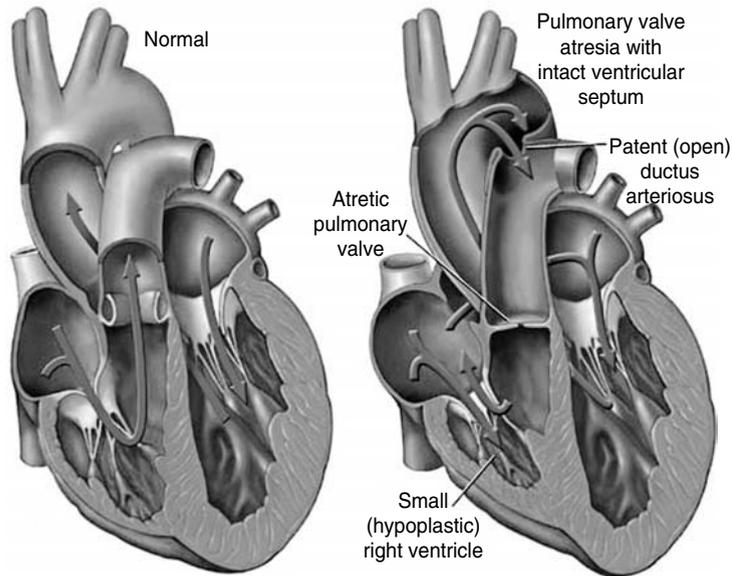
Fig. 6.40 Anatomy of pulmonary atresia with intact ventricular septum (PA/IVS). The right ventricle (RV) is hypoplastic with complete obstruction to outflow due to fusion of the pulmonary valve leaflets. Pulmonary blood flow is supplied by the patent ductus arteriosus (PDA). There is tricuspid regurgitation and right-to-left (R–L) shunting at the atrial level.

communication (ASD or patent FO) and a complete obstruction to RV outflow (PA). RV pressures may be 2–3 times systemic and RA pressure is elevated. RV filling volume in diastole is essentially equal to the volume of blood that is regurgitated back across the tricuspid valve in systole. Consequently, there is an obligatory physiologic R–L shunt at the atrial level, with complete mixing of systemic and pulmonary venous blood in the LA. When the ASD or FO is restrictive, there will be a large right atrial to LAP gradient. This will result in poor decompression of the RA and systemic venous congestion. Pulmonary blood flow is provided by a downstream shunt (PDA).

Persistently high RV pressures in the prenatal and neonatal period may result in enlargement of the Thesbesian veins leading to the development of anomalous fistulous connections between the RV and the epicardial coronary arteries. Retrograde coronary blood flow through these ventriculocoronary connections predisposes the coronary circulation to development of proximal obstructive lesions from fibrous myointimal hyperplasia. As a result of these changes, myocardium distal to any proximal coronary occlusion will be dependent on a high RV pressure to provide retrograde perfusion via ventriculocoronary connections. This

physiology is described as right-ventricle dependent coronary circulation (RVDCC).

Surgical therapy

Coronary angiography is performed in all patients PA/IVS to assess RV and tricuspid valve function and to assess for the presence of RVDCC. Surgical therapy has two objectives: provision of enough pulmonary blood flow to replace the PDA, and if possible, relief of RV outflow obstruction such that forward flow through the tricuspid valve, RV, and PA is established. Decompression of the RV is contraindicated in the presence of RVDCC. Myocardial ischemia or infarction distal to coronary lesions may occur when perfusion pressure via ventriculocoronary connections is reduced by RV decompression. Fistulous connections between the RV and the epicardial coronary arteries in the absence of proximal coronary obstructive lesions are not a contraindication to RV decompression.

Forward flow through the RV may promote continued growth of the RV. If the RV is large and only pulmonary valvular atresia exists, a pulmonary valvulotomy or a RV outflow transannular patch may be all that is necessary. In some cases, balloon dilation of the pulmonary valve in the cardiac catheterization laboratory is sufficient.

Because decompression of the RA and RV will occur as long as the ASD or FO is open, the ASD or FO cannot be closed unless the RV is capable of providing all of the pulmonary blood flow without failing. If the RV is hypoplastic and the valve is severely atretic, a MBTS in combination with a RV outflow tract transannular patch may be necessary to provide adequate pulmonary blood flow. Because the infundibulum may be very hypertrophied and the infundibular muscle usually is quite fibrotic the incision for the transannular patch is carried well down into the body of the RV. The PDA is almost always ligated at the time of the initial procedure.

Following neonatal intervention one of the following options exist depending on the presence or absence of RVDCC and the size of the RV and tricuspid valve. In all of the repairs described the MBTS, if present is ligated.

- *Fontan procedure (TCPC).* Staging to the fenestrated Fontan via a superior cavopulmonary shunt is reserved for patients with RVDCC or for patients with severely hypoplastic RVs.
- *One-and-a-quarter ventricle repair.* In patients with non-RVDCC and some RV mass this repair which consists of a BDG and an atriopulmonary connection between the roof of the RA and the undersurface of the right PA opposite the BDG anastomosis in conjunction with an RV outflow patch and a fenestrated ASD (R–L "pop-off") or ASD closure can be considered. This repair allows a small amount of SVC and IVC blood to cross the tricuspid valve and be ejected by the RV antegrade into the pulmonary bed.
- *One-and-a-half ventricle repair.* In patients with non-RVDCC and mild to moderate RV hypoplasia this repair, which consists of a BDG in conjunction with an RV outflow patch and a fenestrated ASD (R–L "pop-off") or ASD closure, can be considered. This repair allows IVC blood to cross the tricuspid valve and be ejected by the RV antegrade into the pulmonary bed.
- *Two-ventricle repair.* In patients with non-RVDCC and mild RV hypoplasia this repair, which consists of a RV outflow patch and a fenestrated ASD (R–L "pop-off") or ASD closure, can be considered. This repair allows all or nearly all systemic venous blood

to cross the tricuspid valve and be ejected by the RV antegrade into the pulmonary bed.

In all of these repairs the fenestrated ASD can be closed at a later date in the cardiac catheterization laboratory if there is minimal R–L shunting and RA hypertension is not present following temporary balloon occlusion.

Anesthetic management

Goals
These patients are managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11). Subsequent management for the superior cavopulmonary shunt and Fontan procedure is described in later portions of the section on Management of single ventricle physiology.

These patients have ductal dependant pulmonary blood flow. Patients with PA/IVS are particularly vulnerable to myocardial ischemia because even in the absence of RVDCC the coronary arteries are supplied in part retrograde from the body of the RV. Myocardial depression is poorly tolerated both because it may reduce pulmonary blood flow across a restrictive PDA and because coronary blood flow may be compromised if aortic pressure and RV pressure falls.

Post-CPB management

Most of these patients are managed according to the principles described in the section on Management of single ventricle physiology, post-CPB management (see Table 6.11). Subsequent management for the superior cavopulmonary shunt and Fontan procedure if necessary is described in later portions of the section on Management of single ventricle physiology.

Only those patients with an RV large enough to require only a transannular patch will not exhibit single ventricle physiology. For a given cardiac output and $Q_P:Q_S$ patients with a transannular patch and a MBTS will have less of a volume load on the LV. Following decompression of the RV PA/IVS patients are vulnerable to myocardial ischemia because even in the absence of RVDCC

the coronary arteries are supplied in part retrograde from the body of the RV.

Truncus arteriosus

Anatomy

A single great vessel arising from the base of the heart and giving rise to the pulmonary, coronary, and systemic arteries characterizes truncus arteriosus. There is a single semilunar valve, which is usually abnormal, and invariably a large (non-restrictive) conoventricular septal VSD is present. The truncus straddles this large VSD (Fig. 6.41). Truncus arteriosus is classified based on the origin of the pulmonary arteries. In type 1, a short pulmonary trunk originates from the truncus and gives rise to both pulmonary arteries. In type 2, both pulmonary arteries arise from a common orifice of the truncus, whereas in type 3, the right and left pulmonary arteries arise separately from the lateral aspect of the truncus. The VSD usually is of the infundibular or perimembranous infundibular type. The truncal valve is tricuspid in most patients, but multiple cusps (4–7) are common and
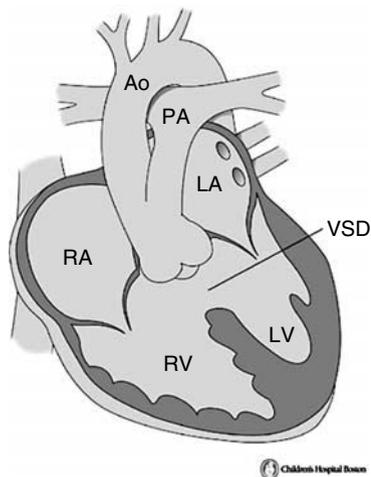
Fig. 6.41 Anatomy of truncus arteriosus. Type 1 truncus arteriosus is illustrated here with a short pulmonary trunk arising from the truncus. There is a large conoventricular septal ventricular septal defect (VSD) with truncal override. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

the valve itself may be regurgitant or stenotic. Extracardiac anomalies are seen in approximately 30% of patients.

Physiology

Truncus arteriosus is a single ventricle physiology lesion amenable to a two-ventricle repair. The large (nonrestrictive) VSD allows equalization of pressures in the RV and LV. As a result, there is bidirectional shunting and complete mixing of systemic and pulmonary venous blood in a functionally common ventricular chamber. This blood is then ejected into the truncal root, which gives rise to the pulmonary, systemic, and coronary circulations. As with all simple shunts, $Q_P:Q_S$ is determined by the ratio of PVR to SVR. However, in truncus arteriosus, the pulmonary and systemic circulations are supplied in parallel from a single vessel, and for a given ventricular output increases in flow to one circulatory system will produce reductions in flow to the other.

As with all single ventricle lesions, a low $Q_P:Q_S$ will reduce arterial saturation, whereas a high $Q_P:Q_S$ will produce ventricular volume overload without a substantial increase in arterial saturation. Shortly after birth the balance of PVR and SVR is such that pulmonary blood flow is high and the patient with truncus arteriosus has symptoms of CHF with mild cyanosis. After cardiac reserve has been exhausted, further decreases in PVR will increase pulmonary blood flow at the expense of systemic and coronary perfusion. This will produce a progressive metabolic acidosis. If truncal valve insufficiency is present, this will obviously impose an additional volume load on the ventricles. Given the high pulmonary blood flow and the transmission of systemic arterial pressures to the pulmonary vasculature present in this lesion development of PVOD is rapid. With development of PVOD there will be a progressive decrease in pulmonary blood flow relative to systemic blood flow and progressive hypoxemia.

Surgical therapy

Because of the risk of early development of PVOD, surgical intervention within the first months of life is undertaken. Definitive repair of truncus arteriosus requires patch closure of the VSD, detachment

of the pulmonary arteries from the truncus, and establishment of right ventricular to PA continuity with a valved homograft. The RV to PA conduit requires placement of the proximal end of the conduit over a ventriculotomy in the RV free wall. The truncal valves must be assessed at the time of surgery. In some instances, valve repair or replacement is necessary to address valvular insufficiency or stenosis. Valvuloplasty is preferred over valve replacement. Valve replacement in a child necessitates subsequent replacements as the child grows. Management of the systemic anticoagulation necessary with a mechanical valve is also difficult in growing children. The RV to PA valved conduit will eventually require replacement as the child grows.

Anesthetic management

Goals
These patients are managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11). This is a nonductal dependant lesion.

Post-CPB management

Goals
1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart-rate-dependent in the post-CPB period.
2 Reduce PVR when necessary through ventilatory interventions.
3 Inotropic support of the left and RV may be necessary for the reasons addressed previously. Dobutamine (5–10 µg/kg/min) or dopamine (5–10 µg/kg/min) is useful in this instance because they provide potent inotropic support without increasing PVR. Milrinone (0.5–1.0 µg/kg/min following a loading dose of 50 µg/kg) should be considered for its inotropic and lusitrophic effects as well as its ability to reduce PVR.

Some degree of RV dysfunction is likely to exist due to the presence of a ventriculotomy and a large VSD patch. This will be particularly problematic in patients with high PVR or early PVOD. Left ventricular volume overload may occur secondary to truncal valve insufficiency.

Interrupted aortic arch

Anatomy
Three types of Interrupted aortic arch (IAA) exist:
- *Type A.* The arch is interrupted distal to the left subclavian artery at the level of the aortic isthmus (similar to very severe coarctation). This type comprises 15% of IAA.
- *Type B.* The arch is interrupted between the left common carotid and left subclavian arteries. The origin of the right subclavian artery is commonly aberrant arising from the descending aorta distal to the interruption. This is the most common manifestation of IAA and comprises 80% of all IAA (Fig. 6.42).
- *Type C.* The arch is interrupted between the innominate and the left common carotid and arteries. This is the least common manifestation of IAA and comprises 5% of all IAA.

In all cases the aorta distal to the interruption is supplied by the DA. There is invariably
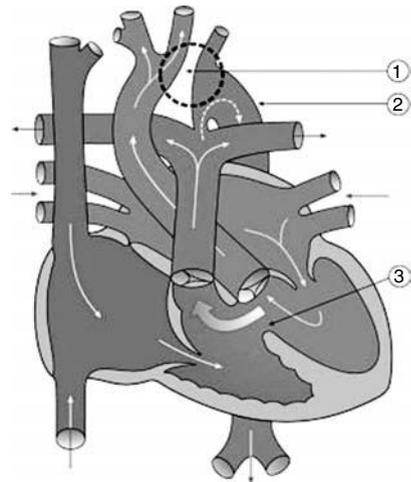
Fig. 6.42 Anatomy of interrupted aortic arch (IAA) with associated ventricular septal defect (VSD). Type B IAA is illustrated here with the interruption between the left carotid and left subclavian arteries (1). There is a large conoventricular septal defect (3) without significant posterior malalignment of the conal septum. The distal aorta (2) and left subclavian artery are supplied by the patent ductus arteriosus (PDA). As a result there will be differential cyanosis with a lower Sao_2 in the lower body and left arm than in the right arm and cerebral circulation.

a large conoventricular septal defect with posterior malalignment of the conal septum. The posterior malalignment can produce subaortic LV outflow tract obstruction. The aortic valve is commonly bicuspid with commissural fusion.

Physiology

IAA is single ventricle physiology lesion with ductal dependent systemic blood flow amenable to a two-ventricle repair. IAA is a complex shunt with complete obstruction to aortic outflow at the level of the interruption. A simple downstream shunt (PDA) provides aortic flow distal to the interruption. Flow to the aorta proximal to the obstruction is supplied by the LV. In addition there is a simple shunt (VSD) and there may be fixed obstruction to LV outflow (subaortic stenosis). There is a physiologic L–R shunt at the level of the VSD. In the presence of significant LVOTO there may be compromise of proximal aortic perfusion due to a large L–R shunt. There is predominantly a physiologic R–L shunt at the level of the PDA. As a result there will be differential cyanosis with a lower Sao_2 in the lower body and arch vessels distal to the interruption than in the arch vessels proximal to the interruption.

The shunt at the level of the PDA is a dependent shunt with net systemic and pulmonary blood flow determined by the ratio of systemic to PVR. Low PVR relative to SVR will allow run-off of blood into the pulmonary circuit (increased physiologic L–R shunting at the PDA) compromising distal aortic perfusion. Closure of the PDA in infants with IAA terminates distal aortic flow severely compromising splanchnic perfusion and usually results in immediate cardiovascular collapse. PGE_1 therapy is lifesaving for these patients.

Surgical therapy

Definitive surgical therapy for IAA involves primary re-anastomosis of the proximal and distal aorta, PDA ligation, VSD closure, and resection of subaortic stenosis if present. Arterial cannulation for CPB requires the use of two arterial cannula. Cannulation is obtained directly in the ascending aorta and in the descending aorta via the PDA. In order to reduce tension on the arch anastomosis it may be necessary to divide and ligate the left subclavian

artery during repair of type B IAA. In addition, it may be necessary to divide and ligate an aberrant right subclavian artery if present to reduce tension on the descending aortic portion of the anastomosis.

Anesthetic management

Goals

These patients are managed according to the principles described in the section on Management of single ventricle physiology, pre-initial repair (see Table 6.11). These patients have ductal dependant distal aortic blood flow. The diastolic blood pressure will be lower and the pulse pressure wider in the distal as compared to proximal aorta. Arterial monitoring sites must be chosen carefully. Right radial artery pressure will reflect distal aortic pressure in the presence of an aberrant right subclavian artery. If the left subclavian artery is divided and ligated during repair, a left radial arterial line will be of little use post-repair.

Post-CPB management

Goals

1 Maintain heart rate (preferably sinus rhythm) at an age-appropriate rate. Cardiac output is likely to be more heart-rate-dependent in the post-CPB period.

2 Reduce PVR when necessary through ventilatory interventions.

3 Inotropic support of the left and RV may be necessary for the reasons addressed previously. Dobutamine (5–10 μg/kg/min) or dopamine (5–10 μg/kg/min) is useful in this instance because they provide potent inotropic support without increasing PVR. Milrinone (0.5–1.0 μg/kg/min should be considered for its lusitrophic effects and it effect on PVR.

Determining whether there is a residual arch obstruction is a priority following termination of CPB. This requires accurate simultaneous measurements of both upper and lower aortic blood pressure obtained with either percutaneously or surgically placed catheters. A significant gradient may necessitate surgical revision. Bleeding from the arch suture lines may be significant. Residual LVOTO may produce LV contractility/afterload mismatch.

Elevated PVR due to LA hypertension and reactive pulmonary vasoreactivity due to high Q_P:Q_S preoperatively may result in RV contractility/afterload mismatch as well. In addition, the long CPB and deep hypothermic circulatory arrest (DHCA) times necessary to complete this procedure may further compromise LV and RV function and produce myocardial edema.

Suggested reading

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Anesthesia for Heart, Heart-Lung, and Lung Transplantation

Heart transplantation

Cardiac transplantation is now common among patients with end-stage cardiac dysfunction that is unresponsive to maximal medical therapy and for which no other surgical options exist. Most adult patients are New York Heart Association (NYHA) functional class IV (symptoms at rest). These patients have an expected 1-year survival of approximately 50–60% with optimal medical therapy. A subgroup of ambulatory NYHA functional class III patients (symptoms with limited exertion) with an impairment of exercise tolerance ($V_{O2max} < 14$ mL/kg/min) predictive of reduced 1-year survival also can be considered for transplantation.

For infants and children, the natural history of end-stage cardiac dysfunction is not as well delineated in large part because of the heterogeneity of the various congenital lesions. In addition, end-stage cardiac dysfunction is more difficult to define. Growth failure secondary to severe cardiac dysfunction is useful in identifying end-stage disease. Progressive pulmonary hypertension, which could preclude transplantation at a later date, also is considered an important indication for transplantation.

Ninety percent of adult patients presenting for cardiac transplantation have a dilated cardiomyopathy (DCM) secondary to ischemic heart disease. Less commonly, patients with end-stage valvular heart disease or with intractable, life-threatening arrhythmias not amenable to medical therapy or insertion of an implanted cardioverter defibrillator (ICD) are transplanted. Cardiac transplantation also has been used for unresectable cardiac tumors, sarcoidosis, amyloidosis, active myocarditis, hypertrophic cardiomyopathies, and refractory angina not amenable to angioplasty or surgical revascularization. Heart transplantation for patients with amyloidosis and sarcoidosis is tempered by evidence that systemic progression of these diseases may limit the long-term effectiveness of heart transplantation. In patients with acute myocarditis there is evidence of higher mortality and rejection rates.

DCM and complex congenital heart disease represent the two major indications for heart transplantation for pediatric patients. In patients younger than 1 year of age, 65% of transplants are for congenital heart disease, primarily hypoplastic left heart syndrome (HLHS). In patients between 1 and 10 years of age, the indications for heart transplantation are divided equally between congenital heart disease and DCM. Most children requiring transplantation for congenital lesions in this age group have had at least one previous cardiac surgical procedure. In patients between 11 and 17 years of age, the primary indication (60%) for heart transplantation is DCM.

Contraindications to heart transplantation are outlined in Table 7.1. Severe osteoporosis, active peptic ulcer, diverticular disease, active infection, and morbid obesity all are conditions that are

Table 7.1 Recipient selection for heart and heart-lung transplantation.

Absolute contraindications

1 History of emotional instability, medical noncompliance, or active substance abuse

2 Fixed pulmonary hypertension (for cardiac transplantation, not for lung or heart-lung transplantation)

3 Significant cerebral vascular disease

4 Active malignancy or life-limiting co-existent disease

Relative contraindications

  1 Physiological age older than 60 years

  2 Significant peripheral vascular disease

  3 Active peptic ulcer or diverticular disease

  4 Severe bronchitis or chronic obstructive pulmonary disease (for cardiac transplantation, not for lung or heart-lung transplantation)

  5 Disease likely to recur in allograft (cardiac amyloidosis or sarcoidosis)

  6 Irreversible hepatic or renal disease (may be considered for combined cardiac and renal or hepatic transplantation)

  7 Immunological sensitization to donor antigens

  8 Severe osteoporosis

  9 Morbid obesity

10 Active infection

11 Diabetes mellitus with end-organ dysfunction

likely to be worsened by the necessity of a lifelong immunosuppressive regiment including steroids. Corticosteroids also complicate the glucose management in diabetes. Nonetheless, carefully selected patients with diabetes without end-organ dysfunction have been shown to have 2- to 4-year survival similar to nondiabetics. Chronic lung disease identified as a forced expiratory volume (FEV) < 50% predicted, a forced expiratory volume in 1 second (FEV$_1$) < 1 L, and a forced expiratory volume in 1 second to forced vital capacity (FEV$_1$:FVC) ratio <1 is believed to predispose postoperative respiratory failure, reduced survival from lung disease alone, and an increased risk of infection on immunosuppression. Survival is favorable for elderly patients, but careful selection is necessary, particularly for patients older than 65 years of age, because they are at increased risk for infectious and steroid complications.

Pathophysiology and adaptation of DCM

The etiologies of DCM can be summarized as follows:

● *Idiopathic.* Idiopathic cardiomyopathy is an irreversible form of DCM for which no clear etiological factors have been identified. Familial and genetic factors, viral and other cyotoxic insults, immune abnormalities, and metabolic, energetic, and contraction abnormalities all have been implicated in the pathogenesis of idiopathic DCM. It is likely that several factors interact to cause disease in susceptible patients.

● *Secondary.* A variety of etiological factors, both acquired and hereditary cause or at least predispose to development of a DCM. The majority of secondary DCMs are irreversible and are due to ischemic heart disease, hypertension, valvular heart disease, or congenital heart disease. Some secondary DCMs are potentially reversible. Toxins (including alcohol and cocaine), pregnancy, infectious agents (including cytomegalovirus and toxoplasmosis), and metabolic abnormalities (including thiamine deficiency and hypo- and hyperthyroidism) are all potentially reversible forms of secondary DCM.

Regardless of the initiating cause, the alterations in ventricular function in DCM are remarkably consistent (Fig. 7.1). Biventricular dysfunction is common in idiopathic and secondary DCM. In ischemic cardiomyopathy, dysfunction may be limited to the left ventricle (LV). Loss of myocardial tissue, as occurs with infarction or from direct myocardial damage, results in overload and subsequent hypertrophy of the remaining active myocardium. For the postinfarction patient, this process is known as ventricular remodeling. Hypertrophy of active myocardium serves to reduce wall stress and energy consumption. However, the process of hypertrophy results in changes that adversely affect myocardial energy balance and ultimately produces progressive myocardial dysfunction. Increases in capillary density do not keep pace with replication of sarcomeres. The distance between capillaries increases resulting in poor substrate delivery to hypertrophied myocardium. In addition, the process of hypertrophy increases
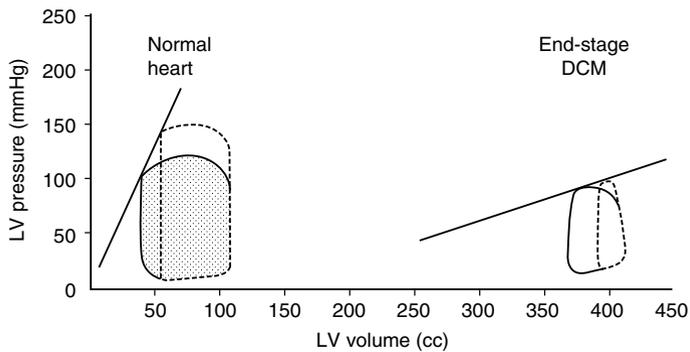
Fig. 7.1 Pressure–volume (PV) loops from a normal heart and a dilated cardiomyopathic (DCM) heart. The DCM heart is dilated, has depressed systolic function, has reduced stroke volume at rest, and is prone to afterload mismatch. Stroke volume at rest for each heart is represented by the solid PV loop. Stroke volume after an increase in afterload with preload and contractility held constant is represented by the dotted PV loop. Note the marked decrease in stroke volume in the DCM as compared with the normal heart with comparable increases in afterload.

the cellular ratio of myofibrils to mitochondria, creating the potential for oxygen imbalance at the cellular level. Eventually, myocardial necrosis results in replacement of myocardium with connective tissue. This produces progressive impairment of contractility, which in turn, stimulates further hypertrophy and progression of myocardial necrosis. Ventricular dilatation occurs as the result of this progressive replacement of myocardium with connective tissue. Eccentric hypertrophy in the surviving myocardium further accelerates the development of ventricular dilatation.

Metabolic down-regulation and uncoupling of cardiac β-receptors is a common feature in DCM. There is also depletion of myocardial norepinephrine (NE) stores. As a result, NE secretion is enhanced in patients with low-output cardiac failure with the degree of elevation paralleling the severity of the failure. Serum NE levels may be two-to-three times normal due to enhanced release and reduced reuptake of NE by adrenergic terminals. The consequence of prolonged elevation of serum NE is gradual down-regulation (reduction in receptor density) of cardiac β_1-receptors and partial uncoupling of cardiac β_1-receptors from adenylate cyclase. Interestingly, there is a greater decrease in the density of β_1-adrenergic receptors in patients with idiopathic cardiomyopathy as compared with ischemic cardiomyopathy. This may be due to long-term adrenergic over-stimulation or anti-β-receptor antibodies in idiopathic cardiomyopathy. Uncoupling of β_1-adrenoreceptors from the effector enzyme adenylate cyclase involves phosphorylation

of the receptors by β-adrenergic receptor kinase. Progressive cardiac dysfunction also produces an increase in the ratio of the inhibitory guanine nucleotide regulatory protein (G_i) to the stimulatory guanine nucleotide regulatory protein (G_S). G_i inhibits and G_S stimulates adenylate cyclase. Uncoupling of β_1-adrenoreceptors and an increased ratio of G_i:G_S both result in reduced levels of cyclic adenosine monophosphate (cAMP) and reduced movement of calcium into myocytes. The consequence of down regulation of β_1-receptors, uncoupling of β_1-receptors, and an increased G_i:G_S ratio is an impaired ability of DCM hearts to produce cAMP. Therefore, the contractile response of the DCM heart to β-adrenergic receptor agonists (epinephrine, dopamine, dobutamine, isoproterenol, and NE) and phosphodiesterase inhibitors (amrinone, milrinone) is markedly impaired. The contractile response to raising intracellular calcium and to cardiac glycosides (digoxin) is retained. In addition, although the depletion of myocardial NE stores does not affect the intrinsic contractile function of the myocardium, it does result in an impaired contractile response to indirect-acting β-adrenergic agonists such as ephedrine.

There is persistent inappropriate activation of the renin-angiotensin-aldosterone system despite absence of salt deprivation and intravascular volume depletion. This induces expansion of intravascular and extravascular volume and promotes fibrotic changes in the heart and kidneys. Counterbalancing this system is the atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP)

system. ANP and BNP are released from secretory granules in the atria and ventricles respectively in response to cardiac chamber distention. Both peptides increase salt and water excretion, suppress the renin-angiotensin-aldosterone system, and induce arterial and venous vasodilation. In compensated heart failure release of ANP and BNP is sufficient to counteract the effects of the renin–angiotensin–aldosterone release induced by mild to moderate reductions in renal perfusion. In decompensated heart failure ANP and BNP release is insufficient to counteract the effects of the renin–angiotensin–aldosterone release induced by moderate to severe reductions in renal perfusion. Elevated plasma levels of BNP are diagnostic for heart failure and the extent of elevation is a predictor of survival.

Therapy for patients with DCM is directed toward treatment of neurohormonal abnormalities and inhibiting or reversing remodeling. Diuretics in combination with angiotensin-converting enzyme (ACE) inhibitors (captopril, enalapril) and beta-blockers (carvedilol, metoprolol) are first-line therapy. Beta-blockers and ACE inhibitors alone and in combination improve symptoms and reduce mortality. Aldosterone inhibiting drugs (spirolactone, eplerenone) may be useful in patients with aldosterone escape in whom ACE inhibition only partially suppresses aldosterone production. Angiotensin-receptor blockers (ARB) such as lorsartan, candesartan, and valsartan are generally reserved for patients who do not tolerate ACE inhibitors. Nesiritide, a BNP analog available in intravenous form, shows some promise in improving symptoms and reducing hospital stay. Short-term use however is associated with an increased risk of renal dysfunction and post-discharge mortality.

Chronic therapy for DCM is problematic. Digoxin has been shown to improve ejection fraction (EF), exercise capacity, and symptoms of heart failure in DCM. It does not substantially improve survival however. Acute, intermittent, and long-term administration of intravenous inotropic agents has not proved as promising. Dobutamine, dopamine and milrinone administration have not been shown to consistently improve exercise capacity or symptoms. In addition, short-term administration of these agents is associated with increased post-discharge mortality particularly in the subset of patients with ischemic heart disease. Administration of these agents is recommended only in the setting of acute hemodynamic compromise in DCM patients unresponsive to conventional therapy.

An alternative to these cAMP mediated inotropic agents is calcium-sensitizing agents. Levosimendan is the only such agent currently clinically available. It increases inotropy in a cAMP-independent fashion by inducing a conformational change in troponin C that increases the sensitivity of troponin C to intracellular ionized calcium. This results in a concentration–response relationship between intracellular calcium and inotropy at lower intracellular ionized calcium levels than seen with cAMP-mediated agents. This agent shows some promise in the chronic treatment of patients with DCM.

Ventricular diastolic function and the atrial transport mechanism

Diastolic dysfunction in the form of impaired ventricular relaxation and reduced ventricular compliance is seen in DCM. There is rapid equilibration of left atrial and ventricular end-diastolic pressures producing a restrictive mitral inflow pattern with abrupt premature closure of the mitral valve. Progressive ventricular dilatation produces atrial enlargement due to the longstanding increase in atrial afterload produced by an elevated ventricular end-diastolic pressure. In many instances, the atria will be dilated, hypokinetic, and filled with spontaneous contrast on echocardiographic examination. In these patients, the contribution of atrial systole to ventricular filling will be minimal. As a consequence of these changes, patients with DCM require high mean atrial pressures to ensure adequate ventricular filling.

Myocardial oxygen balance

Oxygen balance is impaired in patients with an ischemic cardiomyopathy. Myocardial blood flow abnormalities also are present in patients with DCM despite the presence of angiography normal coronary arteries. It has been proposed that functional small-vessel abnormalities due to either

increased vascular tone or endothelial abnormalities account for decreased global baseline myocardial blood flow and impaired coronary reserve in DCM. Regional perfusion defects also are seen in 45% of DCM hearts without demonstrable coronary lesions. Furthermore, myocardial ischemia has been detected in patients with DCM who are subjected to pacing-induced tachycardia and to coronary vasodilation from dipyridamole infusion.

Left ventricular systolic function

When a patient presents for transplantation, an EF of 10–20% is likely. Compensation for the progressive reduction in contractility occurs by use of preload reserve. As contractility decreases, end-systolic volume (ESV) increases for a given afterload. Increases in preload initially can be used to normalize stroke volume (SV) under these conditions. Preload reserve is exhausted when the sarcomeres are stretched to their maximum diastolic length. When this occurs, there will be no further augmentation of the velocity of shortening by increasing diastolic fiber length, and the ventricle behaves as if preload were fixed. For a given level of contractility, after preload reserve has been exhausted, additional increases in afterload will be accompanied by parallel decreases in SV. This is defined as a state of afterload mismatch. Patients with end-stage DCM will have exhausted preload reserve and will exhibit afterload mismatch (see Fig. 7.1). In addition, patients with DCM have a fixed SV due to exhaustion of preload reserve and an inability to decrease ESV by increasing contractility.

The result of this compensation process is progressive ventricular dilatation. Dilatation of the ventricle has several important consequences. Ventricular dilatation can produce mitral insufficiency secondary to dilation and deformation of the valve annulus. This type of functional mitral insufficiency is common in DCM. Dilatation of the ventricle also results in elevated wall stress (wall stress $= [P \times r]/2h$) at the conclusion of isovolumic contraction for a given left-ventricular end-systolic pressure (LVESP). Because wall stress is synonymous with afterload, ventricular dilatation further compromises systolic function by producing increased afterload at a given systolic blood pressure.

Right ventricular function and the pulmonary vasculature

In instances in which DCM produces biventricular dysfunction, the right ventricle (RV) will exhibit the same alterations in systolic function, afterload sensitivity, and diastolic dysfunction described for the LV. The prolonged elevations of left atrial pressure (LAP) seen in progressive DCM have profound effects on the pulmonary vasculature and right ventricular function. Early in the disease, elevated LAP is transmitted to the pulmonary venous system and there is reversible passive elevation of the pulmonary artery pressures while pulmonary vascular resistance (PVR) remains normal (see Fig. 5.13). Right ventricular function remains unchanged. As the disease progresses, reactive changes occur in the pulmonary vasculature. Prolonged perivascular edema results in arterial intimal fibroelastosis and nonreversible elevations in PVR due to obliterative changes in the distal pulmonary vasculature known as pulmonary vascular occlusive disease (PVOD). Progression of this process presents a large increase in right ventricular afterload similar to that seen in severe mitral stenosis (see Fig. 5.13). Similar changes occur in infants and children with congenital heart disease.

The RV is poorly adapted to generate pressures that approach systemic. As a result, afterload mismatch occurs, the RV fails, and RV output falls. Peripheral edema and hepatic congestion ensue. RV failure and dilation may lead to functional tricuspid regurgitation and worsening symptoms of right heart failure. In the steady state, RV output and LV output must be equal. Therefore, LV output is also limited by RV failure. In cases of severe RV dysfunction or in the presence of systemic pulmonary artery pressures, there is leftward shift of the intraventricular septum further compromising LV filling and function.

When the postischemic donor RV is acutely exposed to the elevated PVR of the recipient, severe right heart failure develops secondary to afterload mismatch. Data from the Registry of the International Society for Heart and Lung Transplantation has consistently demonstrated a continuous

relationship between preoperative PVR and postoperative mortality. In addition pre-transplant PVR in excess of 5 Wood units and a transpulmonary gradient in excess of 15 mmHg both have been clearly associated with increased postoperative mortality in adults. As a result, increased irreversible PVR elevations remains an absolute contraindication to heart transplantation (see Table 7.1).

Most centers perform provocative testing in their patients with elevated PVR using oxygen, nitric oxide (NO), sodium nitroprusside, prostaglandin E_1 or a combination of these drugs in patients with a PVR > 4 Wood units or a pulmonary vascular resistance index (PVRI) > 6 Wood units/m^2. It has been demonstrated that adults in whom PVR can be reduced using sodium nitroprusside or prostaglandin E_1 to <2.5 Wood units while maintaining a systolic blood pressure >85 mmHg have a postoperative mortality similar to patients with a resting PVR < 2.5 Wood units. Mortality in patients with a pre-transplant PVR > 5 Wood units and TPG > 15 mmHg who demonstrate a reversible component to their pulmonary hypertension do not have increased mortality. Typically a PVR < 5 Wood units after drug therapy presents an acceptable risk. Because aggressive postoperative use of inodilators and selective inhaled pulmonary vasodilators (NO, prostacyclins) is now routine and because PVR naturally tends to drop in the period following transplantation outcome in patients with elevated PVR has improved.

In children, a PVRI in excess of 6–7 Wood units/m^2 and a transpulmonary gradient >15 mmHg have been associated with increased postoperative mortality. Most centers will consider transplantation if a PVRI < 4–6 Wood units/m^2 and a transpulmonary gradient <15 mmHg can be obtained with some combination of inotropes, oxygen, NO, sodium nitroprusside, or prostaglandin E_1 prior to transplantation.

Effect of heart-rate alterations on hemodynamics

Patients with DCM have a fixed SV and, as a result, are dependent on maintenance of their heart rate to maintain cardiac output. With exhausted preload reserve, reductions in heart rate will not be accompanied by increases in SV as seen in the normal heart. Therefore, reductions in heart rate will be accompanied by cardiac output decreases. Heart-rate increases will reduce diastolic filling time and will reduce end-diastolic volume (EDV) and SV. Heart rate increases generally will result in no change in cardiac output because the reduction in SV will be offset by the increase in heart rate. Elevations in right and LAPs by volume infusion to compensate for reduced diastolic filling time are not practical because they will increase systemic and pulmonary venous congestion. For patients with an ischemic DCM, heart-rate increases may exacerbate myocardial ischemia.

Effect of afterload alterations on hemodynamics

Reduced contractility is represented by a linear left ventricular pressure–volume relationship that has a less positive slope and is shifted rightward. As the result of impaired contractile function, patients with DCM have enhanced sensitivity to afterload (see Fig. 7.1). Small increases in afterload result in comparatively large increases in ESV. For a given EDV; this results in a large reduction in SV. Conversely, afterload reduction with maintenance of EDV will produce concomitant increases in SV. This partly explains the unequivocal success of vasodilator therapy such as ACE inhibitors in improving NYHA functional class and reducing mortality in patients with end-stage DCM. Aggressive perioperative afterload reduction is difficult considering the low systolic blood pressure of most patients with DCM.

The donor

The following guidelines are used to select donors after the diagnosis of irreversible brain death has been made. Echocardiographic assessment of donor ventricular and valvular function is routine. The final decision as whether to accept a donor heart is made by the harvesting surgeon following visual inspection of the heart and overall assessment of donor suitability and hemodynamic stability.

• Age less than 55 years. Most centers have become more lenient given the shortage of suitable donors. For a patient who has had a long waiting list interval

and who has been difficult to cross-match the risk of taking a heart from an older donor who is a good cross-match may be preferable to the risk of dying on the waiting list.

- Absence of significant cardiac disease or trauma. Severe myocardial contusion usually is identified by a history of blunt chest trauma, CPK-MB and troponin elevations, and echocardiographic evidence of severe ventricular dysfunction. Patients who have suffered cardiac arrest are not necessarily excluded from consideration but require subsequent evaluation of function both clinically and echocardiographically. Generally, a desirable donor heart is maintained with less than 10 µg/kg/min of dopamine.
- Low probability of coronary artery disease. Coronary angiography is not commonly employed in evaluation of younger donors. Many centers evaluate male donors older than 45 years of age and female donors older than 55 years of age with coronary angiograms.
- No active infection or malignancy with the possibility of metastases.
- Negative serologies for human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) or hepatitis B and C. Donors are also tested for toxoplasmosis and cytomegalovirus (CMV).
- ABO compatibility and human lymphocyte antigen (HLA) screen. The donor and recipient must be ABO blood type compatible. HLA typing for cardiac transplantation is not routine. The recipient's blood is tested against a standard panel of blood cells containing a diverse human lymphocyte sample. This screen is called the panel reactive antibody (PRA) screen. If the PRA has 5–15% reactivity, most centers will proceed with transplantation based on ABO compatibility. If the PRA is greater than 15%, then a lymphocyte cross-match between donor and recipient blood can be performed. This is a time-consuming process, as donor blood must be transported to the transplant center. Pre- and post-transplant therapy with intravenous IgG or plasmapheresis may be indicated. Recently, some success with ABO incompatible transplants has been achieved in infants due to the immaturity of infant ABO isohemagglutinins. Table 7.2 outlines the transfusion strategy that must accompany ABO incompatible transplantation to prevent immunization.

- Recipient donor size match. For adult patients, the donor's body weight should be within 60–150% of the recipient's weight. For infants and children the donor's weight should be between 80 and 160% of the recipient's body weight. Hearts transplanted into infants and children demonstrate normal cardiac chamber dimensional growth. Most centers prefer donors at the upper limits of size for their adult and pediatric patients with pulmonary hypertension, although data to support this practice are lacking.

Aggressive hormone replacement therapy (HRT) is currently utilized by many centers in the subset of heart donors with depressed LV function (left ventricular ejection fraction (LVEF) < 45%) with or without hypotension. HRT can be summarized as follows:

- Triiodothyronine (T$_3$) supplementation: 4.0 µg bolus followed by an infusion of 3.0 µg/h.

Table 7.2 Transfusion strategy for ABO incompatable heart transplantation.

ABO of heart recipient	ABO of transfused blood products			
	ABO of donor heart	Plasma	Red cells	Platelets
O	AB	AB	O	AB
O	B	AB or B	O	AB or B
O	A	AB or A	O	AB or A
B	AB	AB	O or B	AB
B	A	AB	O or B	AB
A	AB	AB	O or A	AB
A	B	AB	O or A	AB

● Vasopressin supplementation: 1.0 unit bolus followed by 0.5–4.0 units/h infusion to treat diabetes insipidus and normalize systemic vascular resistance (SVR) (800–1200 dynes/s/cm^5).

● Steroid supplementation: methylprednisolone 15 mg/kg bolus.

● Insulin supplementation: 1.0 units/h minimum, increase to keep blood sugar 120–180 mg/dL.

Anesthetic management of the recipient

Goals

1 Avoid increases in afterload; afterload reduction can be attempted with caution, but EDV must be maintained.

2 Maintain preload.

3 Maintain or enhance contractility.

4 Maintain heart rate.

5 Avoid hypercarbia, hypoxemia, and acidosis that tend to cause pulmonary hypertension and may result in acute RV decompensation.

Preoperative evaluation

Cardiac transplant patients typical1y undergo extensive medical evaluation. A summary of this evaluation is readily available to the anesthesiologist through the transplant coordinator. Several unique management problems are common in patients DCM. Use of an antifibrinolytic should be considered for patients at risk for postoperative bleeding.

Ventricular arrhythmias

More than 70% of DCM patients have asymptomatic, nonsustained ventricular tachycardia seen on ambulatory monitoring. Antiarrhythmic therapy is problematic for these patients considering the negative inotropic and arrhythmogenic effects of many of the agents, the altered drug pharmacokinetics in heart failure, and the low efficacy of these agents for patients with severe LV dysfunction. In addition, although therapy can reduce ventricular arrhythmias and improve exercise tolerance and ventricular function, reduction in the incidence of sudden death is unproven. An ICD may be necessary for patients with symptomatic ventricular arrhythmias if medical therapy is not effective or cannot be tolerated.

Thromboembolic phenomena

Patients with an EF less than 30% and patients with atrial fibrillation are particularly at risk for the formation of atrial and ventricular mural thrombi and subsequent systemic or pulmonary embolization. In addition, patients with left ventricular aneurysms as the result of extensive prior infarction are also at higher risk for mural thrombus formation. Long-term oral anticoagulation, primarily with coumadin, is common for patients with DCM. This will complicate the management of hemostasis after termination of cardiopulmonary bypass (CPB).

Preoperative mechanical ventricular support and the total artificial heart

At present, the limiting factor in the number of patients who can be offered a heart transplant is the availability of donor hearts. In the United States, it is estimated that although 40 000 patients per year could benefit from a heart transplant, only approximately 2200 heart transplants are performed per year. Furthermore, 20% of suitable transplant candidates die before a donor heart can be found. As a result, mechanical assist devices and the total artificial heart are used as a bridge to cardiac transplantation until suitable donor hearts arc found.

Previous cardiac surgical procedures

All patients who have undergone previous cardiac surgical procedures arc likely to have prolonged dissection times and are at risk for bleeding. Adequate intravenous access is a necessity. All blood products must be CMV compatible and transfused through leukocyte filters. Many patients with ischemic DCM will have undergone prior coronary artery bypass surgery. Nicking or cutting of the existing extracardiac conduits (internal mammary arteries and reverse saphenous veins) can severely compromise myocardial perfusion. Likewise, surgical manipulation of these conduits may result in embolization of atherosclerotic plaques into the distal coronary vascular bed with subsequent transmural myocardial ischemia. A determination of how much myocardium is supplied by the conduits

that are patent can be made from the most recent catheterization report.

Many children with congenital heart disease will have undergone prior procedures. Physical examination should include an evaluation of the limitations to vascular access and monitoring sites imposed by previous surgery and catheterizations. A child who has undergone a palliative shunt procedure may have a diminished pulse or an unobtainable blood pressure in the arm in which the subclavian artery has been incorporated into the shunt. Children who have undergone multiple palliative procedures may have poor peripheral venous access and previous surgical cut-down sites may exist. Children having multiple cardiac catheterizations may have absent or compromised femoral arterial and venous access. Such findings have obvious implications regarding arterial and venous catheter placement, sphyingomonometric blood pressure monitoring, the use of pulse oximetry, and the mode of induction.

Premedication

Most patients will have been called into the hospital on short notice and many will have eaten solid food in the previous 6–8 hours. In addition, patients will have taken their initial doses of oral immunosuppressive drugs, usually cyclosporine and azathioprine or mycophenolate moftil. Cyclosporine usually is administered with 10–20 mL of liquid. To reduce the risk of aspiration in adults and older children, a nonparticulate antacid such as bicitra (30 mL) should be given in addition to intravenous metaclopromide 10 mg and an H_2-receptor blocker such as ranitidine 50 mg. For infants and smaller children, a period of 2–3 hours of NPO (nothing by mouth) status is sufficient and usually transpires before induction. Premedication with midazolam 0.03–0.05 mg/kg in divided doses works well to reduce anxiety. In older children with previous multiple opioid and benzodiazepine exposures, intravenous ketamine in doses of 0.5–1.0 mg/kg may be necessary as well. In children without intravenous access, oral premedication as will probably be necessary. Supplemental oxygen should be administered, because hypoxemia will exacerbate existing pulmonary hypertension.

Preinduction

Some transplant patients will be receiving intravenous inotropic and vasodilator therapy when they arrive for surgery. These agents should be continued via a reliable intravenous route. Sterility is of the utmost importance because the patients will be immunosuppressed. All patients should have two large-bore peripheral intravenous lines. Electrocardiogram (ECG) monitoring should allow assessment of V_5, I, II, III, aV_R, aV_L, and aV_F. Normally two leads (II and V_5) are monitored simultaneously intraoperatively. A radial artery catheter is placed with local anesthesia before induction of anesthesia. It is placed after induction in infants and children. Patient size or the presence of complex intracardiac anatomy generally precludes placement of a pulmonary artery catheter in infants and children. Pulmonary artery pressures are monitored post-CPB with a surgically placed transthoracic PA catheter. Some centers do not place a pulmonary artery catheter in adult patients for heart transplantation. The advantages of a pulmonary artery catheter are discussed in Chapter 3. The disadvantages as they apply to cardiac transplant patients are:

• Technical difficulty in advancing the catheter in patients with a dilated RV and low cardiac output.

• An increased risk of atrial and ventricular ectopy leading to hemodynamic compromise.

• An increased risk of infection.

• The catheter must be withdrawn into the sterile sheath during excision of the recipient's heart.

• The catheter must be re-advanced across new suture lines into the donor heart as CPB is terminated.

Nonetheless, central venous access is necessary for pressure monitoring and drug infusion in both pediatric and adult patients. Some centers prefer that the right internal jugular vein not be used perioperatively because it is the preferred route to obtain the endomyocardial biopsies used to monitor rejection postoperatively. Placement of a central large-bore venous sheath for use as a reliable site of rapid fluid administration is warranted if peripheral access is poor. Multiplane transesophageal echocardiography (TEE) is utilized to manage pediatric and adult patients pre- and

post-CPB. After transplantation TEE is used to assess left and right ventricular function, measure pulmonary artery pressures (using a tricuspid regurgitation jet), and guide management of pulmonary artery hypertension and RV dysfunction if necessary.

Induction and maintenance

The choice of specific induction agents is less important than the realization that patients with DCM have limited contractile reserve; dependence on preload, and limited ability to respond to acute increases or decreases in afterload. In addition, the circulation time will be slow given the low cardiac output state. These patients require an induction that will blunt the hemodynamic response to laryngoscopy and tracheal intubation without undue myocardial depression, vasodilation, and hypotension. Careful titration of etomidate (0.1–0.3 mg/kg) in combination with 5–10 µg/kg of fentanyl or 1–2 µg/kg of sufentanil is useful for induction. A full 0.3 mg/kg dose of etomidate is often not necessary to induce hypnosis and loss of consciousness in these patients. This drug combination has minimal direct effect on heart rate, myocardial contractility, peripheral vascular resistance, or venous capacitance. An overall diminution in central sympathetic tone will also contribute to circulatory depression. Thiopental and propofol are less well tolerated. A nondepolarizing muscle relaxant in a dose $2 \times ED_{95}$ such as vecuronium or pancuronium 0.02 mg/kg or cisatracurium 0.04 mg/kg is used to assure prompt control of the airway. Pancuronium is generally reserved for those patients in who a low baseline heart rate. In infants and children the vagolytic and sympathometic effects of pancuronium can be used to counteract the vagotonic effects of fentanyl or sufentanil. Alternatively, rocuronium (1.0 mg/kg) or succinylcholine (1–2 mg/kg) can be used to perform a modified rapid sequence induction (cricoid pressure during positive pressure ventilation) in the patient with questionable NPO status.

Anesthesia can be maintained with additional doses of opioid in conjunction with a benzodiazepine (usually midazolam in increments of 0.01–0.03 mg/kg) or a low inhaled concentration of isoflurane or sevoflurane. Nitrous oxide (N_2O) is not a good choice as an adjuvant agent; it has a weak myocardial depressant effect that normally is counteracted by the sympathetic outflow it produces. In patients with DCM where elevated catecholamine levels, down-regulated β-receptors, and reduced myocardial NE stores are present, the myocardial depressant effects will predominate.

In the instance of a child without intravenous access a careful inhalation induction with 100% oxygen and sevoflurane following oral medication (ketamine and midazolam) can be considered. Once intravenous access is obtained anesthesia can be maintained as described above. An alternative for induction and maintenance in infants and children with intravenous access is a high-dose narcotic technique (50–75 µg/kg of fentanyl or 5.0–7.5 µg/kg of sufentanil) in conjunction with a benzodiazepine (usually midazolam) or a low inhaled concentration of isoflurane or sevoflurane and pancuronium. Caution must be used when benzodiazepines are used in conjunction with synthetic opioids, as they are synergistic in their effects on venous capacitance and SVR. This technique is a good choice in infants and children as postoperative intubation ventilation for at least 24 hours is usually necessary.

Regardless of the choice of induction and maintenance agent, episodes of hemodynamic compromise must be treated promptly. Bradycardia associated with hemodynamic compromise can be effectively treated with a small dose of pancuronium (0.015–0.05 mg/kg) if vecuronium or cisatracurium has been used. Atropine should be used cautiously. Atropine administration may initiate tachycardia, and atropine, unlike β$_1$-adrenergic agents, increases heart rate without any reduction in the duration of systole. Therefore, for equal increases in heart rate, atropine will cause a greater reduction in the duration of diastole and will compromise subendocardial perfusion to a greater degree than a β$_1$-adrenergic agent. Ephedrine (a direct- and indirect-acting β- and α-agonist) 0.03–0.07 mg/kg is a reliable agent to increase heart rate without compromising diastole. In addition, the augmentation in diastolic blood pressure obtained is beneficial when hypotension accompanies bradycardia.

Tachycardia is detrimental for patients with ischemic DCM and should be treated to avoid subendocardial ischemia and hemodynamic compromise. The first strategy should be to terminate noxious stimuli and then increase the depth of anesthesia as necessary. The use of short- or long-acting beta-blockers is not recommended considering the presence of severely depressed systolic function. If hypotension due to reduced SVR occurs, small doses of phenylephrine (0.5–1.5 μg/kg) and volume infusion (5 mL/kg) to increase preload to preinduction levels usually will correct the problem. Phenylephrine reliably increases SVR. Caution must be exercised when α-adrenergic agonists are administered to patients with severe systolic dysfunction. The goal should be to normalize SVR. Overzealous use of phenylephrine will increase afterload, induce afterload mismatch, and severely reduce SV. If the patient fails to respond with a prompt increase in aortic blood pressure, an inotropic agent should be started to avoid a downward spiral of ventricular dilatation, increased wall stress, reduced SV and further hypotension. Dobutamine or dopamine 3–5 μg/kg/min are reasonable choices; dopamine increases SVR more than dobutamine. Using noxious stimulation such as laryngoscopy and intubation to treat hypotension in the lightly anesthetized patient with DCM must be avoided. These stimuli will produce a sudden, dramatic increase in afterload. The subsequent afterload mismatch will produce ventricular dilatation and may produce an additional reduction in blood pressure.

When surgical stimulation (skin incision, sternotomy, sternal spreading, and aortic manipulation) produces hypertension, additional doses of sufentanil (0.5–2.5 μg/kg) or fentanyl (5–25 μg/kg) are indicated. On occasion control of hypertension requires the use of vasodilator agents or adjuvant anesthetic agents. Judicious use of low inspired concentrations of isoflurane or sevoflurane is usually effective. Sodium nitroprusside is a ready titratable, potent arteriolar dilator and can be used effectively to treat hypertension. An infusion can be started at 0.25 μg/kg/min and titrated upward. However, because sodium nitroprusside is a potent arteriolar dilator, it has the potential to induce a coronary steal in the presence of the appropriate anatomy.

This may be of concern in patients with DCM of ischemic origin. Nitroglycerin dilates large coronary vessels and does not dilate arterioles; therefore, it is not implicated in the steal phenomena. Nitroglycerin has it greatest dilating capacity on the venous beds and arterial dilation occurs only at higher doses. Despite this, when used in appropriate doses, nitroglycerin and nitroprusside have been shown to be equally effective in treatment of hypertension. For treatment of hypertension, nitroglycerin is started at 0.5 μg/kg/min and may be increased up to 5 μg/kg/min.

Operative procedure

Three surgical techniques exist for orthotopic heart transplantation: the biatrial technique (Figs 7.2–7.4), the bicaval technique, and the total technique. These procedures are performed through a median sternotomy with hypothermic CPB, bicaval cannulation, and aortic cross-clamping. After commencement of CPB using the biatrial technique the recipient's heart is excised to just above the atrioventricular groove, leaving: a large cuff of left atrium containing all four pulmonary veins, a large cuff of right atrium containing the superior vena cava (SVC) and inferior vena cava (IVC), the ascending aorta just distal to the aortic valve, and the main pulmonary artery just distal to the pulmonic valve.

The donor left and right atria are anastomosed to the cuffs of the recipient left and right atria while the donor and recipient aorta and pulmonary artery are anastomosed. This technique creates large atrial cavities with abnormal geometry. This results in a less than optimal contribution of atrial systole to ventricular filling. In addition, the distorted anatomy contributes to the development of functional mitral and tricuspid regurgitation. It also is associated with the development of atrial septal aneurysms, atrial thrombus, and sinus node injury.

These problems have led to application of the more anatomical bicaval and total techniques. Currently, the bicaval technique is the most common technique used. These techniques result in better atrial function, a lower incidence of early and late atrial arrhythmias, and less tricuspid regurgitation.

(a)

(b)
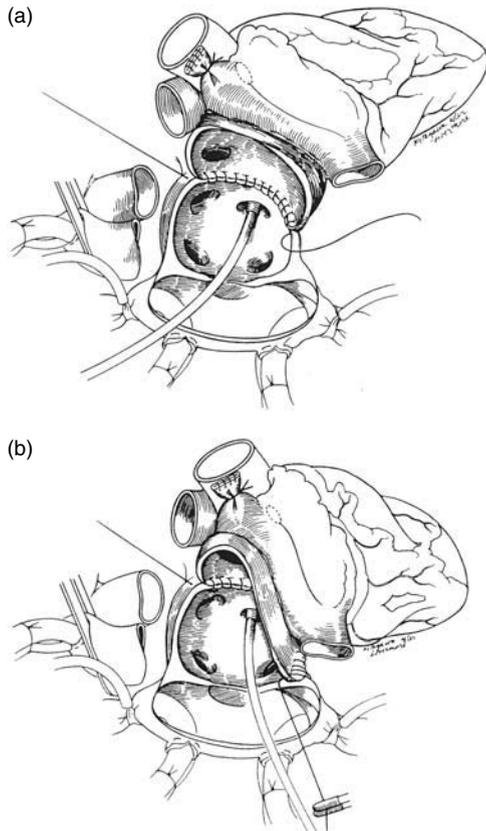
Fig. 7.2 Operative technique for biatrial orthotopic heart transplantation. (a) The recipient heart has been excised leaving a cuff of right atrium containing the superior vena cava (SVC) and inferior vena cava (IVC) and a cuff of left atrium containing all four pulmonary veins. The beginning of the left atrial anastomosis is depicted. The sinoatrial (SA) node of the donor heart is depicted by the dashed oval in the right atrium. The donor SVC is ligated. (b) Details of the anastomosis between the recipient and donor left atria.

(a)

(b)

Fig. 7.3 (a) The left atrial anastomosis is complete and the new intra-atrial septum is being completed. (b) The right atrial anastomosis is being completed using a portion of the donor IVC.

Whether they will result in long-term freedom from pacemaker implantation and better cardiac function remains to be determined.

In the bicaval technique, the recipient's atria are completely excised, leaving the SVC, the IVC, and a small cuff of left atrium containing all four pulmonary veins. In the total technique, the recipient's atria are completely excised, leaving the SVC, the IVC, and two small cuffs of left atrium: one containing the two right pulmonary veins and the other containing the two left pulmonary veins. In the bicaval technique, there are five anastomoses: the donor SVC, IVC, and posterior left atrium are anastomosed to the recipient SVC, IVC, and one pulmonary vein cuff while the donor and recipient aorta and pulmonary artery are anastomosed. In the total technique there six anastomoses: the donor SVC, IVC, and posterior left atrium are anastomosed to the recipient SVC, IVC, and two pulmonary vein cuffs while the donor and recipient aorta and pulmonary artery are anastomosed.

For children with congenital heart lesions, the technical aspects of the surgical procedure are more challenging. For example, for patients with HLHS, the aorta must be reconstructed. For children having undergone a Fontan or bidirectional Glenn procedure, a caval reconstruction may be necessary. Pulmonary artery (PA) reconstruction may be
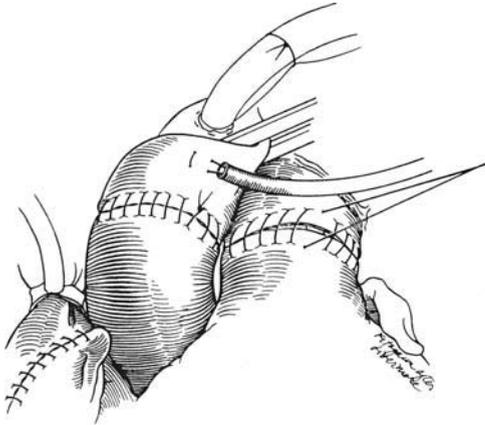
Fig. 7.4 Details of the completed aortic and pulmonary artery anastomoses. The aortic cannula and cross-clamp are depicted. In an effort to reduce the ischemic interval, the surgeon may release the aortic cross-clamp after completion of the atrial and aortic suture lines and complete the pulmonary artery anastomosis while the heart is being re-perfused.

necessary for patients with pulmonic atresia or RV to PA conduits.

Post-CPB management

Goals

1 Maintain sinus rhythm at 100–120 b/min in adults and older children and at 130–150 b/min in neonates and infants. Atrial or atrioventricular (AV) sequential pacing may be required.

2 Avoid pulmonary artery hypertension by treating hypercarbia, hypoxemia, and acidosis.

3 Aggressively treat pulmonary artery hypertension with vasodilator therapy to avoid RV failure. If RV failure does occur, inotropic support of the RV and pulmonary vasodilation may be necessary.

4 Maintain right atrial pressure (RAP) and LAP to optimize SV in the setting of increased ventricular stiffness.

5 Inotropic support of the LV may be necessary if the ischemic interval is long.

Preparation for termination of CPB

The following issues need to be considered when formulating a plan for termination of CPB in a patient with a newly transplanted heart.

Impaired systolic function

Systolic dysfunction in the donor heart may occur for a variety of reasons.

● *Ischemia-reperfusion injury.* This is the most common cause of allograft systolic dysfunction post-CPB. Preservation of the donor heart involves application of the aortic cross-clamp and delivery of cold cardioplegia to induce arrest in diastole, followed by cold storage at 4°C. The ischemic interval, the time from when the aortic cross-clamp is applied in the donor until the aortic cross-clamp is removed after implantation of the heart in the recipient is extremely important. The longer this ischemic interval, the more likely there is to be biventricular systolic dysfunction secondary to myocardial fibrosis. Because there is an incremental increase in mortality with ischemic times greater than 3.5 hours, it is desirable to keep the interval at less than 4 hours. In an effort to reduce the ischemic interval, the surgeon may release the aortic cross-clamp after completion of the atrial and aortic suture lines and complete the pulmonary artery anastomosis while the heart is being reperfused. Prolonged and excessive inotropic support of the donor heart before cross-clamping also is undesirable because it contributes to post-transplant ischemic dysfunction.

● *Brain death.* Abrupt increases in intracranial pressure as the source of brain death result in greater degree of myocardial ischemia and necrosis (particularly of the RV) than gradual increases in intracranial pressure. There is evidence that early survival following heart transplantation is reduced in patients receiving hearts from donors dying of gunshot wounds to the head and from donors dying from spontaneous intracranial hemorrhage. Donors who experience brain death as the result of a sudden rise in intracranial pressure exhibit a hyperdynamic cardiovascular response, massive increases in plasma epinephrine, and histological evidence of severe myocardial ischemia and necrosis.

● *Hyperacute rejection.* This rare event is caused by ABO blood group incompatibility or cytotoxic recipient antibodies directed against donor lymphocytes. It presents as cyanosis and mottling of the allograft in conjunction with profoundly impaired systolic function. It is impossible to separate these patients from CPB for any extended period of time.

The only therapy available is excision of the allograft with placement of a total artificial heart. This type of rejection is preventable by careful donor and recipient ABO typing and PRA screening.

- *Myocardial contusion*. Patients with severe myocardial contusions are excluded as donors. Patients with lesser degrees of dysfunction from blunt trauma may exhibit impaired systolic function in the post-CPB period.
- *Myocardial infarction*. As a result of the careful screening of donors this is a very rare cause of immediate allograft dysfunction. With an increase in the acceptable age for donors, this is likely to become a more common problem.

RV afterload mismatch

Impaired right ventricular performance is a particular risk in the presence of recipient pulmonary hypertension. RV afterload mismatch may occur as the result of severely depressed RV systolic function and normal pulmonary artery pressure (PAP) and PVR or, more commonly, as the result of less severely depressed RV systolic function and elevated PAP and PVR. This may result in acute allograft RV dysfunction severe enough to prevent termination of CPB. Therapy in this setting will need to be directed toward inotropic support of the RV and selective reduction of PVR.

Sinus and AV node dysfunction

Ischemic injury to the sinus and AV node may produce bradycardia, nodal rhythm, or heart block. Sinoatrial (SA) node dysfunction is much more common and approximately 10–20% of patients need permanent atrial pacing. In some instances, an appropriate sinus rate can be obtained with isoproterenol. In other instances, atrial or AV sequential pacing is necessary.

Impaired diastolic function

The post-ischemic state of the transplanted heart is characterized by increased ventricular stiffness and limited preload reserve resulting in a fixed SV. Increases in heart rate obtained with pacing will reduce diastolic filling time (see Fig 5.8). This, in turn, will produce reductions in EDV and SV for a given ESV. The net result will be little or no change in cardiac output. Atrial or AV sequential pacing is likely to be superior to ventricular pacing due to the presence of an appropriately timed atrial systole. For a given right or left atrial pressure, atrial pacing or AV sequential pacing will provide a higher ventricular EDV than ventricular pacing.

Inotropic support is useful for patients with limited preload reserve in both sinus and paced rhythms because SV can be augmented at a given afterload by reducing ESV. Inotropic agents allow SV to be maintained as heart rate increases, thereby producing increases in cardiac output. This occurs because the reductions in EDV produced by reduced diastolic filling time are offset by the reductions in ESV produced by enhanced contractility. Optimal heart rate is 100–110 b/min for adults and older children, whereas 130–150 b/min is optimal for neonates and infants. Higher heart rates result in progressive reductions in SV such that cardiac output remains constant or falls.

Termination of CPB

Terminating of CPB is discussed in detail in Chapter 10. Particular attention must be paid to deairing the heart. Severe ventricular dysfunction may follow ejection of air down the coronary arteries. The RV is particularly at risk because of the anterior location of the right coronary ostia. TEE is valuable in guiding the deairing process.

A dose of methylprednisolone (usually 10 mg/kg in children and 500 mg in adults) will be given after aortic cross-clamp removal. In some institutions, the dose will be given after termination of CPB.

Historically, isoproterenol, which is a potent chronotrope, dromotrope, inotrope, and vasodilator, has been used to enhance cardiac output during the immediate post-CPB period. Isoproterenol works well for patients in whom minimal inotropic support of the RV and LV is necessary. This is most likely when the donor heart requires minimal inotropic support before cross-clamping, the ischemic interval is short, and recipient pulmonary artery pressure is low or mildly elevated. Generally, isoproterenol is infused at 0.01–0.05 μg/kg/min (adults) or 0.05–0.25 μg/kg/min (children). At these doses, heart rate is maintained in an age-appropriate range, inotropic support of the RV and

LV is provided, and PVR and SVR are reduced. Higher doses of isoproterenol increase the incidence of hemodynamic changes that are unfavorable to the myocardial energetics of the post-ischemic heart. Isoproterenol increases myocardial oxygen consumption (MVo_2), reduces aortic diastolic blood pressure, is arrhythmogenic, and increases heart rate. All of these variables tend to exacerbate myocardial ischemia. Furthermore, as the dose of isoproterenol increases, it may be difficult to maintain systemic blood pressure due to prohibitive decreases in SVR. Due to these side effects, doses in excess of 0.01–0.05 µg/kg/min (adults) or 0.05–0.25 µg/kg/min (children) are rarely useful as a means of providing additional inotropic support or as a method of increasing heart rate. For this reason many centers have moved away from isoproterenol as first line therapy in cardiac transplant patients using other inotropic agents and pacing as necessary.

When isoproterenol is ineffective in producing the desired heart rate, atrial or AV sequential pacing should be initiated. This combination will allow maintenance of SV as heart rate is increased. When isoproterenol is ineffective in producing the desired inotropic effect, alternative inotropic agents should be promptly initiated. The need for additional inotropic support can be determined with either TEE or a pulmonary artery catheter. TEE will reveal ventricular dilatation and global hypokinesis. Regional wall motion abnormalities are also possible, but the ischemic insult usually is diffuse. Atrial enlargement and dilation of the mitral or tricuspid valve annulus with subsequent mitral or tricuspid regurgitation also is possible. Pressure monitoring will reveal an elevated central venous pressure (CVP) (>15 mmHg), elevated pulmonary artery occlusion pressure (PAOP) (>20 mmHg), or both. Cardiac output will be reduced (<2.0 L/min/m^2). The advantage of the pulmonary artery catheter is that it allows measurement of PAP and calculation of PVR and SVR. PAP can be estimated with TEE using a tricuspid regurgitation jet and the CVP measurement.

The properties of the various inotropic agents are reviewed in detail in Chapter 4. The choice of agent should be tailored to the clinical picture. Epinephrine 0.01–0.10 µg/kg/min (adults), 0.05–0.50 µg/kg/min (children), or dopamine 5–10 µg/kg/min is a better choice than dobutamine or milrinone when SVR and systemic blood pressure are low. Dobutamine 5–10 µg/kg/min or milrinone 0.50–0.75 µg/kg/min after a 50 µg/kg loading dose are better choices when PAP and PVR are elevated. Milrinone is a fairly potent inodilator with salutatory effects on PVR. Its use in adults often requires a simultaneous infusion of NE (0.01–0.10 µg/kg/min) to maintain SVR and blood pressure. This is generally not necessary in infants and children.

When RV afterload mismatch exists with preserved LV systolic function, there will be low cardiac output, low systemic blood pressure, elevated CVP, elevated PAP, and low PAOP. TEE will reveal a dilated right atrium and ventricle with an under filled, hyperkinetic LV. Tricuspid regurgitation will be likely.

Therapy for RV failure involves inotropic support and pulmonary vasodilatation. Pulmonary vasodilatation with intravenous agents is problematic because simultaneous reduction of SVR occurs. Simultaneous reduction of a normal SVR may compromise RV and systemic organ perfusion. Isoproterenol has historically been used during the post-cardiac transplant setting. Although isoproterenol is a potent inotrope and a pulmonary vasodilator, it is not a selective pulmonary vasodilator. Its β_2 effects cause parallel reductions in PVR and SVR. Other intravenous pulmonary vasodilators have been evaluated in heart transplant patients. Prostaglandin E_1 (PGE_1), prostacyclin (PGI_2), sodium nitroprusside (SNP), and nitroglycerin (NTG) are pulmonary vasodilators. Unfortunately, they are not selective pulmonary vasodilators because they cause reductions in SVR as well. In theory, PGE_1 should be a selective pulmonary vasodilator because it undergoegs a pronounced first-pass elimination in the lungs while PGI_2, SNP, and TNG are metabolized in one circulation time. In reality, all four drugs reduce PVR while causing a decrease in SVR such that the ratio of PVR:SVR is unchanged or, in the case of PGI_2, slightly increased. Efforts to reduce PVR with PGE_1, PGI_2, SNP, and TNG may require simultaneous

use of inotropes and vasoconstrictors to maintain systemic blood pressure. The simultaneous use of inotropic support is of benefit to the afterload mismatched RV as well. Use of PGI$_2$ to reduce PVR seems to result in better maintenance of SV and cardiac output than PGE$_1$, TNG, and SNP due to less of a venodilating effect.

The use of the inhaled selective pulmonary vasodilator NO has revolutionized treatment of pulmonary hypertension and associated RV afterload mismatch. Aerosolized, inhaled PGI$_2$ has a similar profile to inhaled NO. These agents are selective for the pulmonary circulation as no substantial concentrations are delivered to the systemic circulation following inhalation. NO delivered at 20 ppm selectively reduces PVR in all heart transplant recipients. Evidence suggests that the peak effect in reducing PVR with NO occurs at 20–40 ppm. Continuous aerosolized PGI$_2$ is delivered at 5–50 ng/kg/min. These agents are discussed in more detail in Chapter 6.

In addition to pharmacologic methods, efforts to reduce PVR with ventilatory interventions are essential. This topic is reviewed in detail in Chapter 6. A combination of a high fraction of inspired oxygen (FiO$_2$), an arterial partial pressure of oxygen (PaO$_2$) > 60 mmHg, an arterial partial pressure of carbon dioxide (PaCO$_2$) of 25–32 mmHg, a pH of 7.50–7.60, and low inspiratory pressures without high levels of positive end-expiratory pressure (PEEP) will produce reliable reductions in PVR.

It is important to rule out a mechanical cause of increased impedance to RV ejection when RV dysfunction exists in the presence of low pulmonary artery pressures. Kinking of the pulmonary artery anastomosis has been observed to cause mechanical obstruction of the RV. Kinking may be observed directly by the surgeon. Alternatively, it may be detected by TEE. It also is diagnosed readily by direct measurement of a pressure gradient between the RV and PA.

When univentricular or biventricular failure is severe and refractory to inotropic and vasodilator agents, a ventricular assist or circulatory assist device may be necessary to support circulation until the ventricles can recover.

Noncardiac surgery in the post-cardiac transplant patient

The success of heart transplantation makes it likely that anesthesiologists will encounter patients with transplanted hearts for a variety of noncardiac surgical procedures. Currently, the steepest drop in survival following adult heart transplant occurs in the first 6 months (to approximately 90% survival). For patients surviving beyond 1 year the conditional half-life (time to 50% survival) is 12 years. There is a steady linear decrease in survival beyond 6 months of approximately 3.4% per year. Similar results exist in children with the conditional half-life 17.5 years in the 1–10 year age group and 13.7 years in the 11–17 year age group. Infant conditional survival appears to be similar to that in the 1–10 year age group.

Some of the surgical procedures are purely elective, whereas others are likely to be urgent or emergent. Most surgical procedures are the direct result of complications of immunosuppressive therapy. These complications are listed in Table 7.3. The most commonly used immunosuppressive agents are summarized in Table 7.4. The incidence of complications requiring general surgical consultation in heart transplant patients is 35–40%. Many of these complications require operative intervention. Progression of atherosclerotic vascular disease also results in surgical intervention for aortic and peripheral vascular surgery. Finally, heart transplant patients undergo all types of elective surgery, including cosmetic surgery.

Table 7.3 Complications of immunosuppression that may require operative intervention.

Gingival hyperplasia – cyclosporine

Pancreatitis – azathioprine, corticosteroids

Cholelithiasis and cholecystitis – cyclosporine

Malignancies

Complications of corticosteroid use: cataracts, retinal detachment, aseptic bone necrosis, perforated viscus, and gastrointestinal hemorrhage

Complications of infection

Table 7.4 Immunosuppressive agents.

Agent	Classification	Mechanism of action	Clinical use
Prednisone methylprednisolone	Corticosteroid	Nonspecific blockade of T-cell cytokine and cytokine receptor production	Maintenance therapy Treatment of rejection
Cyclosporine	Calcineurine inhibitor	NFAT (nuclear factor) mediated inhibition of IL-2 promoter gene	Maintenance therapy
Tacrolimus (FK506)	Calcineurine inhibitor	NFAT (nuclear factor) mediated inhibition of IL-2 promoter gene	Maintenance therapy
Azathioprine	Antimetabolite, 6-mercatopurine derivative	Inhibitor of T-cell proliferation	Adjuvant therapy
Mycophenolate mofentil (MMF)	Inhibitor of *de novo* purine synthesis	Inhibitor of T-cell proliferation	Adjuvant therapy in lieu of azathioprine
Sirolimus	Anti-proliferative agent (rapamycin inhibitor)	Blocks G_1 to S phase of the cell cycle, inhibitor of T-cell proliferation	Adjuvant therapy in lieu of azathioprine or MMF
Everolimus	Anti-proliferative agent (rapamycin inhibitor)	Blocks G_1 to S phase of the cell cycle, inhibitor of T-cell proliferation	Adjuvant therapy in lieu of azathioprine or MMF
OKT3	Monoclonal antibody	Antibody to T-cell receptor complex (native and activated T cells)	Induction therapy
Basiliximab	Monoclonal antibody	Antibody to IL-2 receptor (activated T cells)	Induction therapy
Daclizumab	Monoclonal antibody	Antibody to IL-2 receptor (activated T cells)	Induction therapy
Rabbit antithymocyte γ-globulin (RATG)	Polyclonal antibody	Antibody to T cells (native and activated T cells)	Induction therapy

IL, interleukin.

Physiology of the transplanted heart

Autonomic nervous system

Regardless of the surgical technique used, the orthotopically transplanted heart is devoid of sympathetic and parasympathetic innervation. The most important consequence of this is an altered baroreceptor response. Normally, vagal afferent fibers from the atria and ventricles produce tonic inhibition of central sympathetic outflow. When atrial and ventricular volumes are reduced, vagal afferent outflow is reduced and central sympathetic outflow increases. In addition, activation of carotid and aortic baroreceptors by hypotension increases central sympathetic outflow. The result is direct sympathetic stimulation of the heart and generation of circulating catecholamines.

In the transplanted heart, no direct sympathetic stimulation of the heart is possible. Response to activation of baroreceptors in the patient with a transplanted heart is dependent on generation of circulating catecholamines for inotropic and

chronotropic response. It normally takes several minutes to generate appropriate levels of circulating catecholamines. Although systemic catecholamine generation in response to arterial hypotension is enhanced, reflex systemic catecholamine release in response to reduced atrial and ventricular volumes is impaired due to atrial and ventricular vagal deafferentation. As a result, abrupt decreases in blood pressure will not be compensated for quickly.

The response of baroreceptors to endogenous and exogenous vasopressors in heart transplant patients is normal, but feedback to the donor heart is absent. Therefore, increases in blood pressure will be accompanied by a reflex decrease in recipient atrial rate but not in donor atrial rate. As a result, there will be no reflex decrease in the transplanted heart rate in response to phenylephrine or NE-induced hypertension. Likewise, Valsalva or other vagal maneuvers will not elicit a heart rate response.

Early in exercise, increases in cardiac output are acquired by increases in SV, with EDV increasing and ESV remaining unchanged. As exercise progresses, cardiac output increases as the result of systemic catecholamine-induced increases in heart rate with maintenance of SV. Cardiac denervation produces presynaptic super-sensitivity due to denervation-associated loss of neuronal catecholamine uptake. As a result, there is increased sensitivity to catecholamines that are taken up by adrenergic nerve terminals (epinephrine, NE) with no increase in sensitivity to catecholamines that are not taken up (isoproteronol).

Some degree of reinnervation of the LV with efferent sympathetic fibers is present in 80% of transplant patients 3 years after transplantation. Reinnervation seems to be progressive but is likely not complete until 15 years after transplantation. Patients with reinnervation have improved heart rate and contractile response to exercise and better exercise tolerance than patients without reinnervation. The ability of some transplant patients to experience angina is consistent with reinnervation with sympathetic afferents. Reinnervation of cardiac vagal afferents is unlikely however. There is some evidence that over time the recipient

(old) AV node may affect the donor (new) AV node via conduction over the suture line. In summary, sympathetic efferent and afferent reinnervation may occur in some patients during the years after cardiac transplantation. When reinnervation occurs, it has physiologic importance.

Heart rate

The resting atrial rate of the transplanted human heart is approximately 90–110 b/min. This is significantly greater than the resting atrial rate of the innervated human heart and demonstrates that the predominant effect on sinus rate in man is a slowing effect of the parasympathetic system. Heart rate increases with exercise in heart transplant patients are achieved through stimulation of cardiac β_2-receptors by circulating catecholamines. The increases in heart rate do not occur until after several minutes of exercise and they parallel the increase in serum catecholamines. Despite this, the heart-rate response with exercise in transplanted hearts is attenuated relative to that seen in normal hearts due to the lack of efferent innervation of the SA node.

LV systolic function

The LV of the transplanted heart exhibits normal contractile function. Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) are reduced, whereas SV and EF remain normal or low normal due to the parallel reductions in EDV and ESV. LV mass is increased due to concentric hypertrophy as the result of the arterial hypertension, which accompanies cyclosporine immunosuppression.

RV systolic function

The RV exhibits normal systolic function. Right ventricular end-diastolic volume (RVEDV) and right ventricular end-systolic volume (RVESV) are larger than normal, and RV wall thickness is increased. This is probably secondary to the persistent tricuspid regurgitation present in most patients. In patients with preoperative pulmonary hypertension, persistence of RV dilatation and tricuspid regurgitation is the result of remodeling of the donor RV in response to recipient pulmonary circulation.

The dilation and tricuspid regurgitation may persist despite resolution of pulmonary hypertension.

Atrial function

Following the biatrial technique, both right and left atrial areas are larger than normal. These patients have reduced right and left atrial emptying compared with normal subjects; the portion of total atrial emptying contributed by the recipient atrium is much less than that contributed by the donor atrium. In addition, the asynchronous contraction of donor and recipient atrium results in wide variations in diastolic flow. Following the bicaval technique, patients have right atrial emptying comparable to normal subjects. Left atrial emptying, although reduced compared with normal subjects, is superior to that seen in biatrial technique patients. In addition, the left and right atrial dimensions are smaller in patients with the bicaval or total technique as compared with the biatrial technique.

Diastolic function

LV diastolic dysfunction occurs immediately after orthotopic cardiac replacement and is related to the post ischemic state. This dysfunction is characterized by a restrictive ventricular filling pattern that improves during the first several months after transplantation. This restrictive pattern may manifest clinically as reduced preload reserve in response to exercise and afterload increases. The etiology of this continued dysfunction is unclear. It may be inherent to the small allograft LVEDV. Whether patients who receive hearts from donors smaller than themselves may be at particular risk for reduced preload reserve is debatable. Rejection episodes are known to impair diastolic function, but it is unclear whether recurring rejection episodes produce progressive LV and RV diastolic dysfunction in the form of a restrictive/constrictive pattern.

There also is deficient acceleration of LV relaxation during exercise, which along with restrictive inflow, contributes to the elevations in left ventricular end-diastolic pressure (LVEDP) and LAP seen during exercise. This impairment of relaxation may be due to loss of adrenergic tone due to denervation, ischemic injury at the time of harvest, or immunosuppression-induced arterial hypertension.

Issues unique to heart transplant patients

Cardiac transplant patients have a unique set of management issues, in addition to those associated with the denervated heart. They are outlined below.

Cardiac allograft vasculopathy

This is currently the late survival-limiting factor after heart transplantation. In adults it accounts for one-third of the late deaths after transplantation as the result of myocardial infarction, congestive heart failure, and sudden death. In children it accounts for 40% of the deaths between 3 and 5 years after transplantation. The incidence of cardiac allograft vasculopathy (CAV) in both adult and pediatric cardiac transplant patients is approximately 10% per year post-transplant with an incidence of approximately 50% at 5 years.

The pathogenesis of CAV is complex, multifactorial, and incompletely understood. It is believed that immunologic mechanisms (number of HLA mismatches and the number and duration of rejection episodes) in conjunction with nonimmunologic risk factors (CMV seropositivity, hyperlipidemia, hypertension, older age at transplantation, diabetes) produce endothelial injury with subsequent myointimal hyperplasia. Unlike atherosclerotic coronary artery disease (CAD), CAV is associated with concentric, diffuse lesions that do not disrupt the elastic lamina and that progress rapidly. Focal, traditional atherosclerotic plaques also are seen in cardiac allografts.

Surveillance for CAV is difficult. Patients with heart transplants may not experience angina or typical ECG changes with myocardial ischemia and infarction due to afferent sympathetic denervation. Noninvasive testing has poor sensitivity and specificity. Intravascular ultrasound (IVUS) is the gold standard for detection of CAV but it is technically demanding, expensive, and limited by the size of the catheter to investigation of vessels of 1 mm in diameter or more. Considering these limitations, transplant centers currently use yearly coronary angiography as a screen for CAV. More frequent angiograms may be indicated to monitor progression in individual patients.

Therapeutic options are limited. More invasive approaches involve angioplasty and coronary stent placement. With this approach, short-term morbidity and success is similar to that seen in atherosclerotic disease, but the restenosis rate is high and long-term prognosis remains poor. Drug eluting stents may prove to be more effective in the long-term. Finally, in the most severe cases, coronary artery bypass surgery and retransplantation have been used. The diffuse nature of the coronary lesions makes bypass surgery an option only in selected cases. The survival rates for retransplantation are significantly less than for initial transplantation and the incidence of malignancy is twice that of first transplants.

Hypertension

Arterial hypertension is present in 75% of transplant patients at long-term follow-up. This is not related to the conventional risk factors associated with hypertension but to immunosuppression mediated increases in SVR and to denervation of cardiac volume receptors. Immunosuppression with calcineurin inhibitors (particularly cyclosporine versus tacrolimus), and corticosteroids is implicated. Therapy is necessary to prevent severe LV hypertrophy and impaired ventricular function. This usually requires treatment with multiple classes of antihypertensive agents. Calcium entry blockers and ACE inhibitors often are used as first-line therapeutic agents.

Atrial and ventricular arrhythmias

The incidence of atrial and ventricular arrhythmias during initial hospitalization after transplantation is 55% and 79%, respectively. At late follow-up, the incidence of atrial and ventricular arrhythmias is 40%. In general, atrial arrhythmias during the initial hospitalization are benign, except for atrial fibrillation. Development of atrial fibrillation is associated with a threefold increase in the risk of death. The risk of death is particularly high in patients who develop atrial fibrillation more than 2 weeks after transplantation.

Permanent atrial pacing is required in approximately 10–20% of both pediatric and adult recipients with symptomatic and asymptomatic bradycardia. Development of bradycardia seems to be related to a longer ischemic interval for the donor heart.

Subacute bacterial endocarditis (SBE) prophylaxis

Bacterial endocarditis is a rare complication in heart transplant patients. Nonetheless, because of the extent of the suture lines and the immunosuppressed status of the patient, SBE prophylaxis is recommended the American Heart Association (AHA).

Rejection

Most patients have at least one acute rejection episode despite adequate immunosuppression. These episodes usually occur within the first 3 months after transplantation with decreasing incidence thereafter. Surveillance during the first year is accomplished with endomyocardial biopsies of the RV via the right internal jugular vein every week for the first 4–8 weeks. Some centers do not perform biopsies in children younger than 6 months old or less than 5 kg in weight unless it is to confirm suspected rejection. Biopsies are graded from 0 to 3 based on histologic criteria. No rejection is 0R, mild rejection is 1R, moderate rejection is 2R, and severe rejection is 3R. After the first year, an annual biopsy is performed in most institutions in conjunction with coronary angiography to evaluate CAV. If clinical evidence of rejection exists, more frequent biopsies may be indicated to document rejection and to assess regression of histologic changes with treatment.

Mild rejection frequently resolves spontaneously and is not treated. Mild rejection by biopsy usually is not associated with clinical evidence of allograft dysfunction such as hypotension, elevated jugular venous pressure, rales, sinus rate >110, atrial fibrillation, bradycardia, or systolic dysfunction by echo. Moderate or more severe rejection is accompanied by evidence of allograft dysfunction and is treated. Although normal allografts have maintained coronary vasodilator reserve, moderate allograft rejection is associated with impaired reserve. Normal reserve returns after treatment of rejection. Rejection also is accompanied by

an attenuated coronary vasodilatory response to nitroglycerin.

First-line therapy for moderate rejection is oral or intravenous pulsed steroids. In the approximately 10% of cases in which mild rejection by biopsy is associated with allograft dysfunction, pulsed steroid therapy is necessary. Severe rejection usually is treated with steroids and, in some institutions, a lympholytic agent such as polyclonal antithymocyte globulin (ATG) or murine monoclonal antibody (OKT3) is added.

Response to drugs

The response to various drugs is altered in heart transplant patients secondary to the denervated state of the allograft:

- *Digoxin*. Digoxin prolongs AV node conduction in a biphasic manner. The initial effect is mediated vagally and is absent in the transplanted heart. The chronic effect is mediated directly and is present in the transplanted heart. The inotropic properties also are directly mediated and present.
- *Muscarinic antagonists*. Atropine, glycopyrrolate, and scopolamine produce competitive inhibition of acetylcholine at the muscarinic receptors of post-gangionic cholinergic nerves such as the vagus. As a result, these drugs will not increase heart rate in the denervated transplanted heart. The effects of these drugs on other organs with muscarinic cholinergic innervation will remain.
- *Acetylcholinesterase inhibitors*. The contention that agents such as neostigmine and edrophonium have no cardiac effects while they continue to have systemic muscarinic effects has been challenged recently. Bradycardia after administration of neostigmine, which was reversed with atropine, has been demonstrated in a heart transplant patient. In addition, sinus arrest after administration of neostigmine and glycopyrrolate for reversal of neuromuscular blockade reversal has been reported in heart transplant patients. Neostigmine produces direct stimulation of cholinergic receptors on cardiac ganglion cells with subsequent release of acetylcholine. In addition, there is allograft denervation hypersensitivity of both the postganglionic neurons and the muscarinic myocardial receptors. These factors, combined with

intrinsic allograft SA node dysfunction may produce severe SA node dysfunction or sinus arrest after acetylcholinesterase inhibitor administration in heart transplant patients.

- *Beta-adrenergic agonists*. There is increased sensitivity to catecholamines that are taken up by adrenergic nerve terminals (epinephrine, NE) with no increase in sensitivity to catecholamines that are not taken up (isoproterenol), Improvements in systolic function with β-adrenergic agents are obtainable during acute rejection episodes.
- *Beta-adrenergic antagonists*. These agents retain their usual activity. The sinus rate of both the donor and recipient slow equally, demonstrating that the predominant effect is caused by blockade of circulating catecholamines. There also will be a normal increase in the refractoriness of the AV node.
- *Calcium entry blockers*. These agents directly suppress the sinus and AV nodes and, thus, should have normal activity. Nonetheless, the negative chronotropic and dromotropic effects of verapamil have been demonstrated to be more pronounced in the transplanted heart. There will be no reflex tachycardia from agents with strong vasodilator properties such as nifedipine.
- *Vagolytic and vagotonic agents*. Drugs with vagolytic activity (pancuronium, demerol) will not increase heart rate, whereas drugs with vagotonic activity (fentanyl, sufentanil) will not decrease heart rate.
- *Adenosine*. The magnitude and duration of adenosine's negative chronotropic and dromotropic effects is 3–5 times greater in the transplanted heart.
- *Ephedrine*. Cardiac drugs that are both direct and indirect acting will have a diminished effect because only the direct effect will be present.

Anesthetic considerations for noncardiac surgery in patients post heart transplantation

A variety of regional and general anesthetic techniques have been used safely and successfully in the anesthetic management of patients with heart transplants. In patients without evidence of allograft dysfunction, the following principles are useful:

1 Aseptic technique is essential.

2 Appreciate that compensation for acute alterations in preload, afterload, and contractility

are incomplete and delayed; postural effects are magnified.

3 Heart rate and blood pressure increases due to inadequate anesthesia will be delayed until circulating catecholamine levels increase.

4 Bradycardia will compromise cardiac output. Baseline SV is reduced and any reflex increase in SV in response to bradycardia is delayed. Atropine will not increase heart rate. Isoproterenol and ephedrine will increase heart rate.

5 Acetylcholinesterase inhibitors (neostigmine, edrophonium) for reversal of neuromuscular blockade may have cardiac effects. Anticholingeric agents (atropine, glycopyrrolate) must be given to block the peripheral muscarinic effects.

6 CVP monitoring, when indicated, may have to be obtained via a route other than the right internal jugular vein.

7 Reflex bradycardia will not accompany administration of vasopressor agents (phenylephrine), nor will directly induced bradycardia accompany administration of agents with vagotonic activity.

8 Reflex tachycardia will not accompany administration of vasodilator agents (sodium nitroprusside, nifedipine, hydralazine), nor will directly induced tachycardia accompany administration of agents with vagolytic activity.

9 Stress-dose steroid coverage should be administered to patients receiving steroids as part of their immunosuppression.

Heart-lung transplantation

Heart-lung transplantation can be considered for patients with end-stage cardiopulmonary disease unresponsive to maximal medical therapy for which no surgical options exist except combined heart-lung replacement. Increasingly, in an effort to make maximum use of donated organs, double lung transplantation (DLT) and single lung transplantation (SLT) are being used for patients with pulmonary disease without secondary severe cardiac dysfunction. The number of heart-lung transplants peaked in 1989 (at approximately 250) and has continued to decline (74 in 2003) as the result of the increased of the use of DLT and SLT. In the USA approximately three pediatric HLTs are performed each year.

For adults, the primary indications for HLT, based on 2005 Registry data, are Eisenmenger syndrome secondary to congenital heart disease (32%), idiopathic pulmonary arterial hypertension (25%), and septic lung disease such as cystic fibrosis and bronchiectasis (15%). Other indications include emphysema, α_1-antitrypsin deficiency, and interstitial pulmonary fibrosis. For children, the primary indications are congenital heart disease (40%), primary pulmonary hypertension (24%), and cystic fibrosis (16%).

Single lung transplantation

SLT can be considered for patients with end-stage lung disease without significant cardiac dysfunction. Generally, patients with an LVEF > 35% and a right ventricular ejection fraction (RVEF) > 25% are considered candidates. The 2005 Registry data indicate that, for adults, SLT is used primarily for patients with obstructive lung disease from emphysema (53%), idiopathic pulmonary fibrosis (24%), and α_1-antitrypsin deficiency (8%). Increasingly, SLT is being used sparingly (1.5%) for patients with pulmonary hypertension from idiopathic pulmonary arterial hypertension and from Eisenmenger syndrome in whom there is not coexistent severe cardiac dysfunction. For patients with obstructive lung disease the BODE index (B, body mass index; O, airflow obstruction as measured by FEV_1; D, dyspnea as measured by the dyspnea scale; E, exercise capacity as measured by the 6-minute walk test) is useful in selecting candidates for transplantation.

For children, most lung transplantations are performed in the 11–17-year-old age group. SLT is used much less frequently than in adults and is used for patients with Eisenmenger syndrome in conjunction with repair of intracardiac lesions.

Double lung transplantation

DLT is also considered for patients with end-stage pulmonary disease without significant cardiac dysfunction. Two approaches to double lung transplantation exist: bilateral sequential single lung transplantation (BSSLT) and *en-bloc* DLT. Patients

with an LVEF > 35% and a RVEF > 25% are suitable candidates. The trend has been to reserve DLT for patients in whom SLT is not an option. Based on 2005 Registry data the primary indications for DLT in adults are cystic fibrosis (32%), emphysema (23%), idiopathic pulmonary fibrosis (10%), α_1-antitrypsin deficiency (9%), and idiopathic pulmonary arterial hypertension (7%). In addition, DLT has been used in conjunction with cardiac repair in adults with Eisenmenger syndrome.

In children, the primary indications are cystic fibrosis (38%), idiopathic pulmonary arterial hypertension (19%), and Eisenmenger syndrome in conjunction with a repair of intracardiac lesions (10%).

Living donor lobar lung transplant (LDLLT)

In the subset of patients deemed too ill to survive long enough to receive a cadaveric SLT or BSSLT this somewhat controversial procedure can be considered. It requires two donors, one donates the right lower lobe the other the left lower lobe. The recipient's native lungs are excised. The majority of these transplants (85%) are in patients with cystic fibrosis. In these patients their small stature allows two lobes from ordinary size donors to provide adequate lung tissue.

Contraindications to HLT, SLT, DLT, and LDLLT are similar to those for heart transplantation and are outlined in Table 7.1. In addition, the following absolute contraindications exist: severe scoliosis or thoracic cage deformity, irreversible, significant respiratory muscle dysfunction, numerous transpleural systemic to pulmonary artery collateral vessels, severe tracheomegly or tracheomalacia, and Burkholderia cepacia genomovar III lower respiratory tract infection in cystic fibrous patients.

Specific disease states

Obstructive lung disease

The most common indication for lung transplantation is obstructive lung disease secondary to emphysema or α_1-antitrypsin deficiency. Patients considered for transplantation generally have an $FEV_1 < 1\,L$, a requirement for supplemental oxygen at rest, and carbon dioxide retention. Pulmonary hypertension is uncommon in these patients. Concomitant CAD must be ruled out because many of these patients have long histories of smoking.

Both SLT and BSSLT have been used for these patients. SLT is relatively contraindicated in two subsets of emphysema patients: those with severe bullous disease and those with bronchiectasis. Severe bullous disease may result in preferential ventilation of the nontransplanted lung. Bronchiectasis introduces the risk of leaving an infected lung in communication with the transplanted lung in an immunocompromised patient. These subsets of patients usually are considered for BSSLT.

In other patients, both SLT and BSSLT provide good early functional results. BSSLT provides better long-term functional results but is associated with a higher operative mortality. Therefore, some centers consider BSSLT in younger emphysema patients.

Pulmonary fibrosis

These patients have restrictive pulmonary physiology. Patients considered for transplantation generally have a $FVC < 1.5\,L$ and a $FEV_1 < 1.2\,L$, a requirement for supplemental oxygen at rest, and carbon dioxide retention. Moderate to severe pulmonary hypertension is common in these patients.

SLT provides good function results in these patients as the transplant lung is preferentially ventilated and perfused. Preferential ventilation of the transplant lung occurs because it is more compliant than the native lung. Preferential perfusion of the transplant lung occurs because PVR is higher in the native lung.

Idiopathic pulmonary arterial hypertension (IPAH)

Patients in whom the cause of pulmonary hypertension is unexplained are said to have IPAH. This disease entity was formerly known as primary pulmonary hypertension (PPH). For the diagnosis of IPAH to be made, the secondary causes of pulmonary hypertension must be ruled out.

Common causes of secondary pulmonary hypertension include mitral stenosis, congenital heart disease, pulmonary embolism, and pulmonary venous obstruction. Seventy-three percent of IPAH patients are female; the mean age at presentation is 34 years, and the 5-year survival rate is 20%. Survival is enhanced by coumadin anticoagulation therapy, presumably because the presence of low cardiac output and pulmonary vascular endothelial injury places these patients at risk for pulmonary thrombosis and worsening pulmonary hypertension. High-dose calcium channel blockers also improve survival, but only in the subgroup of patients who experience a greater than 25% decrease in PVR and pulmonary artery pressure. Continuous PGI_2 (epoprostenol, Flolan®) infusion improves survival and functional status. However, it usually is reserved for patients with NYHA functional class III–IV. Newer therapies include bostensin (an endothelin-1 inhibitor), sildenafil (a phosphodiesteraste-5 inhibitor), and treprostinil (a PGI_2 analog which can be infused subcutaneously).

All patients with IPAH have RV dysfunction. IPAH produces RV afterload mismatch and subsequent RV hypertrophy. Chronic exposure to the loading conditions that produce hypertrophy results in progressive ventricular dysfunction as the result of progressive fibrosis and cell death. RV dilatation with dilation of the tricuspid valve annulus and TR are common. Opinion regarding the best procedure for patients with IPAH continues to evolve. HLT is the procedure of choice in IPAH patients with severe end stage RV dysfunction or severe biventricular dysfunction. At present, the trend is to offer all other IPAH patients SLT or BSSLT. This strategy has evolved because: (i) except in cases of end-stage RV systolic dysfunction, substantial recovery of the RV is possible with the normalization of pulmonary artery pressures, which occurs after SLT and DLT; and (ii) use of SLT and BSSLT makes better use of the limited organ supply. Currently, 85% of lung transplants done in patients with IPAH are BSSLT.

Eisenmenger syndrome

This syndrome occurs in patients with congenital heart disease and pulmonary hypertension severe enough to cause reversal of left-to-right shunts. Eisenmenger syndrome evolves in patients with intracardiac or great vessel left-to-right shunts. Initially, the left-to-right shunt produces increased pulmonary blood flow and eccentric hypertrophy of the cardiac chambers involved. With a ventricular septal defect (VSD), there will be eccentric hypertrophy of the LV and RV; with an atrial septal defect (ASD), there will be enlargement of the right atrium, left atrium, and RV. Prolonged exposure of the pulmonary vasculature to increased pulmonary blood flow and pressure leads to development of pulmonary hypertension and pulmonary vascular occlusive disease (PVOD). PVOD produces right ventricular concentric hypertrophy. As PVOD advances and PVR approaches and then exceeds SVR, intracardiac shunting becomes bidirectional and then right to left. In the short term, the processes of eccentric and concentric hypertrophy provide appropriate adaptation. However, chronic exposure to the loading conditions that produce hypertrophy results in progressive ventricular dysfunction as the result of fibrosis and cell death. As a result, these patients usually have severe biventricular dysfunction and generally are not candidates for SLT and BSSLT. When LV function is preserved, repair of the congenital cardiac defect can be performed in conjunction with SLT and BSSLT procedures. As with IPAH, there is debate as to whether SLT is the appropriate operation for patients with pulmonary hypertension secondary to Eisenmenger syndrome.

Cystic fibrosis

Cystic fibrosis is a multisystem disease and is the most common fatal inherited disease among Caucasians. Pulmonary involvement is inevitable, and 95% of affected adults die of respiratory complications. Airway obstruction secondary to viscous secretions, edema, and reactive airways leads to air trapping and an increase in functional reserve capacity (*FRC*), residual volume (*RV*), and total lung capacity (*TLC*). FEV_1 and *FVC* are reduced. In addition, lung damage occurs as the result of bacterial infections. Most patients with cystic fibrosis eventually are colonized by *Pseudomonas aeruginosa*. This pathogen is responsible for producing extensive

tissue damage both directly and by antigenic stimulation of the immune system. Recurrent infections and remissions are the norm. Aerosol administration of recombinant human DNase (rhDNase) reduces the risk of infectious exacerbations requiring parenteral antibiotics and improves pulmonary function. rhDNase reduces the viscoelasticity, reduces the adhesiveness, and improves the mucociliary transportability of cystic fibrosis sputum.

Chronic hypoxemia, acidosis, and physical loss of pulmonary vessels and lung tissue produce pulmonary hypertension and cor pulmonale. Right ventricular hypertrophy and dilatation develop. Chronic exposure to the loading conditions that produce hypertrophy results in progressive ventricular dysfunction as the result of progressive fibrosis and cell death.

In cases in which severe right ventricular dysfunction exists, HLT is the procedure of choice. In cases in which right ventricular function is normal or slightly impaired, BSSLT is used by some centers in place of HLT. SLT is not an option for patients with cystic fibrosis because the transplanted lung will quickly become contaminated and infected by secretions from the remaining lung. SLT with contralateral pneumonectomy has been used but has not been widely accepted.

Additional management problems are presented by the presence of pancreatic insufficiency. Eighty-five percent of patients with cystic fibrosis have pancreatic insufficiency severe enough to cause steatorrhoea and malabsorption. Insufficient caloric absorption and the anorexia of chronic disease combined with the increased caloric demands of chronic infection may result in malnutrition. Enteral and parenteral feeding may be necessary. Vitamin K deficiency may result in prolongation of the prothrombin time. Glucose intolerance is common (40% of adults) and diabetes mellitus occurs in 25% of adult patients.

Subclinical liver disease and hepatomegly secondary to fatty infiltration are common. Only rarely is liver dysfunction severe enough to cause hepatocellular dysfunction and hypersplenism. As a result, thrombocytopenia and coagulation factor deficiencies are rare.

The donor

Only 5–20% of all solid organ donors are suitable lung donors. Potential lungs are rejected because of blunt thoracic trauma, the potential of aspiration during resuscitation, overaggressive fluid resuscitation, and neurogenic pulmonary edema. The guidelines used to select donors for lung transplantation are summarized below:

1 Age younger than 65 years.
2 Adequate gas exchange. The donor should have a $PaO_2 > 250$ mmHg on $FiO_2 = 1.0$ and PEEP = 5 cm H_2O or $PaO_2 > 100$ mmHg on $FiO_2 = 0.4$ and PEEP = 5 cm H_2O. Pulmonary compliance should be normal with static pressure <20 mmHg and peak pressure <30 mmHg at a tidal volume of 15 mL/kg.
3 Normal bronchoscopic examination.
4 Normal serial chest radiographs.
5 No history of pulmonary disease. A smoking history is acceptable in some centers.
6 Donor recipient size match. Some programs compare donor and recipient lung size using chest radiograph measurements. A growing practice is comparison of donor and recipient total lung capacity from nomograms based on age, height, and sex. In patients with obstructive lung disease, an allograft with 15–20% greater volume than that predicted for the recipient can be used as these patients have huge pleural cavities.
7 No active severe infection or malignancy with the possibility of metastases.
8 Negative serologies for HIV or hepatitis B or C.
9 ABO compatibility and HLA screen.

The guidelines used to select donors for HLT are the combination of those for heart transplantation and those for lung transplantation.

Harvest of the lungs usually is accomplished in conjunction with harvest of the heart. The vena cavae are transected, an incision is made in the left atrial appendage, and the aorta is cross-clamped and cold cardioplegia is given. At this point, the pulmonary artery is injected directly with 500 µg of PGE_1 followed by infusion of 3–4 L of iced preservative solution which is vented out an incision in the left atrial appendage. The lungs are partially inflated (60%) with FiO_2 of 0.4 and the trachea or bronchi is stapled and divided. The heart-lung

block is then removed. When the heart and lungs are to be used for separate recipients, adequate portions of pulmonary artery and left atrial-pulmonary vein cuff must be allocated to each recipient. The lungs are immersed in a cold crystalloid solution at 4°C and transported. Although the maximum ischemic time is 6–8 hours, the optimal ischemic time should not exceed 5–6 hours because short- and intermediate-term patient survival may be effected.

Operative procedure and patient positioning

HLT is performed through a median sternotomy with hypothermic CPB, bicaval cannulation, and aortic cross-clamping. The recipient undergoes resection of the heart-lung block, leaving only a right atrial cuff in continuity with the IVC and SVC, the cut end of the distal trachea, and the cut end of the proximal ascending aorta. The donor heart-lung block is implanted with anastomoses of the right atrium, distal trachea, and ascending aorta.

SLT is performed through a standard thoracotomy with the patient in the lateral thoracotomy position. The donor lung block contains a cuff of left atrium with two pulmonary veins, the bronchus, and the branch pulmonary artery. The other donor lung and the donor heart can be used for two other recipients. One lung ventilation (OLV) is established and a pneumonectomy is performed, followed by implantation of the donor lung with anastomoses at the left atrium, bronchus, and branch pulmonary artery. This procedure often can be performed without CPB.

Two very different surgical procedures are used for DLT. The *en-bloc* procedure is performed on CPB with hypothermia, bicaval cannulation, aortic cross-clamping, and cardioplegic arrest of the recipient heart. A median sternotomy is used. The donor double lung block consists of the two lungs, the distal trachea, the main pulmonary artery, and a large left atrial cuff with all four pulmonary veins. The donor heart can be used for another recipient. The block is implanted with anastomoses at the trachea, posterior left atrium, and main pulmonary artery after bilateral recipient pneumonectomies.

This procedure is associated with poor healing of the tracheal anastomosis and reduced long-term survival compared with BSSLT and has been largely abandoned.

BSSLT is the other approach to DLT. This procedure often can be performed without CPB, which is considerably more challenging for the anesthesiologist. This procedure is performed with the patient supine through a sternal bithoractomy. Proper positioning is necessary to provide adequate exposure for the thoracotomy portion of the incision. One approach is to position the patient's arms suspended over the head. This is cumbersome and consumptive of the small amount of space available at the head of the table. In addition, it exposes the patient to an increased risk of brachial plexus injuries. With proper positioning of two rolls, one on either side of the patient's spine extending from the cervical to the lumbar region, the arms can remained tucked at the patient's side. Each donor lung block contains a cuff of left atrium with two pulmonary veins, the bronchus, and the branch pulmonary artery. The donor heart can be used for another recipient. OLV is established and a pneumonectomy is performed, followed by implantation of the donor lung with anastomoses at the left atrium, bronchus, and branch pulmonary artery. The procedure is then repeated for the next donor lung.

Use of CPB
The indications for use of CPB are summarized in Table 7.3.

HLT and *en-bloc* DLT
HLT and *en-bloc* DLT both require hypothermic CPB with aortic cross-clamping as described previously.

SLT and BSSLT
Elective CPB is used for SLT and BSSLT for the following subsets of patients:
- Infants and small children.
- Patients with pulmonary hypertension.
- Patients undergoing lung transplantation and simultaneous repair of intracardiac defects.

For all other patients with SLT and BSSLT, CPB is initiated only when hemodynamic, gas exchange, or

Type of transplant	CPB	OLV
HLT	Full hypothermic, aortic cross-clamp	No
En-bloc double-lung transplant	Full hypothermic, aortic cross-clamp, cardioplegic arrest	No
SLT, BSSLT		
Infants, small children	Full normothermic	No
Intracardiac defect repair	Full hypothermic, aortic cross-clamp, cardioplegic arrest	No
Pulmonary hypertension	Partial normothermic	Yes
All others	Partial normothermic if necessary	Yes

Table 7.5 Indications for cardiopulmonary bypass (CPB) and one-lung ventilation (OLV) in lung transplantation.

BSSLT, bilateral sequential single lung transplantation; CPB, cardiopulmonary bypass; HLT, heart–lung transplantation; OLV, one-lung ventilation; SLT, single-lung transplantation.

technical difficulties are encountered in the course of the procedure. Most SLT and BSSLT patients without pulmonary hypertension can be managed without CPB. There is a higher incidence of need for CPB in patients with restrictive lung disease. Intra-operative criteria that predict the need for use of CPB in patients with restrictive lung disease include an arterial oxygen saturation (Sa_{O_2}) < 90% with an Fi_{O_2} of 1.0, baseline mean PA pressure > 40 mmHg, mean PA pressure > 50 mmHg with the pulmonary artery clamped, severe systemic hypotension, and a cardiac index < 2.0 L/min/m^2. Avoiding CPB when possible is important because use of CPB contributes to postoperative graft dysfunction in the form of an increased arterial:alveolar oxygen ratio, increased severity of radiographic pulmonary injury, and prolonged postoperative intubation. It does not appear that use of CPB effects long-term outcome.

Full CPB is used for infants and small children and for all patients undergoing simultaneous repair of an intracardiac lesion. Aortic cross-clamping and cardioplegic arrest are only necessary when intra-cardiac defects are repaired. Normothermic partial CPB is used for all other cases of SLT and BSSLT. Cannulation of the ascending aorta and the right atrium is used for bilateral SLT and right SLT. For patients undergoing left SLT, descending aorta and pulmonary artery cannulations have been used. Alternatively, femoral vein and artery cannulation can be used.

Anesthetic management

Goals

1 Patients with obstructive lung disease may exhibit auto-PEEP, stacking of breaths, and hemodynamic compromise with positive pressure ventilation. Ventilatory interventions will be necessary.

2 Pre-existing LV or RV dysfunction requires that contractility be maintained or enhanced.

3 Avoid hypercarbia, hypoxemia, and acidosis that will exacerbate pulmonary hypertension and may result in acute RV decompensation.

4 Avoid increase in the PVR:SVR ratio in patients with Eisenmenger syndrome. This will increase right-to-left shunting and worsen hypoxemia.

Preoperative evaluation

Lung transplant patients typically undergo extensive medical evaluation. A summary of this evaluation is readily available to the anesthesiologist through the transplant coordinator.

Premedication

Most patients are called into the hospital on short notice and many will have eaten solid food in

the previous 6–8 hours. In addition, patients will have taken their initial doses of oral immuno-suppressive drugs, usually cyclosporine and aza-thioprine or mycophenolate moftil. Cyclosporine usually is administered with 10–20 mL of liquid. It is important to verify that these medications have been taken. To reduce the risk of aspiration in adults and older children, a nonparticulate antacid such as bicitra 30 mL can be given in addition to intra-venous metaclopromide 10 mg and an intravenous H_2 receptor blocker such as ranitidine 50 mg. For infants and smaller children a period of 2–3 hours of NPO status is sufficient and usually transpires before induction.

Premedication for adults and children is most safely and effectively titrated by the anesthesiol-ogist before induction and while lines are placed and the history and physical examination are completed. Midazolam 0.03–0.05 mg/kg in divided doses works well to reduce anxiety. Supplemental oxygen should be administered because hypoxemia will exacerbate existing pulmonary hypertension.

Preinduction

Some transplant patients will be receiving intra-venous inotropic and vasodilator therapy when they arrive for surgery. These agents should be con-tinued via a reliable intravenous route. Sterility is of the utmost importance because the patients will be immunosuppressed. Patients with bronchospas-tic disease should receive bronchodilator therapy before induction. Likewise, patients with cystic fibrosis should receive nebulized acetylcysteine or rhDNase to help break up tenacious secretions.

Adults

All patients should have two large-bore periph-eral intravenous lines (14-gauge). If the patient's arms are suspended over the head, venous access in or below the antecubital fossa is not practical because flow will be impaired. Placement of one or more introducer sheaths in the internal jugular vein for use as reliable sites of rapid fluid admin-istration is warranted if peripheral access is poor or the arms are to be suspended over the head. ECG monitoring should allow assessment of V_5, I, II, III, aV_R, aV_L, and aV_F. Baseline recording

of all seven leads should be obtained for compar-ative purposes. Normally, two leads (II and V_5) are monitored simultaneously intraoperatively. If a left thoracotomy incision is used, V_5 is not an option because the lead will be in the operative field. A radial or femoral artery catheter is placed with local anesthesia before induction of anesthesia. When a femoral artery catheter is used, it should be placed in femoral artery contralateral to the one that will be cannulated if CPB is used.

Most centers place a pulmonary artery catheter in adults for SLT and BSSLT. The catheter can be placed after induction in patients who are unable to lie flat or to cooperate. Some centers use PA catheters that allow continuous cardiac output and mixed venous oxygen saturation (Svo_2) moni-toring. The PA catheter is an important tool in managing the patient during pneumonectomy and clamping of the pulmonary artery. In addition, information obtained from the PA catheter is used to determine whether completion of the proce-dure without CPB is feasible. It is not necessary to direct the pulmonary artery catheter into the contralateral pulmonary artery in patients under-going SLT. The catheter can be pulled back into the main pulmonary artery before pulmonary artery clamping and then advanced into the contralateral pulmonary artery.

For HLT some centers do not place a PA catheter for the same reasons outlined for heart transplant patients. As with heart transplantation, some cen-ters prefer that the right internal jugular vein not be used as an access site in HLT patients in order that it can be used later for obtaining endomyocardial biopsies.

Multiplane TEE is used to help manage the patient pre- and post-CPE. After transplantation, TEE is used to assess left and right ventricular function, measure pulmonary artery pressures (using a tri-cuspid regurgitation jet), and guide management of pulmonary artery hypertension and RV dys-function if necessary. In addition, TEE is used to assess the pulmonary arterial and pulmonary venous anastomoses after lung transplantation. TEE also has proved useful in detection and treat-ment of dynamic, infundibular RV outflow tract obstruction after lung transplantation. Patients with

RV hypertrophy may have apposition of the walls of the infundibulum in systole, when RV afterload is reduced after donor lung implantation. Hypovolemia and inotrope use tend to exacerbate this problem.

A thoracic or lumbar epidural can be used both intraoperatively and for postoperative pain management in SLT and BSSLT patients. The catheter can be placed preoperatively in those patients who are unlikely to require CPB. For patients requiring CPB, the epidural catheter is placed postoperatively after reversal of heparinization and correction of coagulation deficiencies. Some centers prefer to place all epidural catheters postoperatively as it is often impossible to predict whether a patient will require CPB. In thoracic catheters, 0.0625–0.125% bupivacaine and fentanyl $10\,\mu g/mL$ at 4–8 mL/h can be infused. In lumbar catheters preservative-free morphine 0.05 mg/mL at 5–10 mL/h can be used.

Children

Placement of an intravenous catheter before induction is optimal with induction proceeding as described for adult patients. Patients with preserved ventricular function, an appropriate NPO interval, and cardiopulmonary stability will likely tolerate an inhalation induction. ECG monitoring should allow assessment of V_5, I, II, III, aV_R, aV_L, and aV_F. Baseline recording of all seven leads should be obtained for comparative purposes. Normally, two leads (II and V_5) are monitored simultaneously intraoperatively. If a left thoracotomy incision is used, V_5 is not an option because the lead will be in the operative field. A radial or femoral artery catheter is placed after induction of anesthesia. CVP monitoring is placed after induction. For older children undergoing SLT or BSSLT with or without CPB, a PA catheter is placed. For all other children, an appropriately sized double-lumen central venous line is placed. The right internal jugular vein is the preferred site. A pediatric multiplane TEE probe can be used for children weighing less than 15–20 kg and the adult multiplane TEE probe for children weighing more than 20–30 kg to help manage the patient pre- and post-CPB as described previously for adult patients.

For older children undergoing SLT and BSSLT, a lumbar or thoracic epidural catheter can be placed for postoperative pain management.

Management of OLV

The indications for use of OLV are summarized in Table 7.3. In procedures performed with full CPB, lung isolation and OLV are not necessary. These procedures can be managed with a standard single-lumen endotracheal tube. The anesthetic plan for SLT and BSSLT in adults and older children must include a method of lung isolation and OLV because these procedures are being performed increasingly without CPB or with partial CPB. When partial CPB is used, OLV to the perfused, nonoperative lung is necessary. Four methods of lung isolation and OLV are available.

Endobronchial intubation

A standard endotracheal tube (ETT) is used and then a bronchoscope is used to direct the ETT down the main stem bronchus of the lung that is to be ventilated.

Advantages
- Applicable to any size patient with use of an appropriate-sized ETT.
- Placement is easy with the appropriate-sized fiberoptic bronchoscope. When the right main stem bronchus is intubated, visualization of the right upper lobe (RUL) bronchus is possible with the bronchoscope. This helps prevent occlusion of the RUL bronchus by the balloon of the ETT.
- Suctioning of secretions via the ETT before endobronchial intubation is easy because a large suction catheter or fiberoptic bronchoscope can be used.
- When the procedure is completed, the ETT does not have to be replaced.

Disadvantages
- Some deflation of the nonventilated lung will occur passively, but most will occur by absorption of gas. For patients with emphysema, this will result in slow, poor lung deflation and poor operating conditions.

• Suctioning of the nonventilated lung and application of continuous positive airway pressure (CPAP) to the nonventilated lung is impossible.

• In taller patients, a standard ETT may not be long enough to extend far enough into the main stem bronchus to provide isolation.

Single-lumen endotracheal tube plus a bronchial blocker

This technique involves use of a Fogarty catheter or Arndt blocker and a standard ETT. Laryngoscopy is performed and the blocker is placed in the trachea, followed by placement of the endotracheal tube. Alternatively the blocker can be placed within the lumen of the ETT. In either case, a fiberoptic bronchoscope is used to guide the bronchial blocking catheter down the appropriate bronchus.

Advantages

• Applicable to any size patient with use of an appropriate-sized ETT and bronchial blocker. Fogarty catheters with balloon sizes from 0.5–3.0 mL are available. Arndt blockers are available in 5-, 7- and 9-French catheters with high-volume low-pressure balloons. Placement is easy with the appropriate-sized fiberoptic bronchoscope.

• Suctioning of secretions via the ETT before placement of the blocker is easy because a large suction catheter or fiberoptic bronchoscope can be used.

• When the procedure is completed, the ETT does not have to be replaced and the Fogarty catheter can be removed.

Disadvantages

• Deflation of the blocked lung must occur by absorption of gas. For patients with emphysema, this will result in slow, poor lung deflation and poor operating conditions.

• Suctioning of the nonventilated lung and application of CPAP to the nonventilated lung is impossible.

• Maintaining the position of the blocker in the main stem bronchus during surgical manipulation may be difficult or impossible. In patients with cystic fibrosis undergoing BSSLT, this introduces the risk of contamination of the first lung transplanted with secretions from the remaining diseased lung.

• Visualization of the RUL bronchus with a fiberoptic bronchoscope is impossible with the blocker in the right main stem bronchus. As a result, occlusion of the RUL bronchus by the balloon of the blocker may occur due to the high takeoff of the RUL bronchus. This makes surgical excision of the right lung and the subsequent transplant bronchial anastomosis technically difficult.

• The Fogerty catheter balloon is a high-pressure low-volume balloon that may compromise bronchial mucosal blood flow.

Univent tube

This is a standard endotracheal tube with a 3-mm outer diameter bronchial blocker, which passes through a 4-mm channel incorporated within the lumen of the endotracheal tube. The bronchial blocker has a 2-mm internal diameter lumen. These tubes are available with internal diameters from 6.0 to 9.0 mm in 0.5 mm increments and in a 3.5 mm uncuffed and 4.5 mm cuffed version. Because of the presence of the enclosed bronchial blocker, the external diameter of these tubes is considerably larger. The external diameter of the 8 mm Univent tube is 13 mm which is the same as the external diameter of a 39-French double-lumen endotracheal tube (DLT). The external diameter of the 3.5 mm Univent tube is same as a 6 mm ETT or a 26-French DLT. Optimal placement of the bronchial blocker requires use of a fiberoptic bronchoscope.

Advantages

• The arrangement of the blocker as an integral part of the ETT provides better stability of the blocker within the main stem bronchus during surgical manipulation.

• It is easier to place in a patient with a difficult airway than a DLT.

• The internal lumen of the blocker will allow some decompression of the nonventilated lung and will allow the application of CPAP.

• When the procedure is completed, the Univent tube does not have to be replaced with a standard ETT. The bronchial blocker can be withdrawn into the internal channel and the Univent tube can be left in place.

Disadvantages
- Due to the large external diameter, these tubes are useful only for adult patients and older children.
- The internal lumen of the blocker is too small to allow adequate suctioning of secretions.
- As with a standard bronchial blocker, occlusion of the RUL bronchus by the balloon of the blocker may occur.
- The bronchial blocker balloon is a high-pressure low-volume balloon that may compromise bronchial mucosal blood flow.

Double-lumen endotracheal tube (DLT)

DLTs are available in sizes from 26-, 28-, 32-, 35-, 37-, 39-, 41-, and 43-French. The outer diameter of a 26-French DLT is equivalent to a 6.0 mm ETT and thus is appropriate size for a patient weighting approximately 30 kg or 8–10 years of age. Both right- and left-sided tubes are available. Right-sided tubes have a side lumen in the bronchial tube that must be positioned over the RUL bronchus so that the balloon of the bronchial lumen does not occlude the RUL bronchus. Fiberoptic bronchoscopy is necessary to ensure proper positioning of both right- and left-sided DLTs.

Advantages
- Deflation and suctioning of the nonventilated lung is easily accomplished.
- Application of CPAP to the nonventilated lung is easy.
- The endobronchial tube is not dislodged easily with surgical manipulation.
- Visualization of the RUL bronchus with the DLT in place is accomplished easily with a fiberoptic bronchoscope.

Disadvantages
- Alignment of the RUL lumen of a right-sided DLT with the patient's RUL can be difficult, particularly in the presence of thick secretions.
- The smallest available DLT is appropriate for children aged 7–8 years.
- Suctioning tenacious secretions through the small lumens of the DL tube is more difficult than through the lumen of a standard ETT.

- When the procedure is completed, the DLT must be exchanged for a standard ETT.

A left-sided DLT is the method of choice for lung isolation in adult and pediatric patients undergoing SLT and BSSLT. The left DLT provides greater versatility and ease of placement. A left-sided DLT, when properly placed, with use of a fiberoptic bronchoscope does not compromise surgical exposure for the left pneumonectomy and the subsequent transplant bronchial anastomosis. Consideration should be given to use of a bronchial blocker or Univent tube in patients with a difficult airway. When a left-sided DLT is needed, placement is accomplished as follows:

1 The trachea is intubated such that the tracheal cuff is just below the vocal cords and the tube is rotated 90° to the left. The trachea cuff is inflated and the patient is ventilated. The bronchial lumen will be located just above the carina in most normal-sized patients.

2 An appropriate-sized fiberoptic bronchoscope is introduced down the bronchial lumen and the right and left main stem bronchi are identified. In some instances, it may be necessary to pull the DLT back slightly if the tip of the bronchial lumen is past the carina. For patients with cystic fibrosis or bronchiectasis, thick secretions may make identification difficult. A suction catheter and saline irrigation may have to be introduced down the bronchial lumen to clear secretions. Suctioning through the bronchoscope is difficult considering the small caliber scopes that can fit down the DLT. Alternatively, aggressive cleanout with an SLT and a large bronchoscope can be accomplished before placement of the DLT.

3 The bronchoscope is advanced down the left main stem bronchus and the left upper lobe bronchus is identified.

4 While the operator keeps the tip of the bronchoscope above the left upper lobe bronchus orifice, the tracheal balloon is deflated and the DLT is advanced into the left main stem bronchus over the bronchoscope. The tip of the bronchial lumen should be confirmed to be above the left upper lobe bronchus. The tracheal balloon is re-inflated and ventilation continues.

5 The bronchoscope is now placed down the tracheal lumen. Ideally, the tracheal lumen should be

positioned just above the right main stem bronchus with the bronchial balloon below the rim of the orifice of the left main stem bronchus. If the DLT has been advanced too far down the left main stem bronchus, the tracheal lumen may lie within the left main stem bronchus. This is unlikely if the tip of the bronchial lumen lies above the left upper lobe bronchus.

6 If the tracheal lumen is within the left main stem bronchus, the tracheal balloon is deflated and the DLT is pulled back until the tracheal lumen provides unobstructed access to the right main stem bronchus. The bronchial balloon should remain at or below the rim of the left main stem bronchus orifice. The tracheal balloon is re-inflated.

7 After proper positioning is confirmed, the bronchial balloon is inflated while the bronchoscope remains in the tracheal lumen. The bronchial balloon should not herniate out the left main stem bronchus when the balloon is inflated. If the balloon herniates out of the left main stem bronchus, the DLT must be advanced slightly into the left main stem bronchus.

8 Positioning of the DLT should be rechecked with the bronchoscope after the patient has been moved into final position. DLT placement may change after movement of the patient into the lateral decubitus position.

Induction and maintenance

Anesthetic techniques should allow for early postoperative extubation. Many patients with end-stage pulmonary disease will be unable to lie flat due to severe dyspnea. These patients are induced in the sitting position and, as they lose consciousness, they are slowly placed supine. For patients in whom there is a risk of aspiration, induction is performed with the patient in a slightly head up position and cricoid pressure is applied until the trachea is intubated.

Narcotic-induced rigidity with subsequent difficulty ventilating can have disastrous consequences for these patients. Careful titration of etomidate (0.1–0.3 mg/kg) in combination with 5–10 µg/kg of fentanyl or 1–2 µg/kg of sufentanil is useful for induction. A full 0.3 mg/kg dose of etomidate is often not necessary to induce hypnosis and loss

of consciousness in these patients. This drug combination has minimal direct effect on heart rate, myocardial contractility, peripheral vascular resistance, or venous capacitance. An overall diminution in central sympathetic tone will also contribute to circulatory depression. A nondepolarizing muscle relaxant in a dose $2 \times ED_{95}$ such as vecuronium or pancuronium 0.02 mg/kg or cisatracurium 0.04 mg/kg is used to assure prompt control of the airway. Pancuronium is generally reserved for those patients in who a low baseline heart rate. In infants and children the vagolytic and sympathometic effects of pancuronium can be used to counteract the vagotonic effects of fentanyl or sufentanil. These drugs in combination with rocuronium (1.0 mg/kg) or succinylcholine (1–2 mg/kg) can be used to perform a modified rapid sequence induction (cricoid pressure during positive pressure ventilation) in the patient with questionable NPO status. Thiopental and propofol are less well tolerated. Thiopental in particular may exacerbate bronchospasm.

Anesthesia can be maintained with additional doses of opioid in conjunction with a benzodiazepine (usually midazolam in increments of 0.01–0.03 mg/kg) or a low inhaled concentration (0.5–0.75 MAC) of isoflurane or sevoflurane. N_2O is not a good choice as an adjuvant agent; it has a weak myocardial depressant effect that normally is counteracted by the sympathetic outflow it produces.

For patients with obstructive lung disease (emphysema, α_1-antitrypsin deficiency, cystic fibrosis) induction and positive pressure ventilation may produce profound hypotension. The possibility that a pneumothorax is present must always be considered. This cardiovascular compromise is secondary to air trapping or auto-PEEP. This auto-PEEP reduces SV and cardiac output through the following:

• Reductions in venous return to the RV resulting in a decrease in RVEDV.

• Increased impedance to RV ejection by mechanical compression of the pulmonary arterial system resulting in an increase in RVESV.

• Shift of the interventricular septum into the LV, which increases LV stiffness and reduces LVEDV.

This combination is particularly detrimental for patients with compromised RV systolic function and RV afterload mismatch. Treatment requires volume administration to (10–15 mL/kg of a balanced salt solution) to normalize RVEDV and inotropic support to improve RV systolic function and normalize RVESV. Either dopamine 5–10 μg/kg/min or epinephrine 0.01–0.10 μg/kg/min (adults) or 0.05–0.50 μg/kg/min (children) are effective. In addition, ventilation with a rapid initial inflation followed by an inspiratory hold or pause and a long expiration time is necessary (low inspiratory to expiratory time (I:E) ratio). This may require hand ventilation, although pressure-control ventilation with an intensive care unit (ICU) ventilator works well. PEEP should not be used.

TEE is extremely valuable in assessing ventricular filling and contractile function in this setting because filling pressures will not provide an accurate measure of ventricular volumes.

In the most severe instances, intermittent periods of apnea may be necessary. This apneic oxygenation may exacerbate pre-existing pulmonary hypertension via carbon dioxide retention and hypoxemia. Evaluation of pulmonary artery pressures and cardiac output with a PA catheter, RV and LV function with TEE, and arterial saturation with pulse oximetry are necessary to determine the extent of hypoventilation that can be tolerated. Marked acidosis (pH of 6.94) and hypercarbia ($Paco_2$ of 150 mmHg) can be tolerated during lung transplantation as long as systemic blood pressure and oxygen delivery are maintained. In some instances initiation of CPB may be necessary.

Blood loss may be impressive during dissection for pneumonectomy in HLT, SLT, and DLT patients with dense adhesions from previous thoracic surgery or for patients with cystic fibrosis or bronchiectasis. A rapid transfusion device may be necessary in some cases. Some centers use antifibrinolytics or aprotinin in both children and adults when CPB is used or when there are dense adhesions regardless of whether CPB is used. In addition to red cells, component therapy with fresh frozen plasma (FFP) and platelets often is necessary, particularly when CPB is used. Manipulation of the lungs in patients with cystic fibrosis or bronchiectasis

may result in release of endotoxins with subsequent decrease in SVR, hyperpyrexia, and increased metabolic rate. Management of the recipient without use of CPB under these conditions is extremely difficult.

After one or both of the lungs have been implanted and perfused, most centers administer methylprednisolone (usually 10 mg/kg for children and 500 mg for adults). After lung implantation has been completed, 5–10 cm H_2O PEEP is applied and the Fio_2 selected is the lowest necessary to obtain a Pao_2 of 90–100 mmHg. This is done because the post-ischemic lung is vulnerable to oxygen-free radial toxicity. At the termination of the procedure, patients with DLTs have the DLT replaced with a large single-lumen ETT. A large tube size should be used to allow easy access for postoperative fiberoptic bronchoscopy.

Special considerations for SLT and BSSLT

Management of OLV and pulmonary artery clamping for recipient pneumonectomy and allograft implantation in SLT and BSSLT patients without CPB is a challenge. The task is made easier for patients undergoing SLT if the lung with the poorest ventilation and perfusion is removed and replaced. For patients undergoing BSSLT, the lung with the poorest ventilation and perfusion should be removed first and replaced.

Maintenance of body temperature is difficult when CPB is not used. A warming blanket under the patient, an actively humidified breathing circuit, a fluid/blood warmer, and a forced warm air blanket over the patient all are necessary.

One lung ventilation (OLV)

Collapse of the operative lung and OLV is likely to exacerbate air trapping and the subsequent hemodynamic compromise and carbon dioxide retention. Treatment with volume administration, inotropes, and ventilatory interventions is warranted as described previously. Marked hypercarbia with acidosis is likely and generally is well tolerated. Aggressive suctioning may be necessary to facilitate collapse of the operative lung. Pao_2 also is likely to decrease, due to intrapulmonary shunting, until the ipsilateral pulmonary artery is clamped.

Administration of CPAP to the nonventilated lung, insufflation of oxygen to the nonventilated lung, or high-frequency jet ventilation (HFJV) of the nonventilated lung may improve oxygenation.

Clamping of the PA

Recipient pneumonectomy requires clamping of the ipsilateral pulmonary artery. Before clamping of the pulmonary artery, the pulmonary artery catheter is withdrawn into the main pulmonary artery. Palpation by the surgeon will confirm its position proximal to the proposed cross-clamp site. After the ipsilateral pulmonary artery has been clamped, the catheter is advanced into the contralateral pulmonary artery. Clamping of the pulmonary artery may compromise RV function due to afterload mismatch. This is most likely in patients with mild to moderate pre-existing pulmonary hypertension and in those with impaired RV function. This is the primary reason why patients with severe pulmonary hypertension require elective CPB. If there is any doubt regarding the ability of the patient to tolerate pulmonary artery clamping, a trial of clamping is recommended. TEE is used to assess RV function. In addition, increased PAP and CVP, falling cardiac index, and Svo_2 may occur.

Allograft implantation

Immediately after allograft implantation and washout of the preservative solution and prostaglandin, there may be profound, transient systemic hypotension. Treatment requires fluid administration and α-adrenergic support. After implantation of the donor lung, there usually is an immediate reduction in PA pressures and an improvement in pulmonary compliance and gas exchange. This period may be followed by allograft dysfunction characterized by deteriorating gas exchange, decreasing pulmonary compliance, and elevated PA pressures. This is the result of noncardiogenic, reperfusion pulmonary edema. Two factors predispose this process: pre-existing pulmonary hypertension, which results in over-perfusion of the donor lung and a long ischemic interval, which enhances capillary permeability.

PEEP (5–15 cm H_2O) usually is necessary to maintain adequate gas exchange when allograft

dysfunction occurs. Increased capillary permeability and the lack of pulmonary lymphatic drainage in the allograft require judicious crystalloid administration. Excessively large tidal volumes should be avoided because over inflation of the allograft will contribute to elevated PA pressures through mechanical compression of the pulmonary vasculature.

If allograft dysfunction is severe, implantation of the second lung in BSSLT patients may require CPB. If CPB is not used, implantation of the second lung is managed as described for the first lung.

Indications for CPB

The decision to use CPB is individualized for each patient. The use of CPB may become necessary at any time during the procedure. The combination of a cardiac index < 2 L/min/m^2, $Svo_2 < 60\%$, mean arterial pressure (MAP) < 50–60 mmHg, $Sao_2 < 85$–90%, and pH < 7.00 despite aggressive ventilatory and pharmacologic intervention is an indication for use of CPB. CPB is not necessary for increased pulmonary artery pressures unless there is evidence of deteriorating RV function. TEE assessment of RV function is supplemented by use of CVP determinations. Increasing CVP, RV distension, worsening global hypokinesis, and new or worsening tricuspid regurgitation (TR) despite inotropic support with epinephrine, NE, or dopamine in combination with inhaled (NO 20–40 ppm) or intravenous pulmonary vasodilation (milrinone 0.5–1.0 μg/kg/min, nitroglycerin 0.5–5.0 μg/kg/min, PGE$_1$ 0.05–0.20 μg/kg/min, or PGI$_2$ 5–20 ng/kg/min) are indications for use of CPB. NE (0.01–0.10 μg/kg/min) is the most effective agent for maintaining coronary perfusion pressure in patients with RV hypertension but its use must be tempered with the knowledge that it may increase PVR as well.

TEE assessment of LV function is supplemented by use of pulmonary artery occlusion pressure (PAOP) determinations. Hypoxemia, hypercarbia, and reduced systemic blood pressure can all contribute to LV dysfunction. Progressive deterioration in LV function (new wall motion abnormalities, LV distension, new or worsening mitral regurgitation (MR)) despite aggressive

pharmacologic and ventilatory interventions is an indication for CPB.

A metabolic acidosis is difficult to treat because sodium bicarbonate administration will produce carbon dioxide, which must be eliminated by increased alveolar ventilation. Obviously, increasing alveolar ventilation often is not possible in these patients.

Post-CPB management

Preparations for terminating CPB are discussed in detail in Chapter 10. Particular attention must be paid to de airing the heart. Severe ventricular dysfunction may follow ejection of air through the coronary arteries. The RV is particularly at risk due to the anterior location of the right coronary ostia. TEE is valuable in guiding the de-airing process.

Patients undergoing HLT have a denervated heart and are managed in the post-CPB period in the same manner as that described for heart transplant patients.

RV function usually improves dramatically after lung implantation due to the immediate reduction in pulmonary artery pressures. Despite this, patients with *en-bloc* DLT, BSSLT, or SLT may require inotropic support. Patients requiring aortic cross-clamping and cardioplegic arrest are at particular risk for post-CPB right and left ventricular dysfunction. In addition, the presence of lung allograft dysfunction may contribute to post-CPB RV dysfunction as the result of elevated PA pressures.

Postoperative care

In rare instances, extracorporeal membrane oxygenation and independent lung ventilation may be necessary after SLT in patients with pulmonary hypertension secondary to reperfusion pulmonary edema. Postoperative independent lung ventilation with a DLT has been used for patients with SLT to minimize preferential ventilation and air trapping in the native lung in patients with obstructive lung disease. For these patients, the native lung has high compliance and air trapping can result in hyperinflation with subsequent displacement of the mediastinum and compression of the donor lung.

Differential ventilation with hypoventilation of the native lung has been used successfully to avoid this problem. Preferential perfusion of the donor lung occurs after SLT, especially for patients with pulmonary hypertension. In cases of severe V/Q mismatch, selective hypoventilation of the native lung combined with positioning the patient in the lateral position with the donor lung in the nondependent position may be necessary in the postoperative period. This will minimize over ventilation of the native lung and over-perfusion of the donor lung. In patients with SLT with a fibrotic native lung, positioning the patient with the donor lung dependent may help equalize ventilation to the both lungs.

Noncardiac surgery in lung transplant patients

As with heart transplant patients, lung transplant, and HLT patients may require surgical procedures. Some are purely elective, whereas others are likely to be urgent or emergent. Most surgical procedures are the direct result of complications of immunosuppressive therapy. These complications are listed Table 7.2. The incidence of complications requiring general surgical consultation and intervention in lung transplant patients is 16%. In addition, lung transplant patients suffer airway and vascular anastomotic complications that require operative intervention. The incidence of airway complications in SLT and BSSLT is 12–17% per anastomosis with an associated mortality rate of 2–3%. Nine percent of nonlethal airway complications require operative intervention. Similar statistics exist in pediatric patients. The most common intervention required is for treatment of bronchial stenosis. This usually involves flexible and rigid bronchoscopy for laser excision of granulation tissue, stent placement, or balloon dilatation.

Lung transplant and HLT patients present a unique set of management issues.

1 *Loss of cough reflex due to transection of vagal fibers.* This makes the patient with a transplanted lung prone to retention of secretions and at risk for pulmonary infections. The risk of aspiration should not be significantly increased, as the innervation of the larynx, epiglottis, and proximal trachea remain

normal. However, laryngeal nerve injury during dissection can result in loss of protective airway reflexes.

2 *Reduction in lung volumes.* Mild proportional reductions in all lung volumes are seen long term in patients after HLT, DLT, and SLT. These reductions are not due to reduced elastic properties of the transplanted lung but are secondary to the volume constraints of the recipient chest cavity and to the strength and efficiency of the thoracic musculature. In fact, the improvement in elastic recoil and the reduced chest wall distention that follow SLT for emphysema substantially reduce the work of breathing and dyspnea.

3 *Ventilatory response to carbon dioxide.* HLT and DLT patients have total vagal denervation, whereas SLT patients retain vagal innervation to the native lung. HLT, BSSLT, and SLT patients all increase minute ventilation in response to carbon dioxide rebreathing-induced hypercapnia. However, while SLT patients increase both tidal volume and respiratory rate, HLT and BSSLT patients exhibit an increase in tidal volume with little or no respiratory rate response.

4 *Ventilatory response to hypoxia.* Lung transplant patients have an increase in tidal volume and respiratory rate comparable to normal patients in response to hypoxia.

5 *Rejection.* Acute rejection of the transplanted lungs can be diagnosed both clinically and with transbronchial biopsies via a flexible bronchoscope. In the absence of clinical evidence of rejection (dyspnea, fever, diffuse perihilar infiltrate on chest radiograph) biopsies are performed at regular intervals postoperatively, Obviously, if clinical evidence of rejection exists, more frequent biopsies may be indicated to document rejection and to assess regression of histologic changes with treatment. Biopsies are graded from 0 to 4 based on histologic criteria.

Acute rejection of the lungs is very common; approximately 50% of patients experience an acute rejection episode in the first 3–6 months post-transplantation. Rejection of the heart in HLT patients, on the other hand, is uncommon. Because rejection of the heart and lungs is not synchronous, heart biopsies are performed in HLT patients

only if there is clinical evidence of heart rejection. Rejection is treated with oral or intravenous pulsed steroids. Persistent rejection unresponsive to steroids usually is treated with a lympholytic agent such as polyclonal antithymocyte globulin (ATG) or murine monoclonal antibody (OKT3).

1 *Bronchiolitis obliterans syndrome (BOS) and bronchiolitis obliterans (BO).* BOS is a clinical entity characterized by declining FEV_1, FEF_{25-75}, and FEF_{50}/FVC. BOS is graded based on the reduction in FEV_1 compared with the best baseline value (0: $FEV_1 > 90\%$ and $FEF_{25-75} > 75\%$; 1: FEV_1 66–80%; 2: FEV_1 51–65%; 3: $FEV_1 < 50\%$). BO is a pathologic diagnosis based on histologic evidence of fibrous scarring of membraneous and respiratory bronchioles with partial or complete obliteration of the lumen. BOS and BO are the main sources of morbidity and mortality after lung transplantation. The prevalence of BOS and BO for HLT, SLT, and BSSLT patients is at 25% at 1 year, 50–60% at 3 years, 60% at 5 years, and 80% at 10 years in large series. The survival rate for lung transplant patients is 76% at 1 year, 60% at 3 years, 49% at 5 years, and 24% at 10 years.

Once established, BOS and BO follow a progressively worsening course. Patients with BOS and BO ultimately develop severe obstructive pulmonary disease and progressive hypoxemia. Augmented immunosuppression may attenuate this downhill course and improve survival. In severe progressive cases, retransplantation is the only option. However, the results are not encouraging, with a 5-year survival of 45%, as BOS and BO usually reoccur within a short time.

The etiology is multifactorial with rejection and CMV infection both implicated. It is believed that an alloimmune injury occurs with subsequent release of immunologic mediators and production of growth factors that lead to luminal obliteration and scarring of the small airway. Monitoring for BO is accomplished with transbronchial biopsies or open lung biopsy when transbronchial biopsies specimens are equivocal.

2 *Response to drugs.* HLT patients have a denervated heart and have drug responses identical to those described for heart transplant patients.

3 *HLT patients.* These patients will have all of the cardiac problems outlined previously for heart transplant patients.

Anesthetic considerations for noncardiac surgery in patients post lung transplantation

1 Sterile technique is essential.

2 Patients with stenotic airways and patients with BOS and BO may exhibit air trapping and auto-PEEP.

3 Diminished cough reflex makes clearing of secretions difficult. Laryngeal damage will predispose to aspiration.

4 Lymphatic interruption necessitates careful fluid administration to avoid interstitial pulmonary fluid accumulation.

5 Placement of an ETT must take into account the position of the tracheal or bronchial anastomoses.

6 Patients with preoperative carbon dioxide retention may exhibit carbon dioxide retention for 2–3 weeks postoperatively as the central chemoreceptors reset.

7 HLT patients will present the same cardiac challenges as heart transplant patients.

8 Stress-dose steroid coverage should be administered to patients receiving steroids as part of immunosuppression.

Suggested reading

Bengel FM, Ueberfuhr P, Schiepel N *et al*. Effect of sympathetic reinnervation on cardiac performance after heart transplantation. *N Engl J Med* 2001;**345**:731–8.

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CHAPTER 8

Pericardial Disease

Effective perioperative care for patients with pericardial disease depends on a thorough understanding of the physiologic alterations the diseased pericardium imposes on the heart. This chapter reviews the normal physiology of the pericardium, followed by a discussion of the physiologic derangements caused by a pericardial effusion or a constricting pericardium. Diseases that can cause pericardial dysfunction will be discussed, including aspects of illnesses that affect anesthetic management. Finally, the anesthetic management of generic patients with pericardial tamponade and constrictive pericarditis will be reviewed.

The normal pericardium is a dual envelope that surrounds the heart and separates the chambers from the bordering chest wall, pleura, and great vessels. There is a visceral layer that is composed of mesothelial cells adherent to the epicardial surface of the heart, and a thicker, fibrous parietal layer that separates the heart from other thoracic structures. The pericardium contains approximately 25 mL of an ultrafiltrate of plasma. The oblique sinus lies behind the posterior wall of the left atrium (LA), where the pericardium is adherent to the vena cava and pulmonary veins. This defines an area of the pericardial space in which an effusion does not collect unless it is very large or under pressure. The transverse sinus is just inferior to the aortic arch and is often visualized with transesophageal echocardiography (TEE). The low compliance of the normal parietal pericardium is responsible for the pathophysiologic mechanisms seen in pericardial

tamponade and accounts for the difference in presentation in patients with either an acute or chronic effusion.

The normal pericardium is richly enervated and inflammation can result in severe pain or vagally mediated reflexes. The pericardium is an active structure providing myocardial stability, a potential barrier to infection and prostaglandin secretion modulating cardiac reflexes and coronary tone. Afferents from the pericardium travel via the phrenic nerve, entering the spinal cord at C4–C6. Pericardial pain often is symptomatically indistinguishable from a diaphragmatic source. The phrenic nerves travel along the lateral aspects of the pericardium, where they are subject to mechanical or cold induced injury during cardiac surgery. The presenting symptoms of pericardial diseases are related to the innervation of the pericardium and the location of adjacent structures. For example, a large pericardial effusion may present as dyspnea, dysphagia, cough, hiccups, or hoarseness due to compression of adjacent lung, esophagus, diaphragm, or recurrent laryngeal nerve.

There are two principle physiologic expressions of pericardial disease: effusion, with or without tamponade, and constriction. It is essential to realize that both pericardial tamponade and constrictive pericarditis produce ventricular diastolic dysfunction. An understanding of the physiology of these diastolic limitations will provide the anesthesiologist with the knowledge to safely anesthetize these patients.
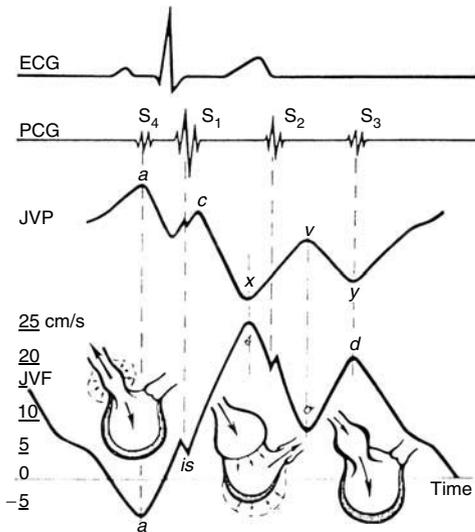
Fig. 8.1 Atrial wave forms, electrocardiogram (ECG) and phonocardiogram (PCG) drawing demonstrating the normal jugular venous pressure (JVP) waveforms and jugular venous flow (JVF). (Reprinted from Kalmanson D, Veyrat C, Chiche P. Atrial versus ventricular contribution in determining systolic venous return. A new approach to an old riddle. *Cardiovasc Res* 1971;**5**:293–302, with permission.)

Normally, venous return to the right side of the heart is accelerated during ventricular systole. This is due, in part, to a reduction in total intrapericardial volume (cardiac structures plus pericardial contents), which generates a pressure gradient from the vena cava to the right atrium. This increased rate of venous flow is represented in the right atrial (RA) waveform by the X descent (Fig. 8.1). The second surge in venous return occurs during the latter phase of atrial systole, when the tricuspid valve opens. This is visualized as the Y descent in the RA waveform (see Fig. 8.1). Analysis of the RA (or central venous) pressure waveform, right ventricular (RV) pressure tracing, and the pulmonary capillary wedge pressure can differentiate pericardial tamponade from constrictive pericarditis.

Pericardial effusion

The clinical manifestations and hemodynamic consequences of blood or other fluid in the
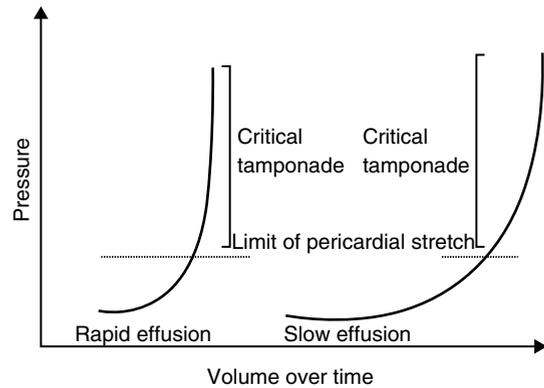
Fig. 8.2 Total intrapericardial pressure as a function of changing intrapericardial volume. Until a critical volume is reached, there is little rise in pressure. Once the critical compliance/pressure relationship is reached, however, small additional increments in volume result in large changes in intrapericardial pressure. (From Spodick DH. Acute cardiac tamponade. *N Engl J Med* 2003;**349**:684–90, with permission.)

pericardial space are determined primarily by the volume and rate of accumulation of the effusion. A slowly accumulating effusion allows time for the parietal pericardium to stretch resulting in sometimes very large, asymptomatic effusions. Conversely, acute pericardial effusions without parietal pericardial stretch can lead to tamponade with resultant cardiogenic shock and death. The compliance curve of the normal pericardium is seen in Fig. 8.2. In either acute or chronic pericardial effusion, when the volume exceeds the limits of pericardial stretch, there is a sharp elevation in intrapericardial pressure. There is a reduction in ventricular filling and stroke volume.

In the operating room environment, the pathophysiology of pericardial tamponade is often observed in acute, hemorrhagic pericardial effusions. This can occur in patients with traumatic cardiac injury, iatrogenic injury (catheterization and pericardiocentesis mishaps), aortic dissection, and post-cardiac surgery bleeding. There is associated hypotension, elevated venous pressure, and a small "quiet" heart (Beck's triad). Hypotension is due to a markedly reduced stroke volume caused by the compression of cardiac chambers by the effusion, especially on the right side. An elevation

in the central venous pressure (CVP) also reflects the restriction to cardiac filling imposed by the tense pericardium. The CVP waveform will demonstrate a prominent X descent, reflecting the accelerated venous return associated with ventricular systole and with the elevation of CVP. Ventricular systole reduces total intrapericardial volume by a quantity equal to the stroke volume, thereby allowing enhanced atrial filling. In addition, the RA waveform will demonstrate the absence of the Y descent, reflecting the increased ventricular end-diastolic pressure due to reduced distensibility induced by the pericardial effusion (Fig. 8.3a,b).

Pericardial tamponade can occur even in the absence of an elevated CVP if the patient is hypovolemic (low-pressure tamponade). This can occur when there is concurrent trauma with exsanguination, excessive diuresis in heart failure patients or in patients with effusion undergoing hemodialysis.

Cardiac echocardiography is the definitive diagnostic technique for documenting the presence and magnitude of a pericardial effusion. Transthoracic echocardiography can be performed rapidly at the bedside with no morbidity. TEE may provide superior image quality, but there is associated risk with insertion of the probe and patient sedation. In the operating room, TEE is indicated in patients undergoing pericardiocentesis and pericardiectomy. Other important imaging techniques include a chest X-ray (widened mediastinum and cardiac silhouette), computerized tomography, and magnetic resonance imaging.

The echocardiographic magnitude of a pericardial effusion is graded as large, moderate, or small. In the supine patient, effusions layer initially along the dependent surfaces of the heart. As the volume of the effusion increases, it appears apically, laterally, and then anteriorly. The typical echocardiographic features suggesting tamponade physiology resulting from an effusion are: RA collapse, which occurs just before ventricular systole; RV collapse in early diastole; and a reduction in RV dimensions during end-diastole (Fig. 8.4a–c). The interventricular septum is displaced posteriorly during early diastole as a consequence of the increase in RV size. The echocardiographic demonstration of RA and RV collapse in the presence of an effusion can be highly predictive
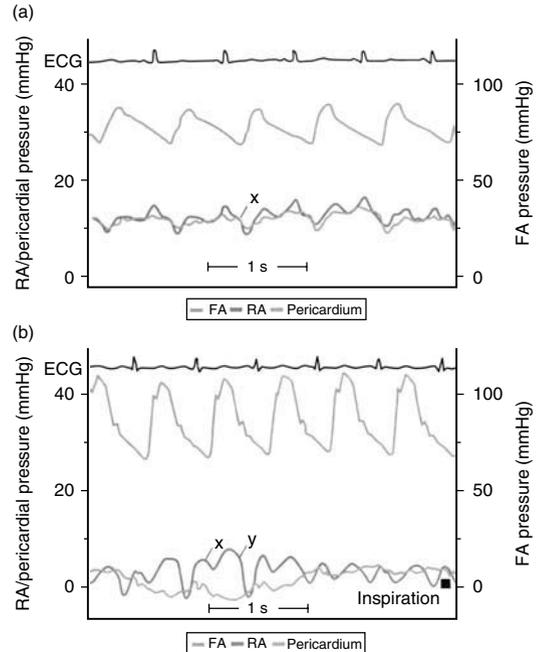
Fig. 8.3 (a) Simultaneous femoral arterial (FA), right atrial (RA), and intrapericardial pressure waveforms from a patient with pericardial tamponade. Note the exaggerated X descent, absent Y descent, equilibration of right atrial and intrapericardial pressures and systemic hypotension. (b) Right atrial pressure (RA) waveform with simultaneous electrocardiogram and femoral arterial pressure waveform (FA). RA tracing demonstrates timing of X and Y descents relative to cardiac cycle. Recordings were taken from a patient with pericardial tamponade after pericardiocentesis. Note the return of the Y descent. Also shown are simultaneous intrapericardial pressure (pericardium) and respiratory cycle (inspiration). ECG, electrocardiogram. (From LeWinter MM, Kabbani S. Pericardial diseases. In: Zipes DP, Libby P, Bonow RO, Braunwald E (eds). *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 7th edn. Philadelphia: Elsevier (Saunders), 2005:1757–80, with permission.)

of tamponade physiology, except in situations in which RV compliance is already low, as in preexisting pulmonary hypertension or a RV infarction. When wall stiffness does not allow intrapericardial pressure to exceed intracavitary pressure, chamber collapse will not be seen.

In the postoperative setting, this presentation may be difficult to discern. The formation of
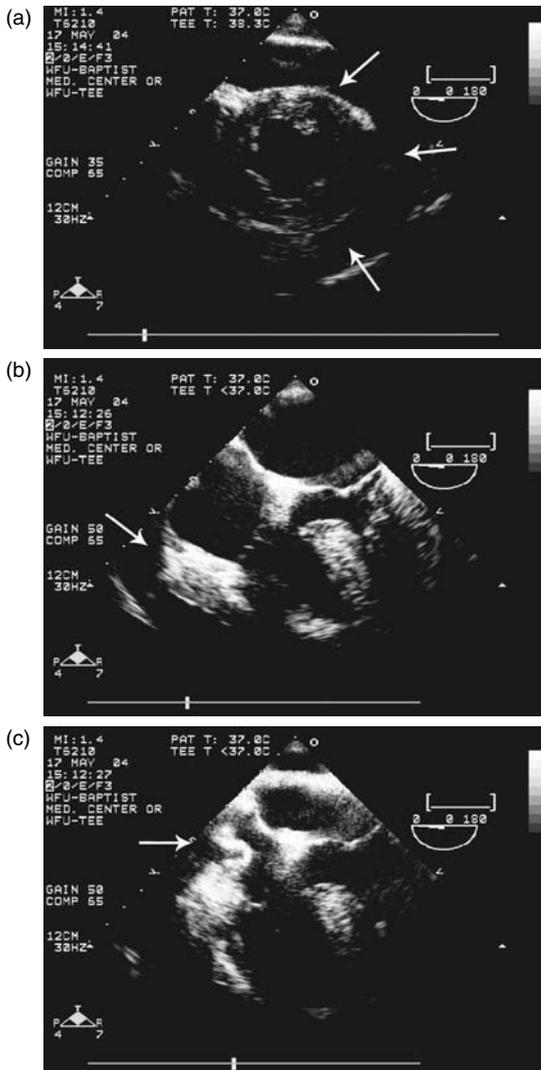
Fig. 8.4 Transesophageal (TEE) images of a patient with a larger pericardial effusion and right atrial collapse. (a) TEE image of the transgastric short-axis view demonstrating a large pericardial effusion along the posterior, lateral, and anterior aspects of the heart (white arrows). (b) TEE mid-esophageal view demonstrating the effusion along the border of the right atrium during ventricular systole (white arrow). (c) The same view showing right atrial collapse during ventricular diastole (white arrow).

pericardial clot alters the distribution of an effusion, as does the presence of adhesions between the heart, pericardium, and anterior mediastinum. In addition, in the setting of a reduced intravascular volume (i.e. hypovolemia from bleeding), patients will manifest a low CVP despite hemodynamically significant pericardial tamponade.

Tamponade physiology can be determined by cardiac catheterization. In patients with straightforward tamponade, RA catheterization reveals an accentuated X descent, absent Y descent, and an elevated CVP (see Fig. 8.3a,b). There will be equalization of RA, RV end-diastolic, and pulmonary capillary wedge pressures. These pressures will equal intrapericardial pressure, when measured during pericardiocentesis. These findings apply only to patients who do not have an underlying condition that alters right or left ventricular compliance, such as prior infarction, pulmonary hypertension, ongoing ischemia, or left ventricular hypertrophy.

Pulsus paradoxus, an exaggeration of the normal 5 mmHg decrease in systolic blood pressure with inspiration, is often seen in pericardial tamponade. A pulsus paradoxus is present when this difference exceeds 10 mmHg. Although a number of mechanisms for pulsus paradoxus have been postulated, echocardiographic studies have provided a coherent explanation. During inspiration, the negative pressure gradient between the periphery and the intrathoracic veins is increased. This increase in negative intrathoracic pressure is transmitted to the intrapericardial structures, accelerating the rate of venous return to the right-sided chambers of the heart. The resultant increase in RV dimensions causes a shift of the interventricular septum to the left, diminishing left ventricular diastolic filling and reducing left ventricular stroke volume and subsequent systolic arterial pressure (Fig. 8.5). This mechanism has been confirmed by pulsed wave Doppler echocardiography. Normally, there is a small increase (<25%) in early tricuspid blood flow velocity and a concomitant small decrease (<10%) in early mitral blood flow velocity with inspiration as compared with expiration. This pattern is exaggerated in the presence of tamponade with early tricuspid flow velocity increasing by as much as 130%, and early mitral flow velocity decreasing

Fig. 8.5 In some patients with pulsus paradoxus there is a septal shift during inspiration limiting left ventricular filling and reducing stroke volume. This may account for the exaggerated reduction in arterial pressure observed during inspiration. (From Goldstein JA. Cardiac tamponade, constrictive pericarditis, and restrictive cardiomyopathy. *Curr Probl Cardiol* 2004;**29**:503–67, with permission.)
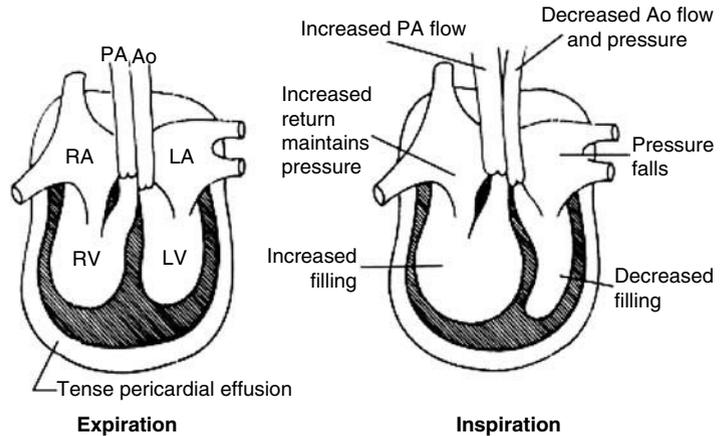
by as much as 50% with inspiration as compared with expiration.

Pulsus paradoxus can be observed in patients with disorders unrelated to pericardial tamponade. These include severe chronic obstructive pulmonary disease, asthma, and pulmonary embolism. Further, pulsus paradoxus may be absent in patients with pericardial tamponade who have coexistent cardiac pathology. Any condition that allows equalization of venous return between the right and left sides of the heart, such as an atrial septal defect, will prevent expression of a pulsus paradoxus. In addition, pulsus paradoxus will not be demonstrable whenever the interventricular shift that accompanies inspiration is prevented by conditions that reduce left ventricular compliance and distensibility such as left ventricular hypertrophy, left ventricular failure, infarction, ischemia, or aortic valve incompetence. Finally, pulsus paradoxus may not be demonstrable in patients with elevated RV end-diastolic pressure due to pulmonary hypertension or pulmonary outflow obstruction. The hemodynamic characteristics of cardiac tamponade are summarized in Table 8.1.

The therapy for hemodynamically significant pericardial tamponade is drainage. The recommended approach for removal of the effusion will depend on the acuity and severity of hemodynamic compromise. Percutaneous pericardiocentesis under ultrasound guidance and local anesthesia can be performed at the bedside and may be life-saving. Blind pericardiocentesis is

Table 8.1 The hemodynamic characteristics of cardiac tamponade.

- Diastolic dysfunction with impaired right heart filling
- Elevated right atrial pressure
- Prominent X descent on central venous pressure waveform
- Blunted or absent Y descent on central venous pressure waveform
- Equalization of diastolic pressures
- Diminished intracardiac chamber volumes
- Diastolic collapse of right atrium and ventricle
- Right ventricular septal shift during late diastole with inspiration
- Decreased blood pressure, cardiac output, and stroke volume
- Increased systemic vascular resistance
- Increased heart rate
- Pulsus paradoxus
- Exaggerated transvalvular flow with respiration

associated with a high rate of complications including pneumothorax, coronary artery or internal mammary artery laceration, and ventricular chamber perforation. These complications are even more likely if there are pericardial adhesions between the pericardium and anterior mediastinum, as in postoperative cardiac surgical patients, patients who have received chest irradiation, or when there is associated pericarditis. The success of pericardiocentesis is partly a function of the etiology of the effusion. Pericardiocentesis under fluoroscopic or

echocardiographic control is very successful for large malignant or uremic effusions, whereas pericardiocentesis for a postoperative effusion, even under fluoroscopic or echocardiographic guidance, has limited success.

Surgery for pericardial effusion and tamponade

The indications and timing of surgery for a pericardial effusion depend on the etiology of the effusion, its rate of accumulation, and the severity of the hemodynamic compromise.

There are three surgical options for permanent drainage of recurrent pericardial effusions: a pericardial window, a partial pericardiectomy, or a full pericardiectomy. A pericardial window creates continuity between the pericardium and pleura or the pericardium and peritoneum. It can be performed under local anesthesia, with the patient in the semi-sitting position. Its advantages include obtaining a pericardial specimen for pathologic examination and minimal physiologic trespass. For these reasons, it is the approach taken most often for patients with malignant pericardial effusions, whose life expectancy from their underlying disease is measured in weeks to months, or for patients with hemodynamically significant uremic pericardial effusions who are awaiting initiation or intensification of hemodialysis. The operative mortality is very low and is primarily a function of the patient's underlying disease. The drawbacks to a pericardial window include a significant incidence of re-accumulation of the effusion, as well as the potential development of constrictive pericarditis.

Pericardioscopy allows visualization of much of the epicardial surface, as well as examination of the intrapericardial structures. It is useful in directing intraoperative biopsy for diagnostic purposes. Because of the possibility of mechanically-induced dysrhythmias during periocardioscopy, preparations for emergent electrical cardioversion or defibrillation must be made before the induction of anesthesia.

In as many as 75% of patients undergoing full or partial pericardiectomy the indication for the procedure is refractory pericardial effusion. Of these, the most common etiologies are neoplastic disease and uremia. The incidence of pericardial tamponade in the period immediately after cardiac surgery may be as high as 1–5%. In these patients, mediastinal exploration for bleeding with clot removal is required when signs and symptoms of tamponade are present.

Anesthetic technique for pericardial effusion and tamponade

Patients undergoing a pericardiectomy for tamponade or recurrent effusion present a unique constellation of problems for the anesthesiologist. The anesthetic considerations in these patients are outlined in Table 8.2. It is essential that the cardiac anesthesiologist obtain a preoperative assessment of the effusion's magnitude, and more importantly, its hemodynamic effect. Except when the patient's condition does not allow time for preoperative echocardiography and/or catheterization, this information should be available and reviewed.

Ventricular filling in diastole is limited to a varying degree by the effusion. This can range from trivial compromise to cardiovascular collapse. Any maneuver that reduces venous return has the potential of further diminishing diastolic filling to the point at which stroke volume becomes inadequate to sustain life. Such maneuvers potentially include positive-pressure ventilation, hypovolemia, and systemic venodilatation.

Initial management of patients with an effusion

The degree of RA and RV collapse is assessed easily with echocardiography, and this information usually is available before induction. Patients with tamponade will require volume infusion to raise CVP and improve RV filling. It may be necessary to increase the CVP to 20 or 30 mmHg in some patients. Most patients with tamponade will have complete emptying of the RV and left ventricle (LV) in systole as a compensatory measure. If echocardiographic examination or previous history suggests systolic impairment, inotrope infusion is warranted to optimize stroke volume. An agent that is not associated with vasodilation (e.g. epinephrine) is indicated. Vasodilation must be avoided as it reduces

Table 8.2 Anesthetic considerations in pericardial effusion and tamponade.

- Administer preoperative sedation or analgesia with caution. These patients are often on the verge of cardiovascular collapse
- In cases of severe tamponade (i.e. patient in extremis or cardiovascular collapse), consider relieving the restriction to diastolic filling before the induction of anesthesia
- Administer positive pressure ventilation with caution until tamponade physiology has been relieved
- Maintain filling pressures high enough to overcome diastolic filling restrictions. The central venous pressure or pulmonary capillary wedge pressure may need to be 20–30 mmHg
- Avoid vasodilation – the resulting hypotension will worsen the diastolic filling dysfunction
- Avoid bradycardia – an elevated heart rate is a normal compensatory mechanism in cardiogenic shock
- Consider inotropic support in the interval before the tamponade is relieved (epinephrine)
- Prepare for a rebound in hemodynamics once the pericardial space is drained in acute tamponade. The sudden rise in blood pressure in patients with normal left ventricular function can be dramatic
- Carefully evaluate the necessity for invasive monitoring. Intra-arterial pressure monitoring is very helpful and can usually be accomplished pre-induction without delay. Central venous access is usually not indicated and may lead to unnecessary delays and increased morbidity in some patients. Intraoperative TEE is helpful in documenting and guiding the pericardial fluid drainage. In addition, TEE can monitor heart function during this interval of unstable and changing hemodynamics

TEE, transesophageal echocardiography.

RV filling and systemic blood pressure in patients who have a fixed stroke volume. Alpha-adrenergic support may be necessary to maintain perfusion pressure. Since the stroke volume is fixed, heart rate must remain normal to high to maintain an adequate cardiac output.

Patients in extremis should undergo pericardiocentesis with local anesthesia, preferably with echocardiographic or fluoroscopic guidance, before the induction of general anesthesia and initiation of positive-pressure ventilation. Although blind pericardiocentesis using an ECG lead on the exploring needle to detect injury current has been used in the past, echocardiographic guidance is now standard. Reference to the pericardial compliance curve (see Fig. 8.2) indicates that the entire effusion need not be drained before induction of general anesthesia. It is necessary to remove only a small volume of fluid to place the patient below the bend of the pericardial pressure–volume curve and effect a dramatic improvement in hemodynamics.

Premedication

Drainage of pericardial fluid is often an urgent or emergent procedure for patients with some degree of hemodynamic compromise. Extreme caution

with premedication is warranted. Midazolam in increments 0.5–1.0 mg is a reasonable approach.

Pre-induction

As for other cardiac surgical procedures, ECG leads for I, II, III, aV$_R$, aV$_L$, aV$_F$, and V$_5$ should be in place before induction. Adequate intravenous (IV) access with at least one large-bore (14- or 16-gauge) catheter should be obtained. Ideally, a radial artery catheter is placed before induction. Central venous access is usually not indicated in most patients.

Induction and maintenance

For the patient with a small, hemodynamically insignificant effusion the anesthetic management will be dictated primarily by the patient's underlying medical condition and the general principles outlined in anesthetic care. For patients with tamponade, great care must be employed if the decision is made to proceed without first relieving some of the effusion percutaneously.

The patient should be prepped and draped before induction in case emergent surgical decompression is needed after induction. Induction with agents with minimal cardiovascular effects is warranted. Etomidate 0.3 mg/kg in combination with fentanyl 1–3 μg/kg or sufentanil 0.2–0.3 μg/kg is

appropriate. Ketamine 1–2 mg/kg IV may be used because it maintains heart rate, contractility, and systemic vascular resistance (SVR). Caution must be exercised for patients who have high existing sympathetic tone because the negative inotropic effects of ketamine will predominate. Muscle relaxants should be chosen to offset any vagotonic effects of the narcotics. Amnesia can be maintained with benzodiapines or low doses of inhalational agents. After the effusion has been relieved, the choice of anesthetic agents should be guided by the patient's underlying disease state and consideration of postoperative ventilatory requirements.

A TEE probe can be inserted after induction and tracheal intubation. This allows online assessment of ventricular filling and contractility. In addition, the completeness of fluid evacuation can be easily assessed.

Drainage of a large effusion and relief of tamponade generally produces a marked improvement in hemodynamics. In some patients, this rapid alteration in fluid status may produce pulmonary venous congestion or pulmonary edema. This is due to the sudden increase in pulmonary venous return to the LA and LV. This is particularly likely if there is reduced LV systolic function or lesions that predispose an elevation of left atrial pressure (i.e. mitral regurgitation, mitral stenosis or poor LV compliance). Treatment will require vasodilation with IV nitroglycerin or a similar agent.

Constrictive pericarditis

Constrictive pericardial disease, like pericardial tamponade, causes a restriction to diastolic filling. In contrast to tamponade, however, all chambers are affected equally and the pattern of restriction to filling is distinctly different. The clinical manifestations of constrictive pericarditis may be quite subtle and easily mistaken for a restrictive cardiomyopathy.

Constrictive pericarditis is an inflammatory process caused by a myriad of processes. The more common causes are idiopathic, infectious (viral > bacterial), neoplastic, autoimmune, uremic, post-irradiation or surgery, post-traumatic, and post-myocardial infarction. Tuberculosis was the most common cause; however, this is no longer true in developed countries.

The underlying pathologic process in constrictive pericarditis is a thickened, fibrotic, scarred, and densely adherent pericardium, with the visceral and parietal layers often fused and occasionally calcified. The antecedent illness may be subclinical pericarditis, with fibrin deposition and subclinical effusion formation; a pericardial effusion with incomplete resorption or drainage; or an infiltrative or reactive process.

Constrictive pericarditis equally impairs late diastolic filling of all heart chambers. Over time, this results in symptoms of biventricular failure. Early in the course of the patient's illness, fluid retention partially compensates for the restriction in diastolic filling by maintaining an elevated central venous volume. This results in a clinical picture similar to right-sided congestive heart failure with ascites, pleural effusions, and peripheral edema. There is a reflex tachycardia serving to maintain stroke volume and cardiac output. Although myocardial systolic function usually is intact, epicardial compression of coronary arteries with resultant ischemia can occur. As stroke volume becomes limited due to inadequate preload, symptoms of chronic low cardiac output prevail, including weight loss, fatigue, muscle wasting, and cachexia.

The physical examination demonstrates an elevation in jugular venous pressure. Cardiac examination reveals a heart with a fixed point of maximal impulse (heart adhered to pericardium) and a pericardial knock. The pericardial knock is heard best in early diastole (the time of maximal filling in pericarditis) along the left sternal border. The knock occurs when the heart rapidly fills and there is abrupt cessation of flow when the pericardial restriction is encountered. The ECG in pericarditis changes as the disease progresses. In the acute phase there is diffuse ST segment elevation and PR segment depression. In later stages, T-wave inversion is present.

An additional finding in constrictive pericarditis is Kussmaul's sign, the apparently paradoxical rise in CVP with inspiration. In pericardial tamponade, the increase in negative intrathoracic pressure associated with inspiration is transmitted to the heart,
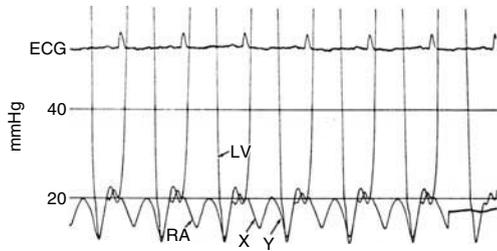
Fig. 8.6 Right atrial (RA) and left ventricular (LV) pressure waveforms obtained from patient with constrictive pericarditis. Prominent X and Y descents give characteristic "M" and "W" appearance to the right atrial pressure waveform. Note also that right and left heart pressures are elevated and equal throughout diastole. (Reprinted from Lorell BH, Grossman W. Profiles in constrictive pericarditis, restrictive cardiomyopathy, and cardiac tamponade. In: Grossman W (ed). *Cardiac Catheterization and Angiography*, 3rd edn. Philadelphia: Lea & Febiger, 1986, with permission.)

resulting in a transient decrease in CVP, stroke volume, and systolic pressure (pulsus paradoxus). In contrast, the thickened unyielding pericardium in constrictive pericarditis prevents the changes in intrathoracic pressure associated with ventilation from being transmitted to the heart. This restriction results in either no change or an increase in CVP at the time of inspiration. This difference in the effect of ventilation has important clinical implications for the anesthetic management of these two groups of patients.

Hemodynamic monitoring is important in patients with constrictive pericarditis and reveals characteristic findings. The CVP waveforms demonstrate prominent X and Y descents, imparting a characteristic "M" or "W" shape to the atrial pressure waveform (Fig. 8.6). There is early diastolic equilibration of pressure within all four chambers, revealed by the equalization of pressures in diastole between the atrium and ventricle. Ventricular filling is initially rapid, due to the increased venous pressure, which is seen as a sharp dip in intraventricular pressure. After the limit to filling imposed by the stiff, unyielding pericardium has been reached, further diastolic filling is halted abruptly. This appears on hemodynamic recordings as a "square root sign" or "dip and plateau," characteristic of constrictive pericarditis (Fig. 8.7a,b).
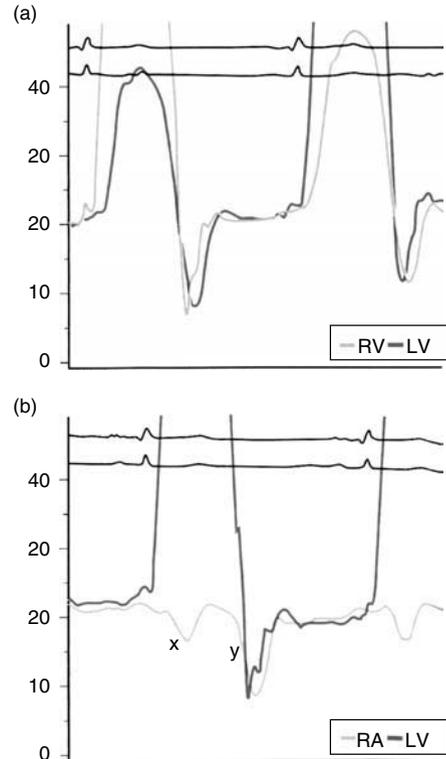
Fig. 8.7 (a) Right (RV) and left ventricular (LV) pressure tracings from a patient with constrictive pericarditis, demonstrating the rapid early diastolic filling, followed by the abrupt cessation of filling once the limit imposed by the pericardium has been reached. This has been described as a "dip and plateau" or "square root" sign. (b) Simultaneous tracing of LV and right atrial (RA) waveforms. Note also the equilibration throughout diastole of right and left ventricular pressures. (Reprinted from Vaitkus PT, Cooper KA, Shuman WP, Hardin NJ. Images in cardiovascular medicine: constrictive pericarditis. *Circulation* 1996;**93**:834, with permission.)

Table 8.3 summarizes the hemodynamic findings in constrictive pericarditis.

Etiology of pericardial disease

The hemodynamic alterations seen in pericardial disease will have a great impact on the anesthetic management of these patients. It is important to remember that the underlying illness causing the pericardial disease may have equal or even greater weight in the considerations necessary for a safe

Table 8.3 Hemodynamic characteristics in pericarditis.

- Diastolic dysfunction with abrupt diastolic filling resistance
- Elevation and equalization of diastolic pressures
- Prominent X and Y descent ("M" or "W" sign)
- Ventricular dip and plateau (square root sign)
- Decreased cardiac output, stroke volume
- Kussmaul's sign
- Pulsus paradoxus uncommon (approximately 33%)
- Pericardial knock present

anesthetic. This section will review the anesthetic implications of those disease states.

Uremia

Pericardial effusions may be seen in as many as 20% of patients with hemodialysis-dependant renal failure. Initiation or intensification of hemodialysis will resolve a hemodynamically significant effusion in two-thirds of patients. Operative drainage for uremic pericardial effusions should be reserved for patients who have not responded to augmentation for their dialysis regimen. The effusion may be hemorrhagic, and if left untreated, may evolve into constrictive pericarditis. Asymptomatic effusions are common in patients with chronic renal failure.

Renal failure alters the anesthetic management of patients with a pericardial effusion or constrictive pericarditis in a number of ways. The preoperative evaluation must include close scrutiny of the patient's coagulation capability due to the impairment of platelet function associated with uremia. Efforts to correct a coagulopathy should be undertaken before surgical intervention for constrictive pericarditis, because surgical hemostasis of raw, bleeding surfaces will be difficult to achieve in the presence of a bleeding disorder. Administration of desmopressin (DDAVP), 0.3–0.4 μg/kg may improve platelet function and coagulopathy in uremic patients.

Renal failure alters the kinetics of many anesthetic agents, especially nondepolarizing muscle relaxants. Cisatracurium is preferred in renal failure patients because of its independence from renal function for metabolic clearance. Although patients with chronic renal failure are adapted to a higher than normal baseline plasma potassium concentration, succinylcholine must be used with caution to avoid the possibility of further hyperkalemia.

Infectious pericarditis

Tuberculosis accounts for approximately 4% of acute pericarditis cases. Initial symptoms are variable with most patients presenting with a fever, weight loss, night sweats, pericardial friction rub, and pleural and pericardial effusions, with 40% demonstrating tamponade physiology. In most patients, tuberculosis pericarditis is self-limiting and clinically seems to be idiopathic in origin until other evidence of tuberculosis is discovered. Many patients with pericardial effusions will require pericardiectomy to treat a reaccumulation of fluid, in spite of initial pericardiocentesis. Up to one-half of patients with acute tuberculous pericarditis can develop constrictive pericarditis requiring pericardiectomy 2–4 months after presentation. Sputum culture is the most frequent positive diagnostic test in those patients who present with acute pericarditis. Acid-fast staining of pericardial fluid is infrequently positive, unlike culture results. Pathologic examination of pericardial biopsy specimens is occasionally positive. Untreated tuberculous pericarditis has a high mortality in the range of 30–40%. Some authors recommend early surgery for a pericardial window, to prevent effusion reaccumulation and possibly the development of late constriction, and early full pericardiectomy if a thickened pericardium is found at that time.

Viral pericarditis can be due to a variety of agents, including coxsackie B, echoviruses, varicella, mumps, hepatitis B, or cytomegalovirus. Viral pericarditis is more common in immunosuppressed patients. Bacterial agents usually are staphylococcus, pneumococcus, or meningococcus. Infection spreads from adjacent sites and occurs in association with hematogenously seeded bacterial endocarditis or from extension of a subdiaphragmatic abscess. Although acute bacterial pericarditis is unusual in the antibiotic era, purulent pericarditis occurs most often in immunosuppressed patients or in the setting of a preexisting effusion (such as with

uremia). Constriction may be a late consequence of incomplete drainage of a purulent effusion. Histoplasmosis is the most common fungal etiology. As with other infectious agents, pericardial involvement is most likely in those patients who are immunosuppressed. If the patient has received amphotericin B, consideration must be given to the possibility of impaired renal function and, less frequently, hemolysis or hypokalemia.

Idiopathic pericarditis

This is the most common cause of acute pericarditis in many series, and certainly includes many cases of viral pericarditis in which the virus is not identified.

Post-myocardial infarction pericarditis

Pericarditis within a few days to a week after myocardial infarction occurs in 5–10% of patients. The typical presentation is new chest pain, associated with an evanescent pericardial friction rub. New chest pain after a myocardial infarction must be differentiated from other, more serious complications of an infarction. The new chest pain of post-infarction pericarditis must be distinguished from that of unstable angina, an extension of the original infarction, or an additional infarction. History, serial ECGs, echocardiograms, and cardiac-specific isoenzyme concentrations will help make the diagnosis. New chest pain associated with a murmur may herald a post-infarction ventricular septal defect (VSD) or post-infarction mitral regurgitation, due to papillary muscle rupture or ischemia. The latter conditions usually are associated with hemodynamic compromise, whereas pericarditis after an acute infarction is not. If there is serious question of differentiating the more benign pericarditis from the other two conditions, echocardiography will resolve the issue quickly. If a patient with post-infarction pericarditis requires surgical intervention, appropriate anesthetic management will be determined primarily by the presence and severity of underlying myocardial ischemia, as well as residual myocardial systolic and diastolic function.

Connective tissue disorders

The systemic manifestations of systemic lupus erythematosus are protean. Pericarditis is the most frequent cardiac manifestation, with tamponade occurring infrequently, and constrictive pericarditis occurring rarely. Myocardial involvement may lead to conduction abnormalities or, infrequently, contractile dysfunction with direct impairment of systolic function. There may be direct involvement of cardiac valves in 20% of patients with lupus. In some, valvular dysfunction may be severe enough to be clinically significant. Rarely, an arteritis can result in clinically significant coronary artery disease. In addition, accelerated atherosclerosis in patients with lupus, in part a consequence of prolonged corticosteroid use, increases the risk of myocardial ischemia and infarction. Patients with lupus severe enough to necessitate operative intervention for effusive, pericardial, or valvular disease usually are receiving systemic steroid therapy and will need prophylactic corticosteroid therapy to protect them from a chronically suppressed pituitary–adrenal axis.

Nonsteroidal anti-inflammatory agents may interfere with platelet thromboxanes, resulting in a coagulation defect. However, fewer than 10% of patients with lupus will have a significant thrombocytopenia. Lupus patients may have a circulating anticoagulant, which presents as an otherwise unexplained prolonged partial thromboplastin time (aPTT). The lupus anticoagulant is a test-tube anticoagulant only interfering with the phospholipid tissue thromboplastins used for the laboratory determination of the partial thromboplastin time and is not associated with a bleeding tendency *in vivo*. In fact, patients with a lupus anticoagulant are at risk for thrombotic events. Therefore, long-term anticoagulation should be considered for patients with a lupus anticoagulant who are undergoing valve replacement.

Pulmonary involvement may result in restrictive lung disease, with a resulting diffusion defect and arterial hypoxemia. Chronic renal failure may be a late result of lupus, with well recognized implications for anesthetic management. Active lupus cerebritis may make conduct of a procedure such as pericardiocentesis difficult or impossible under local anesthesia.

Chronic constrictive pericarditis can occur as a complication of rheumatoid arthritis. Approximately one-third of patients with rheumatoid

arthritis will have pericardial thickening or effusion seen by echocardiography. Pericarditis usually is seen only in those patients with otherwise severe manifestations of their disease. In these patients, constrictive pericarditis usually improves after pericardiectomy. Conduction system abnormalities may be due to myocardial rheumatoid nodules or from inflammatory changes. Severe rheumatoid arthritis is associated with cervical spine disease including atlantoaxial subluxation and the potential for spinal cord or vertebral artery compression. There is possible involvement of the temporomandibular and cricoarytenoid joints further complicating airway management. Most rheumatic pleural effusions will spontaneously resolve, but some will require percutaneous or surgical drainage or decortication for recurrent pleuritis.

Malignancies

Malignant pericardial disease is associated most commonly with cancers of the breast and lung, Hodgkin disease, and other lymphomas. The spectrum of pericardial disease associated with malignancies ranges from acute hemorrhagic pericardial tamponade, to compression syndromes from tumor masses (Fig. 8.8), to constrictive physiology from a noncompliant pericardium encased with infiltrating

Fig. 8.8 This pregnant patient has marked ventricular compression from her liver (white arrow A), and her Hodgkin lymphoma tumor mass (white arrow B). This patient exhibited classic symptoms of a constrictive pericardial disease due to her pregnancy and extrinsic neoplastic pathology.

tumor. Unlike patients with radiation-induced constrictive pericarditis, patients with pericardial disease secondary to a malignancy may present with signs and symptoms of pericardial tamponade, constrictive disease, or a combination of both.

Large mediastinal masses, which can be seen in patients with Hodgkin lymphoma, pose significant risk of intrathoracic airway compression during the institution of positive pressure ventilation independent of endotracheal intubation. The physical presence of such masses should be sought by computerized tomography or magnetic resonance imaging before surgical intervention for pericardial disease. The functional significance of anterior mediastinal masses can be evaluated by flow–volume spirometry. If functional intrathoracic airway compression is present, there often will be a flattening of the expiratory phase of the flow–volume loop in the supine but not sitting positions. Furthermore, many such patients will report symptoms of air hunger or a sensation of chest compression in the supine but not in the lateral or sitting positions. When such signs or symptoms are present, serious consideration must be given to performing the surgical procedure under local anesthesia or after an effective course of radiation or chemotherapy to reduce the size of the mediastinal mass. Fiberoptic intubation with the patient appropriately sedated, but breathing spontaneously, also may reveal the presence of functional airway obstruction that might not be appreciated by routine chest X-ray or computerized tomography.

Current chemotherapy for Hodgkin lymphoma includes several agents with anesthetic implication including bleomycin (pulmonary fibrosis, respiratory failure possibly associated with high inspired concentrations of oxygen), doxorubicin (myocardial dysfunction), and prednisone (suppression of the pituitary–adrenal axis).

Chronic effusions or pericarditis can present months to years after radiation therapy, especially after mantle irradiation for Hodgkin disease, lymphoma, or other thoracic neoplasms. Typically, patients have received 4500 rads or more. The likelihood of pericardial injury varies with total dose of radiation administered, as well as the amount of heart included in the radiation portal. If the primary
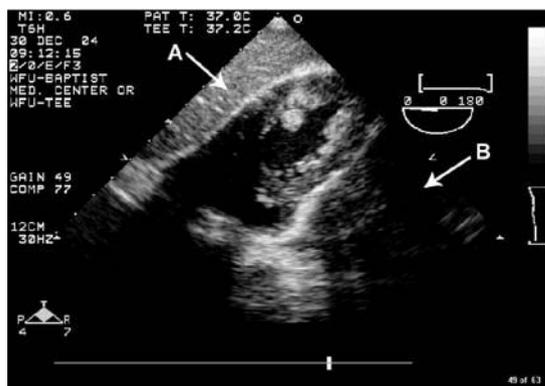
radiation-induced lesion is symptomatic pericardial constriction, then pericardiectomy should be considered. At surgery, the pericardium and adjacent tissue will be very friable and densely adherent; bleeding will be a major intraoperative consideration.

Prior cardiac surgery

Unlike tamponade from most other causes, in which echocardiography demonstrates the effusion to be homogenous, the collection of blood around the heart may usually be loculated (areas of clotted and unclotted blood). Echocardiographic findings typical of effusive tamponade such as RA and RV collapse, Doppler flow variation across the mitral and tricuspid valves with respiration and swinging of the heart within the effusion are not commonly seen in the postoperative period. Localized compression of each of the cardiac chambers, as well as of the pulmonary outflow tract has been reported. Pulsus paradoxus may not be seen due to the presence of hypovolemia. The presence of hemodynamic compromise (hypotension, low urine output, low cardiac output) in combination with the echocardiographic finding of a pericardial separation width of >10 mm has been shown to have 100% sensitivity for detection of postoperative cardiac tamponade.

Postoperative constrictive pericarditis is the most common cause of constrictive pericarditis requiring pericardiectomy, with an overall incidence of 0.2–0.3% of all patients undergoing cardiac surgery. Constrictive physiology may present in the immediate postoperative period or, more typically, months to years later. Povidone-iodine irrigation around the heart may be one etiologic factor in postoperative constrictive pericarditis.

Pericardial closure at the time of the original procedure decreases the incidence of perioperative cardiac tamponade from blood pooling, as well as subsequent constrictive pericarditis that results from organized hematoma around the posterior aspect of the heart. Closure of the pericardium greatly facilitates re-exploration during subsequent cardiac surgery by preventing the right ventricle and anteriorly placed grafts from becoming densely adherent to the anterior chest wall. This not only reduces the amount of bleeding during subsequent surgery but also makes catastrophic entry into cardiac chambers in re-exploration much less likely to occur. However, the pericardium is not closed routinely at the end of cardiac surgery by all surgeons for a number of reasons. For patients with dilated ventricles or those who have developed myocardial edema while supported by cardiopulmonary bypass (CPB), closure of the pericardium may restrict ventricular diastolic filling enough to be hemodynamically significant, especially if pre-existing left ventricular compliance is low (as with aortic stenosis). Furthermore, some surgeons are concerned that pericardial closure may kink or otherwise mechanically distort anterior or lateral coronary grafts, compromising both short-term flow and long-term patency.

Surgery for constrictive pericarditis

Patients with constrictive pericarditis do not present emergently for pericardiectomy. A thorough review of the cardiac catheterization data, echocardiographic examination and other data by the anesthesiologist before the induction of anesthesia is mandatory. Patients undergoing pericardiectomy for constrictive disease present a spectrum of anesthetic challenges different from the patient with pericardial tamponade. Unlike anesthetizing a patient with a pericardial effusion, during which the most difficult aspects of the anesthetic occur before induction and during the early part of an otherwise brief procedure, pericardiectomy for constrictive disease requires ongoing vigilance and often endurance during a long and difficult surgery.

Pericardiectomy for constrictive disease usually involves extensive dissection of tissue which is adherent to thin-walled cardiac chambers, the great vessels, coronary arteries, or aortocoronary saphenous vein grafts. Perioperative mortality can be as high as 10%, with hemorrhage being a significant or primary cause of death. Massive hemorrhage can occur from inadvertent entry into cardiac chambers, or the patient can bleed more slowly, but continuously, from raw dissected surfaces. It is imperative that venous access be adequate to guarantee timely volume, blood, and coagulation factor replacement, as needed. Usually, patients

undergoing pericardiectomy for constrictive disease are explored through a median sternotomy. Many will have undergone prior cardiac surgery, and although pump oxygenator standby is common, CPB is required in only 10% of such patients. The primary reason for avoiding CPB for constrictive pericardiectomy is the need for systemic anticoagulation and excessive. In patients with constriction secondary to prior cardiac surgery, dense adhesions around the heart may incorporate epicardial saphenous vein or internal mammary coronary grafts, and damage during pericardiectomy, with either bleeding or myocardial ischemia, can result.

Although some surgeons will approach the heart through a left lateral thoracotomy and remove pericardium from the LV only, most will use a median sternotomy and resect as much pericardium as is possible. Pericardial resection usually will extend over the entire anterior surface, exclusive of pericardium that overlies coronary artery grafts, laterally to the phrenic nerves, and inferiorly to the diaphragmatic surface. When CPB is not used, the anesthesiologist must expect frequent mechanically-induced dysrhythmias, and therefore have the capability of electrical cardioversion and defibrillation. In addition, frequent manipulation and displacement of the heart during the dissection will cause wide swings in stroke volume and blood pressure. If the extent of the dissection or the potential complications of reentering the chest of a patient who has undergone prior cardiac surgery requires the institution of CPB, then the anesthesiologist must be prepared to deal with ongoing hemorrhage, with surgical hemostasis difficult to achieve. Adequate reserves of red cells, as well as platelets and other blood products, must be immediately available.

Anesthetic technique for constrictive pericarditis

Table 8.4 outlines the goals for anesthetic management in constrictive pericarditis.

Premedication

The principle determinant of preoperative sedation will be the patient's underlying medical condition. For example, a young, otherwise healthy patient

Table 8.4 Anesthetic goals in constrictive pericarditis.

- Maintain adequate central venous volume
- Avoid bradycardia. Diastolic filling is limited by the constricting pericardium, and slow heart rates will result in low cardiac output
- Establish generous venous access. Prolonged, continuous bleeding is common and a major cause of mortality
- Aggressively treat platelet, red cell, and clotting factor depletion
- Positive-pressure ventilation is not detrimental; changes in intrathoracic compliance are poorly transmitted through a stiff, adherent pericardium
- Be prepared for a long, tedious surgery
- Transesophageal echocardiography (TEE) is indicated as there is expected hemodynamic instability and volume swings

with constrictive pericarditis secondary to mantle irradiation for Hodgkin disease years earlier can be premedicated as for any other major operation. The premedication of a patient with severe rheumatoid arthritis undergoing pericardiectomy for constrictive disease who also has an unstable cervical spine will be determined primarily by the need for sedation and topical anesthesia for an awake intubation. If the patient is undergoing pericardiectomy secondary to prior cardiac surgery, premedication will be determined primarily by the adequacy of myocardial revascularization and the presence of residual angina or ischemia. If the patient has residual myocardial ischemia, then premedication considerations are similar to those for primary revascularization.

Except when myocardial ischemia is likely, relative tachycardia need not be avoided. Increased heart rate maintains cardiac output compensating for the restriction in diastolic filling.

Preinduction

Patients are prepared as for coronary artery bypass graft (CABG) or valve surgery. Adequate IV access, including central venous access, is essential. A pulmonary artery catheter with thermodilution capability may be indicated, independent of the etiology of the constrictive disease. The ability to

measure cardiac output, as well as right- and left-sided filling pressures, is often useful, even though myocardial contractility will be normal in many patients with constrictive pericarditis.

Induction and maintenance

Myocardial performance is abnormal in constrictive pericarditis. There is diastolic dysfunction with abnormal filling resulting in either compensated or uncompensated heart failure. Anesthetic agents may further compromise these patients. The induction of anesthesia depends on the etiology of the patient's constrictive pericarditis and the anticipated duration of surgery. Induction may be similar to that used for coronary artery bypass surgery, if the duration of surgery is expected to be lengthy and significant residual ventricular dysfunction is anticipated in the immediate postoperative period. This would include a combination of fentanyl 10–25 μg/kg or sufentanil 1–3 μg/kg, together with a benzodiazepine and inhalational agent. If the etiology of constrictive pericarditis is secondary to prior coronary revascularization, then a significant potential for perioperative myocardial ischemia exists, and ongoing vigilance for myocardial ischemia must be maintained throughout the anesthetic. Sternotomy, dissection, and removal of the pericardium can injure entrapped coronary bypass grafts as well as a grafted internal mammary artery.

Unlike the patient with a pericardial effusion, changes in intrathoracic pressure are not transmitted to the heart through the thickened pericardium in constrictive disease. This eliminates the need to avoid positive pressure ventilation and makes induction and maintenance quite similar to that for coronary revascularization. The primary difference between surgery for revascularization and constrictive pericarditis is that the latter is of shorter duration, with a greater risk of severe hemorrhage. Many of these patients will require inotropic support during surgery and for a period of time after surgery. The patient with constrictive pericarditis may take as long as a month to regain normal hemodynamics and ventricular function.

Suggested reading

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CHAPTER 9

Anesthesia for Surgery of the Thoracic Aorta

Thoracic aorta lesions are among the most clinically challenging and acutely life-threatening lesions encountered by the cardiac anesthesiologist. The perioperative mortality ranges from 10 to 35%. Morbidity, including myocardial infarction (12%), respiratory failure (25%), stroke (3%), and renal failure (9%), remains significant despite aggressive intensive care interventions. The majority of these patients are older and approximately 30% have coexisting pulmonary, vascular, renal, and coronary artery disease placing them at the very highest risk. Despite these significant risks, in many patients operative care remains the best option for long-term survival. For example, the 2-year survival in patients with untreated thoracic or thoracoabdominal aortic aneurysm is 25%, whereas the expected 2-year survival after surgery is approximately 70%.

Aortic disease may present at any age, including the newborn. In younger patients, aortic disease usually presents secondary to congenital defects, Marfan disease (aneurysms), bicuspid aortic valve disease with aneurysm formation, and aortic transaction after blunt chest trauma. In older patients, the disease is associated with atherosclerotic peripheral vascular disease, hypertension, diabetes mellitus, and tobacco abuse.

All patients presenting for aortic surgery require an extensive evaluation by the anesthesiologist. In some cases, the surgery is urgent in nature (aortic transection and aortic dissection) and the evaluation is necessarily limited. Nevertheless, a brief review of all available laboratories, cardiac studies, and radiographic studies is crucial. This information will allow the anesthesia team to quickly assess risk and plan for the operative procedure. Management of preoperative medications, institution of beta-blocker therapy (if indicated), placement of invasive monitoring devices, and surgical strategies can all be determined in the preoperative period. Assembling an appropriate operative team, including perfusionists, nursing staff, and blood bank personnel, is required before any aortic procedure. The operative team must communicate closely before the surgery begins because line placement, drug selection, and blood banking preparation all depend on the extent of the proposed surgery. In any aortic procedure, the anesthesiology team must prepare for blood salvage techniques and be ready for potential massive transfusion of blood and blood products.

There are multiple approaches to the repair of aortic lesions that will affect the conduct of anesthesia. For example, the repair of a type A aortic dissection may require deep hypothermic circulatory arrest (DHCA) with retrograde cerebral cardioplegia. A descending aortic aneurysm repair may employ left heart bypass with monitoring and drainage of lumbar cerebral spinal fluid. This interplay between surgery and anesthesia places aortic surgery among the most challenging in cardiac anesthesiologist's domain.

Classification of aortic lesions

Aortic lesions may be classified into three pathophysiologic subtypes: aortic dissection, aortic

aneurysm, and aortic transection. Aortic transection and acute aortic dissections are surgical emergencies requiring immediate intervention. Aortic aneurysms and chronic aortic dissections often are repaired electively.

Aortic dissection

Acute aortic syndromes include aortic dissection, intramural hematoma, and symptomatic aortic ulcer. Aortic dissection is defined as a separation of the layers of the aortic wall with variable proximal and distal extension. In 90% of the cases, an intimal tear is identified, whereas in the remainder, no intimal tear is observed (Fig. 9.1a,b). In the absence of an intimal tear, it is thought that there is

Fig. 9.1 (a) Transverse section of the descending aorta showing the dissection flap and a point of connection between the true and false lumen (by color flow). (b) This is the same patient demonstrating a transesophageal echocardiography (TEE) long-axis view of the descending aorta. The dissection flap is clearly seen as the point of communication between the true and false lumen.

a rupture of the vasa vasorum with bleeding into the arterial media creating an intramural hematoma. The incidence of aortic dissection ranges from 5–30 cases per million people per year. Pain is the most common presenting symptom; however, there may be a wide range of presentations secondary to distal organ system involvement. The dissection flap may propagate antegrade and/or retrograde involving any side branch of the aorta. There may result malperfusion syndromes, tamponade, and aortic valve regurgitation.

A high clinical index of suspicion is required in order to make a timely diagnosis. Prompt evaluations with computed tomography (CT) scanning, magnetic resonance imaging (MRI), and/or transesophageal echocardiography (TEE) are all highly sensitive and specific modalities to diagnose aortic dissection. Risk factors for aortic dissection include hypertension, aortic medial disease, Marfan syndrome, congenital bicuspid aortic valve, aortic atherosclerosis, and blunt chest trauma. Approximately 70% of patients with aortic dissections have a history of hypertension. Cocaine abuse may be a causative factor in some otherwise healthy individuals. Frequently, the acute event precipitating the dissection is never determined. Iatrogenic injuries from surgical manipulation of the aorta and placement of diagnostic or therapeutic devices into the aorta may result in acute dissection. The ratio of males to females with aortic dissection is approximately 3:1, and the peak incidence is in the 5–7th decades of life. A dissection less than 14-days-old is defined as acute, and a dissection older than 2 weeks is defined as chronic. Approximately 33% of all thoracic aneurysms will present as an acute dissection. Anatomically, 60% of dissections involve the ascending aorta, 20% involve the transverse arch, and 20% involve the descending aorta.

Aortic dissections are described according to either the DeBakey or Stanford classification (Fig. 9.2). DeBakey classified dissections on the initial site of injury and the location of aortic extension. In type I and II dissections, the inciting lesion occurs in the ascending aorta. Type I lesions extend into the descending aorta, whereas type II lesions are limited to the ascending aorta. Both of these dissections may render the aortic valve incompetent

DeBakey Type I   Type II   Type III

Stanford   Type A   Type B

DeBakey
Type I   Originates in the ascending aorta, propagates at least to the
          aortic arch and often beyond it distally
Type II   Originates in and is confined to the ascending aorta
Type III Originates in the descending aorta and extends distally down the
          aorta or, rarely, retrograde into the aortic arch and ascending
          aorta
Stanford
Type A   All dissections involving the ascending aorta,
          regardless of the site of origin
Type B   All dissections not involving the ascending aorta
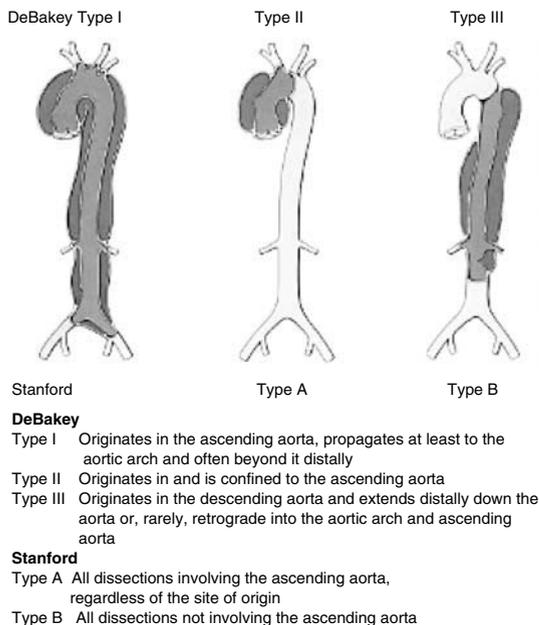
Fig. 9.2 The DeBakey and Stanford classification systems for aortic dissections. (From Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management. Part 1: From etiology to diagnostic strategies. *Circulation* 2003;**108**:628–35, with permission.)

due to retrograde involvement and deformation of the aortic valve annulus. In a type III dissection, the intimal tear is in the descending aorta. Type III lesions are further subdivided into subtype A, which has a retrograde extension into the proximal aortic arch, and subtype B, which has antegrade extension into the descending aorta. In the Stanford classification, type A dissections are those with any involvement of the ascending aorta, and type B dissections involve only the descending aorta distal to the left subclavian artery. Younger patients with underlying connective tissue abnormalities are prone to type A dissections; older patients will commonly present with a type B dissection.

Management of these patients depends on the location of the lesion and extent of the dissection. Medical management involves controlling blood pressure and myocardial contractility. This often is a temporizing measure until the patient can undergo surgical repair. Patients with a Stanford A lesion who undergo surgical repair have a significantly

lower hospital mortality rate than patients who are managed medically. In comparison, patients with a Stanford B lesion do not have a significant difference in mortality with either medical or surgical management (Fig. 9.3). The overall in-hospital mortality is approximately 30% for proximal dissections and 10% for patients with distal dissections. The predictors of in-hospital mortality include proximal dissection, age >65 years, shock, pulse, and neurologic deficits.

Aortic transection

Rupture of the aorta often results from nonpenetrating chest injuries sustained in trauma. Although prompt diagnosis and treatment are crucial for survival, this lesion may remain clinically silent and thus untreated. Anatomically, the heart and distal aorta are mobile components, whereas the aortic arch is fixed by the great vessels. During the deceleration phase of an acceleration–deceleration injury, the arch motion slows with the body while the remaining heart and aortic components continue in motion. This energy creates a shearing force on the aorta leading to injury. Up to 95% of aortic injuries will occur at the isthmus where the aorta is tethered by the ligamentum arteriosum. Additional sites of injury include the aortic hiatus in the diagram, mid-thoracic descending aorta, and origin of the left subclavian artery. Multiple sites of aortic injury occur in up to 20% of patients (Fig. 9.4a–d).

An estimated 10–15% of fatal automobile accident victims suffer aortic rupture. Eighty-to-ninety percent of these patients die at the scene. Among the 10–20% surviving 1 hour after the injury, an additional 30% die within 6 hours, 49% within 24 hours, and 72% within 8 days. Should the patient make it to surgery, the mortality rate for repair of this lesion is approximately 20%.

Aortic aneurysm

Aneurysms are classified by their etiology, location, and shape. Aortic pathology predisposing aneurysm includes atherosclerosis, cystic medial necrosis, syphilitic aortitis, trauma, postoperative false aneurysms, connective tissue disorders and
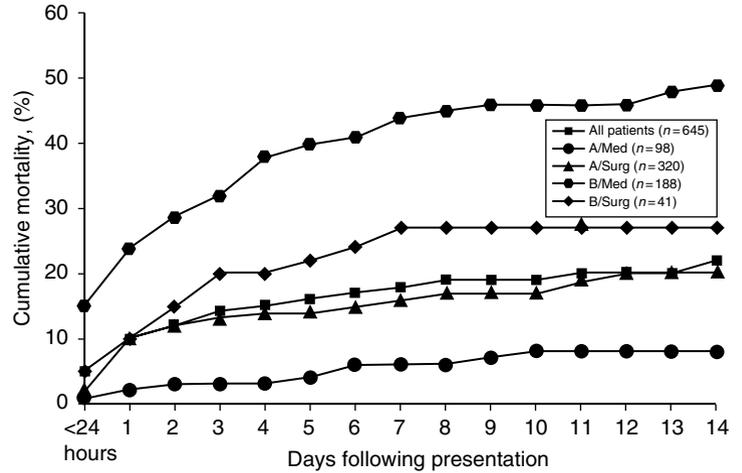
Fig. 9.4 Angiographic studies from four patients with aortic transection following motor vehicle accidents. The defect can have a number of anatomic locations and presentations. (a) Transection in the descending aorta. (b) Transection in the innominate artery. (c) Fusiform transection of the descending aorta. (d) Transection at the ligamentum arteriosum.

(a)   (b)
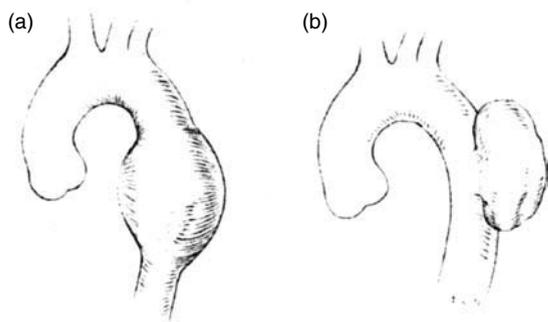
Fig. 9.5 Types of thoracic aortic aneurysms.
(a) Fusiform. (b) Saccular. (From Magilligan DJ Jr,
Ullyot DJ. The heart. I. Acquired diseases. In:
Way LW (ed). *Current Surgical Diagnosis and Treatment.*
Norwalk, CT: Appleton & Lange, 1991:359, with
permission.)

congenital aortic anomalies. Aneurysms with concurrent dissection are more common to the ascending aorta, whereas atherosclerotic aneurysms are primarily localized to the descending aorta. The DeBakey and Stanford classifications, which were discussed under aortic dissections, are commonly used to describe the location and extent of this lesion. Aneurysms are described morphologically as fusiform or saccular (Fig. 9.5a,b). Fusiform aneurysms have a higher operative mortality than saccular aneurysms. The male to female ratio is approximately 2:1, although women have a higher incidence of aneurysm rupture. This disorder tends to affect older patients with the mean age for diagnosis is in the sixth decade of life. A psuedoaneurysm occurs when there is a well-defined collection of blood and thrombus outside of the vessel wall. Exsanguination in a psuedoaneurysm is prevented by the surrounding connective tissue. This defect is sometimes referred to as a contained rupture or false aneurysm.

Larger aortic aneurysms, expanding aneurysms, and symptomatic aneurysms require surgical intervention. Patients with an aortic diameter >55 mm and without surgical intervention have a 2-year survival rate of <25%. The operative mortality for repair is 20–34% for acute dissections and 8–22% for chronic dissections. These patients have a high incidence of coexisting pulmonary, cardiac, and vascular disease complicating their intraoperative and postoperative care.

Diagnosis of aortic lesions

Aortic lesions often present with a constellation of symptoms suggesting the ongoing events. These symptoms are a result of expansion, dissection, or rupture of the aorta (Table 9.1). Severe anterior chest or back pain is the most common presenting symptom. Pain may occur directly from aortic expansion or from involvement of nearby structures. Pain may extend into the neck, shoulders, or abdomen. The intensity of pain may not correlate with the size of the lesion. Up to a half of patients with aortic lesions will be asymptomatic. Possible explanations for the lack of symptoms might include distracting injuries in the patient with trauma, a chronic disease process or other masking coexisting disease processes (i.e. cardiac ischemia). Any patient with a suspected aortic lesion requires immediate evaluation and diagnosis.

Chest radiography is a rapid and easily accessible method for diagnosing aortic lesions (Fig. 9.6). Table 9.2 lists eight classic radiographic signs consistent with aortic injury. Loss of the aortic knob contour is the most consistent finding on chest radiograph for patients with aortic injury. However, radiograph under penetration or venous mediastinal bleeding may cause false-positive studies. The next most common finding is superior mediastinal widening. Radiographs are assessed for the ratio of mediastinal to chest width (M/C). An M/C ratio of >0.25 is consistent with an aortic injury.

More sophisticated imaging techniques such as angiography, CT, MRI, aortography, transthoracic echocardiography (TTE), and TEE provide superior specificity and sensitivity of diagnosis over chest radiographs. Historically, aortography has been considered the "gold standard" in assessing lesions of the aorta. However, this modality is costly, invasive, and time consuming. Additionally, aortography subjects patients to potentially nephrotoxic contrast agents. Although aortography remains the superior diagnostic modality for coronary artery anatomy evaluation and branch vessel involvement, numerous studies have evaluated

Table 9.1 Presenting signs and potential etiologies for patients with thoracic aortic lesions. The frequency of these findings, as calculated from previous studies is indicated when obtainable.

Symptoms/clinical finding	Possible etiology	Frequency (%)
Chest or back pain	Active aortic dissection	>50
No clinical findings	Distracting injuries, chronic dissection	5–50
Angina	Aortic dissection into coronary arteries	5.8
Acute myocardial infarction	Aortic dissection into coronary arteries/thrombus	
Aortic regurgitation	Aortic valve injury/ascending arch injury	10–50
Assymetric upper extremity pulse amplitude	Arch interruption	9–45
Hypertension of the upper extremities	Distal aortic occlusion/rupture	37
Distant heart sounds	Pericardial tamponade/pericardial effusion	
Hypotension	Hypovolemia/aortic dissection	
Pulmonary edema	Lung contusion/myocardial contusion/acute aortic insufficiency	
Hemothorax	Traumatic injury/descending thoracic injury	3
Respiratory difficulty	Bronchial or tracheal compression/atelectasis/pneumonitis/acute aortic insufficiency with pulmonary edema rib fractures	8
Pneumothorax		
Confusion	Hypotension/acute head injury	
Horner syndrome		
Paraplegia	Spinal cord ischemia/trauma	2.3–2.6
Hemoptysis	Erosion of bronchus/pulmonary contusion trauma	
External chest wall abnormalities		35
Jaw pain	Referred secondary dissection	8.8
Hoarseness	Stretching/compression of laryngeal nerve	8.6
Dysphasia	Esophageal compression or erosion	5
Hematemasis	Esophageal compression of erosion	5
Melena	Direct intestinal injury/intestinal infarction	
Anuria or hematuria	Renal injury/renal infarction/hypovolemia	2–3

diagnostic alternatives with promising results (Table 9.3). Several series have shown MRI to be 100% sensitive and specific in diagnosing aortic lesions. Furthermore, MRI or CT in combination with TTE has equivalent sensitivity and specificity to aortography for evaluating such lesions. The limited ability of CT and MRI to evaluate the aortic valve is well supplemented by adding echocardiography.

TEE provides excellent resolution of intrathoracic structures in a rapid, relatively noninvasive fashion. For patients with a suspected thoracic aortic lesion, intraoperative TEE can make or confirm

Fig. 9.6 Posteroanterior roentgenogram of a patient presenting with a chronic transverse arch aortic aneurysm. Note the aneurysm at the aortic knob, the deviation of the trachea and elevation of the left hemidiaphragm. At surgery, the left phrenic nerve was stretched and splayed by the aneurysm. (From Commarata BJ. Anesthesia for surgery of the thoracic aorta. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:259–76, with permission.)

Table 9.2 Chest radiograph findings in thoracic aortic lesions.

Loss of aortic contour
Mediastinal widening
Displacement of the right paraspinous interface
Deviation of the trachea to the right
Displacement of the nasogastric tube to the right
Left hemothorax
Depression of the left mainstem bronchus below 40° from horizontal
Left apical cap

Table 9.3 Sensitivities, specificities, and predictive values of imaging techniques for the diagnosis of thoracic aortic dissection.

Technique	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Angiography	77–88	94–100	95–100	71–84
CT	80–83	88–100	83–100	71–88
MRI	100	100	100	100
TEE	97–99	98–100	98–100	96–99

CT, computed tomography; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; TEE, transesophageal echocardiography.
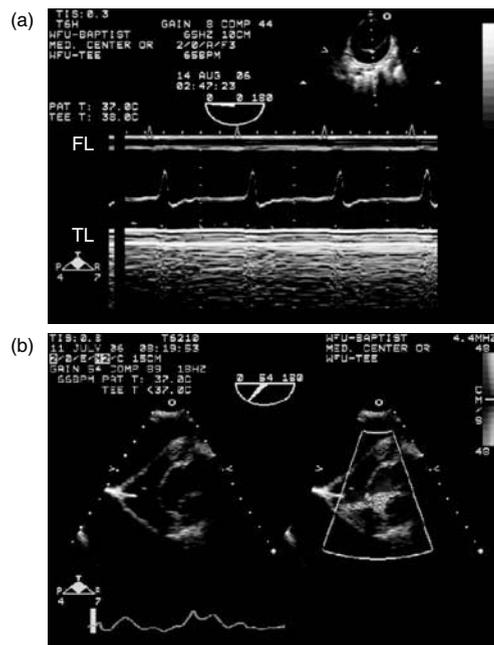
Fig. 9.7 (a) M-mode transesophageal echocardiography (TEE) of a dissection. The true and false lumen are clearly demonstrated. The true lumen will expand during systole. FL, false lumen; TL, true lumen.
(b) Pseudoaneurysm of the aortic root. The defect along the noncoronary cusp is clearly seen with color Doppler.

the diagnosis, locate dissection sites, identify the true and false lumen, evaluate the surgical repair, and assess the adequacy of perfusion during cardiopulmonary bypass (CPB) (Fig. 9.7a,b). In comparison with aortography, TEE provides a higher sensitivity,

significantly shorter examination time and thrombus identification. TEE is indicated intraoperatively to assess myocardial performance, signs of ischemia, heart valve status, and post-repair aortic integrity. For patients with trauma, TEE is highly sensitive and specific for evaluation of aortic injuries.

TEE has several limitations. Lesions of the distal ascending aorta are difficult or impossible to visualize with TEE secondary to interference of the trachea and left main stem bronchus. Examination of the subdiaphragmatic descending aorta is limited. Ultrasonic artifacts sometimes are confused with intimal tears and lead to an incorrect diagnosis. Despite these limitations, TEE is a widely used perioperative and intraoperative diagnostic modality for evaluating patients with aortic injuries.

Airway compression from aortic lesions

The aortic arch saddles the left main-stem bronchus as the vessel makes the transition from ascending to transverse to descending aorta (Fig. 9.8). Ultimately, the descending aorta assumes its location along the posterior wall of the bronchus. A thoracic aortic
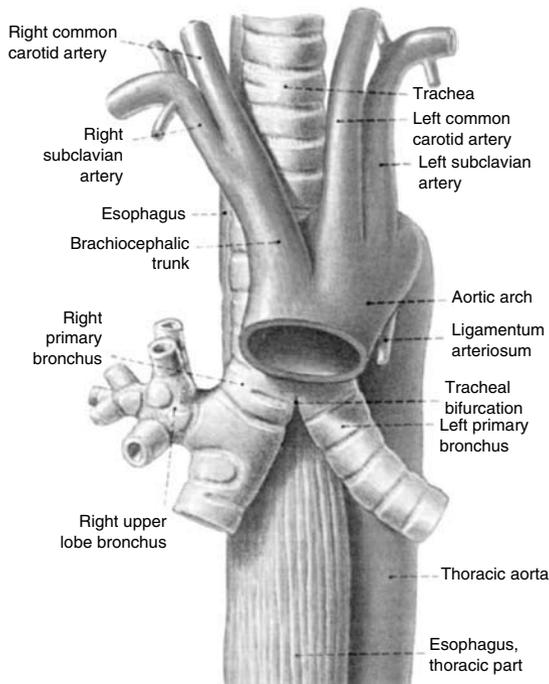
Fig. 9.8 The anatomic relationship of the esophagus, great vessels and the trachea. (Adapted from Clemente CD. *Anatomy: A Regional Atlas of the Human Body*, 2nd edn. Baltimore/Munich: Urban & Schwarzenberg, 1981:181, with permission.)

lesion can impinge upon and damage the trachea or main-stem bronchus, leading to tracheomalacia and respiratory distress (Fig. 9.9a,b) Thoracic aortic lesions usually cause compression or deviation of the left main-stem bronchus; however, the right main-stem bronchus and trachea also may be compromised.

Symptoms of airway compression may be exacerbated by changes in body position. A preoperative history and examination revealing stridor, wheezing, cough, or tracheal deviation should raise suspicion of aortic impingement and possible tracheomalacia. Unilateral vocal cord paralysis, which results from compression of the recurrent laryngeal nerve between the aorta and trachea, may present clinically as voice hoarseness. Preoperative pulmonary function testing with flow–volume loop analysis will reveal an intrathoracic obstructive process in severe cases. Radiographic studies may be useful in delineating the extent of airway compromise caused by aortic lesions.

Surgical approach and management

Patients with a suspected aortic dissection require immediate diagnosis, invasive monitoring, and treatment. Medical management focuses on pain and blood pressure control to reduce disease extension. Narcotics are effective for pain control, and a wide variety of vasoactive agents including beta-blocking agents, sodium nitroprusside, and angiotensin-converting enzyme (ACE) inhibitors can be used for blood pressure control. The therapeutic goal is to reduce the shear forces along the dissection flap. Patients with hemodynamic instability or significant comorbidity (i.e. pericardial tamponade, acute aortic regurgitation, shock) often require emergent intubation and preparation for surgery.

Ventilation

The location of the aortic lesion will dictate the surgical approach necessary for repair. Ascending and transverse aortic arch lesions are repaired through a median sternotomy without the requirement for one-lung ventilation (OLV). These patients can be
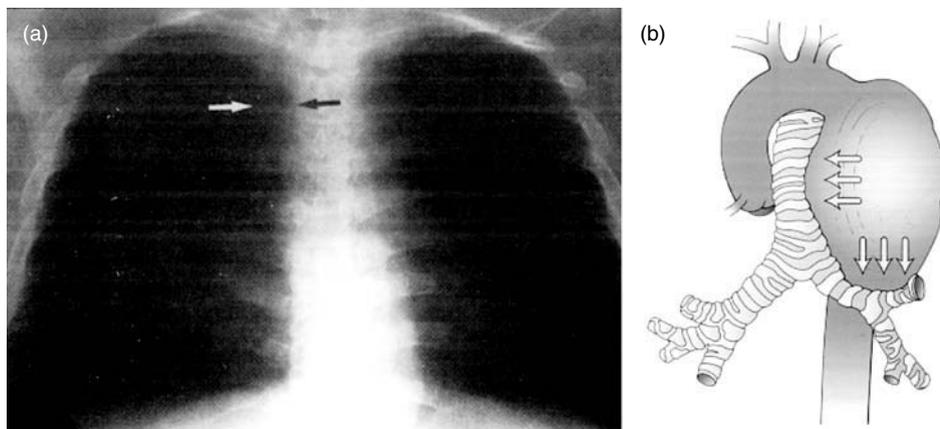
Fig. 9.9   (a) The trachea is markedly deviated secondary to an aortic aneurysm. (b) The trachea and left mainstem bronchus may be compressed from an aortic aneurysm. Left-sided double lumen endotracheal tubes may be difficult to place in these patients. (From Hunt D, Schwab F. Chest trauma. In: Rosen P, Doris P, Barkin R *et al.* (eds). *Diagnostic Radiology in Emergency Medicine*. St. Louis: Mosby Year Book, 1992:77–100 and Smith MS, Grichnik KP. Anesthetic considerations for lung transplantation and thoracic aortic surgery. In: Miller RD, Reves JG (eds). *Atlas of Anesthesia, Vol. VIII: Cardiothoracic Anesthesia*. Philadelphia: Current Medicine (Churchill Livingstone), 1999:6.1–18, with permission.)

managed with a single lumen endotracheal tube. Lesions of the distal transverse arch and descending aorta are repaired through a left thoracotomy. Surgical exposure is enhanced and trauma to the left lung is minimized by providing OLV with the left lung collapsed. Caution is indicated as the aneurysm may impinge on the trachea or bronchus resulting in tube malposition, airway damage, or aortic rupture.

Aortic cross-clamping

Aortic cross-clamping at some level is required for repair of all thoracic aortic lesions. The placement of the aortic cross-clamps for repair of various aortic lesions is summarized in Fig. 9.10(a–f). Aortic cross-clamping creates potential for end-organ ischemia. The organs at risk vary with the position of the cross-clamps.

Spinal cord ischemia is a potential consequence of aortic cross-clamping. Anatomically, the blood supply to the spinal cord is derived from several sources. A single anterior spinal artery arises from the vertebral arteries at the level of the foramen magnum and supplies the anterior two-thirds of the spinal cord. A pair of posterior spinal arteries arises from the posterior inferior cerebellar arteries and supplies the remainder of the cord. The vertebral, deep cervical, intercostal, and lumbar arteries also contribute to spinal cord perfusion as the anterior and posterior radicular arteries (Fig. 9.11). The largest radicular artery is the arteria radicularis magna or artery of Adamkiewicz, which supplies the majority of blood to the lower two-thirds of the spinal cord. The origin of this vessel is localized to T9–T12 in over 60% of patients. Therefore, in contrast to the upper spinal cord, the lower cord has a relatively limited blood supply with fewer collateral vessels and is at risk for ischemia during aortic cross-clamping or hypotensive periods. Ligation of intercostals arteries at the time of surgery is controversial. Ligation of lower intercostal arteries is associated with a greater the risk of neurologic deficit (Fig. 9.12).

Spinal cord perfusion pressure (SCPP) is the difference between mean arterial pressure (MAP) and the cerebrospinal fluid (CSF) pressure. Efforts to improve perfusion necessitate either an increase in MAP or a reduction in CSF pressure. Lumbar drains reduce CSF volume and pressure thereby augmenting SCPP (Fig. 9.13a,b). The literature is contradictory on the benefit of CSF fluid drainage in patients; however, many institutions routinely employ this
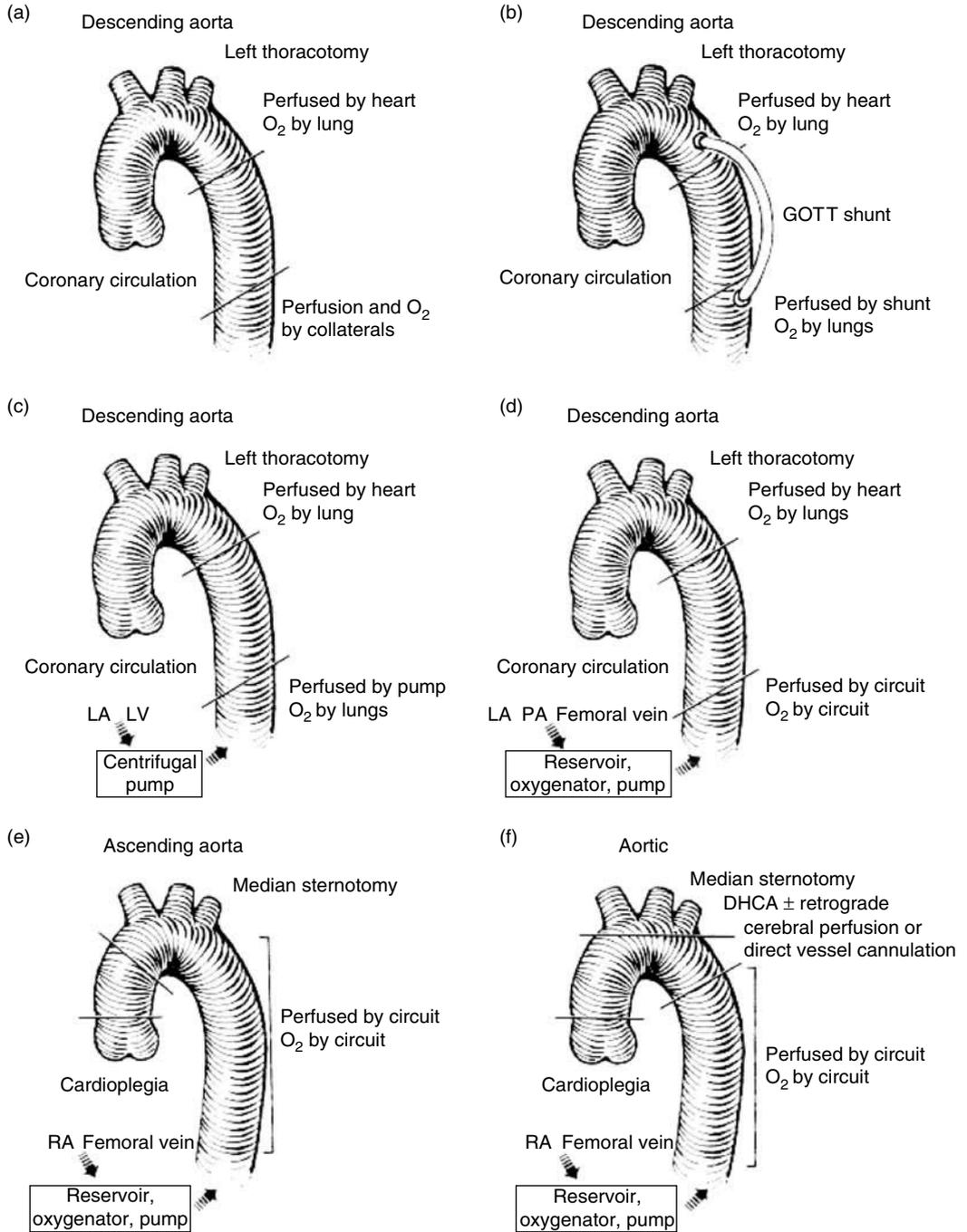
Fig. 9.10 Location of aortic cross clamp (—), surgical approach, and circulatory adjuncts for repair of aortic lesions. (a–d) Descending aorta. (e) Ascending aorta. (f) Aortic arch. (From Commarata BJ. Anesthesia for surgery of the thoracic aorta. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:259–76, with permission.)
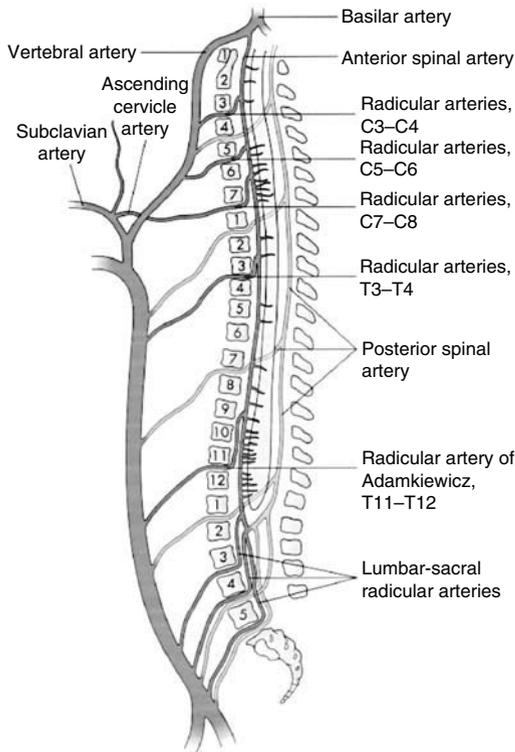
Fig. 9.11 Blood supply of the spinal cord. (From Smith MS, Grichnik KP. Anesthetic considerations for lung transplantation and thoracic aortic surgery. In: Miller RD, Reves JG (eds). *Atlas of Anesthesia, Vol. VIII: Cardiothoracic Anesthesia.* Philadelphia: Current Medicine (Churchill Livingstone), 1999:6.1–18, with permission.)

Fig. 9.12 Percentage of patients with neurologic deficit by intercostal artery and artery status. The lower to position of the artery on the spine, the higher the risk of deficit with ligation. (From Safi HJ, Miller CC III, Carr C *et al*. Importance of intercostal artery reattachment during thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 1998;**27**:58–68, with permission.)

modality with good result. There are numerous case reports of patients with new onset paraplegia after surgery with resolution of symptoms after CSF fluid drainage.

Some centers employ selective cooling of the spinal cord via lavage of the subarachnoid space. Corticosteroids, thiopental, N-methyl-D-aspartate receptor antagonists, papaverine, and magnesium also have undergone studies evaluating their protective effects on the spinal cord. Although many agents have shown success in the laboratory, clinical efficacy is difficult to establish. The single best intervention to reduce spinal cord injury is limiting the aortic cross-clamp time to an absolute minimum.

Among the most common perioperative injuries associated with repair of thoracic aorta lesions is postoperative paraplegia. The incidence of paraplegia after thoracic aortic repair ranges from 2–40%, depending on the site of the lesion and the degree of aortic involvement and aortic dissection. Patients with dissection have at least a twofold greater incidence of postoperative paraplegia when compared with those without dissection. Despite numerous animal and human studies, the precise mechanism of spinal cord injury during aortic cross-clamping remains uncertain. Contributing factors include aortic cross-clamp time, extent of aneurysm, presence of hypotension or shock, urgency of operation, aneurysm with concurrent dissection, diabetes, and advanced patient age. The spinal cord will tolerate a limited period of ischemia before irreversible cellular injury occurs (Fig. 9.14). A cross-clamp time of <30 minutes is usually safe and carries a minimal risk for postoperative paraplegia. Thirty to sixty minutes of cross-clamp time leaves patients more vulnerable to injury, whereas times >60 minutes approach a 90% incidence of paraplegia. Therefore, for repairs exceeding 30 minutes, patients may benefit from extracorporeal circulatory techniques to augment end-organ perfusion.

Somatosensory-evoked potentials (SSEPs) and motor-evoked potentials (MEPs) can be used to
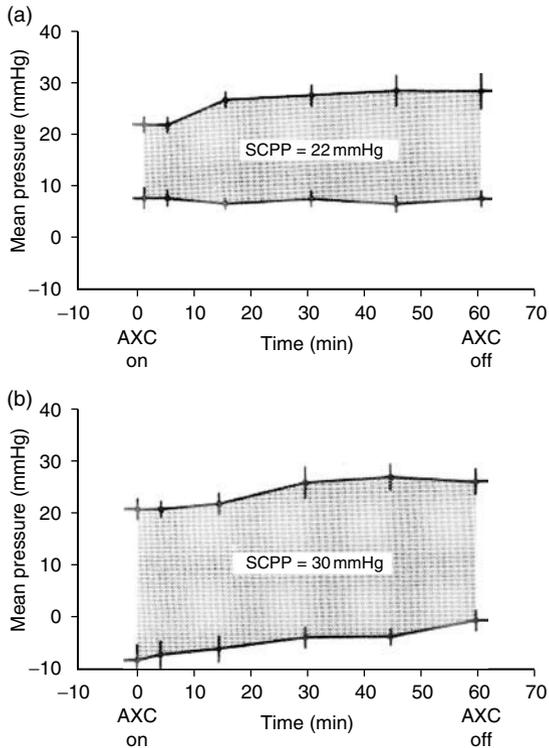
Fig. 9.13 Spinal cord perfusion pressure (SCPP) (distal aortic pressure, upper line; cerebral spinal fluid pressure, lower line) was lower in the control group of dogs (a) than in the cerebrospinal fluid (CSF) drainage group of dogs (b). AXC, aortic cross-clamp. (From McCullough JL, Hollier LH, Nugent M. Paraplegia after thoracic aortic occlusion: influence of cerebrospinal fluid drainage. Experimental and early clinical results. *J Vasc Surg* 1988;**7**:153–60, with permission.)

Fig. 9.14 Relative risk of ischemic spinal cord injury relative to aortic cross-clamp time. (From Svensson LG, Loop FD. Prevention of spinal cord ischemia in surgery. In: Bergan JJ, Yao JST (eds). *Arterial Surgery: New Diagnostic and Operative Techniques*. New York: Grune & Stratton, 1988:273–85, with permission.)

detect intraoperative spinal cord ischemia. Both evaluate amplitude and latency of signal transduction as a marker of neuronal integrity (Fig. 9.15). SSEP involves stimulation of upper or lower extremity peripheral nerves with signal observation at the cervical spine and scalp. The electrical signal, which is carried by the dorsal columns, assesses the integrity of afferent long tracts within the spinal cord. SSEP monitoring also may be helpful in assessing the adequacy of distal perfusion via extracorporeal circulation. This type monitoring is not routinely employed at all centers. Some data find no reduction in postoperative neurological deficits associated with the use of SSEP monitoring.

Also, the predominantly efferent anterior horn area seems to be most sensitive to ischemia. SSEP monitoring directly assesses the dorsal column but can only indirectly monitor these motor areas within the cord. SSEP monitoring cannot differentiate between peripheral and central ischemia causing observed changes. Motor-evoked potential monitoring detects the area of interest in the spinal cord, but it is technically difficult outcome data regarding its use is contradictory.

Renal insufficiency is common after procedures of the thoracic aorta with an incidence of approximately 10%. Reported risk factors for postoperative renal failure include reduced left ventricular (LV) function, need for reoperation, renal ischemic time exceeding 30 minutes, postoperative respiratory insufficiency, preexisting renal dysfunction, urgent or emergency procedures, and large volumes of blood loss during the procedure. Adequate hydration and renal perfusion pressure are important for renal protection. Several therapeutic interventions to avoid this complication are advocated; however, clinical efficacy is uncertain. Most clinicians agree that intraoperative urine output of 0.5–1.0 mL/kg/h is considered a measure of adequate renal perfusion and function; however, this assumption may be invalid. Common pharmacologic interventions include "renal dose" dopamine

Fig. 9.15 Somatosensory evoke potentials (SSEPs) and motor evoked potentials (MEPs) latency and amplitude determinations during aortic surgery. (From Meylaerts SA, Jacobs MJ, van Iterson V *et al.* Comparison of transcranial motor evoked potentials and somatosensory evoked potentials during thoracoabdominal aortic aneurysm repair. *Ann Surg* 1999;**230**:742–9, with permission.)

(2–4 μg/kg/min), fenoldopam, and mannitol. Mannitol induces an osmotic diuresis and acts as an oxygen-free radical scavenger. There are little data supporting the use of dopaminergic agonists for renal protection in this clinical scenario. The anesthesia team should focus on appropriate hydration prior to aortic cross-clamping and maintenance of distal perfusion pressure. Extracorporeal circulatory techniques may be beneficial in providing blood supply to an otherwise ischemic kidney during aortic cross-clamping.

Distal aortic arch and descending thoracic aortic lesions

These lesions are repaired through a left thoracotomy with the aid of OLV. A number of options exist in the management of these lesions.

Simple aortic cross-clamping

Conceptually, the simplest method for repairing distal aortic arch and descending thoracic aortic lesions involves cross-clamping the aorta and proceeding with the surgical procedure. As shown in Fig. 9.10a, the aorta is clamped proximally and distally to the lesion. Coronary and cerebral perfusion are uninterrupted by this arrangement and distal aortic perfusion is either temporarily interrupted or occurs via collateral vessels. Pulmonary blood flow continues normally. This method produces proximal aortic hypertension, which may produce LV afterload mismatch, LV distension, mitral regurgitation (MR), and myocardial ischemia. Pharmacologic management of LV function during this period is challenging. Aortic cross-clamp time ideally is limited to <30 minutes.

To provide flow to the areas below the distal clamp, several techniques have been developed. The concept behind all of them is diversion of blood from the heart for distribution to the distal aorta. This serves two purposes: it provides blood flow to the areas distal to the aortic cross-clamp, and it offers a nonpharmacologic method to control proximal aortic hypertension and LV distension during the cross-clamp period. The available methods are described below.

Passive shunting

The work of Gott and colleagues developed the tri-dodecymethyl ammonium chloride–heparin shunt consisting of sized, nonthrombogenic plastic tubing. The segment of tubing is placed into the aorta between the proximal clamp and the aortic valve, and the other end of the tubing is placed into the aorta beyond the distal clamp (Fig. 9.10b). This method has several advantages and disadvantages.

Advantages
● The shunt provides a method for distal perfusion without the need for systemic heparinization.
● The shunt is quickly and easily placed.

Disadvantages
● Precise control of shunted blood is impossible to regulate.
● Other problems include bleeding from the insertion sites, accidental dislodgement during the procedure, migration of the proximal end of the shunt across the innominate or left carotid artery, blockage of the surgeon's field of view, kinking of the shunt, embolic stroke, and death.

Left heart bypass

Left heart bypass removes a fraction of oxygenated blood from either the left atrium or the left ventricle for delivery to the distal aorta or femoral artery (Fig. 9.10c). A centrifugal pump is used in this arrangement. No oxygenator is needed because oxygenated blood from the left heart is used.

Advantages
- The amount of blood diverted from the left atrium to distal aorta can be precisely controlled. Communication with the perfusionist is essential.
- The system is relatively easy to insert.
- Minimal heparinization is needed (activated clotting time (ACT) = 150 seconds).
- Patients undergoing left heart bypass have smaller differences between the upper and lower extremity mean arterial pressure, higher intraoperative urine output, lower incidence of postoperative azotemia, and less blood loss in comparison with patients with a passive shunt.

Disadvantages
- No blood or fluid can be added to the bypass system because there is no reservoir. Large-bore peripheral or central venous access is a necessity.
- The absence of a heat exchanger does not allow the patient to be actively warmed or cooled.

A 4% incidence of postoperative renal failure is associated with left heart bypass, as compared with 9% and 11% for simple cross-clamping and CPB, respectively. However, left heart bypass has not eliminated complications from aortic surgery. A 3% early mortality rate, 1.5% reversible renal failure rate, and 2.3% incidence of permanent spinal cord injury have been reported despite using left heart bypass for patients undergoing repair of descending thoracic aortic lesions.

Partial cardiopulmonary bypass

Partial cardiopulmonary bypass (CPB) exists when only a portion of the systemic venous drainage to the heart is captured and returned to the CPB circuit (Fig. 9.10d). During partial CPB, the remaining portion of systemic venous return is to the right atrium. This blood makes its way to the pulmonary bed, where gas exchange occurs. The blood then returns to the left atrium and left ventricle, where it is ejected into the systemic circulation. For partial CPB to be effective the heart must be beating with ejection and the lungs must be ventilated. In the absence of ventilation, systemic venous blood that enters the right atrium ultimately will reach the systemic circulation without gas exchange having occurred. This will result in hypercarbia and hypoxemia.

The source of venous blood for this technique can be the femoral vein, left atrium, or pulmonary artery. The right atrium is poorly accessible from a left thoracotomy. Arterial outflow from the CPB circuit is delivered to a distal aortic site or to the femoral artery. The CPB circuit contains a venous reservoir, a heat exchanger, and an oxygenator. The oxygenator portion of the circuit is redundant when the left atrium is used as the source of venous blood.

Advantages
- The patient can be actively warmed. This is a major advantage if hypothermia becomes a problem.
- Blood and fluid can be added easily to the system via the venous reservoir.
- All shed blood can be scavenged by the cardiotomy suction and returned to the venous reservoir without the need for a cell-saver system.
- Precise control of the amount of blood diverted from the heart to the distal aorta is possible. The perfusionist partially occludes the venous drainage line with a clamp and controls arterial outflow with the pump head to determine the balance between proximal and distal blood flow. Close communication with the surgeon and perfusionist is essential.

Disadvantages
- Full systemic anticoagulation with heparin is necessary.
- Left heart bypass with partial CPB requires intensive vigilance to hemodynamics by both the anesthesiologist and the perfusionist. There is a shared circulation in place. It is possible for the perfusionist to divert too much blood from the heart thereby depriving the heart, head, and upper extremities adequate blood supply. The use of an upper and

lower arterial line as well as intraoperative TEE assist the team in assessing upper body and lower body blood flow.

Ascending aorta and aortic arch lesions

Ascending aortic and aortic arch lesions require full CPB. They are repaired through a median sternotomy. The clamps interrupt coronary circulation necessitating cardiac arrest and cardioplegia. All of the systemic venous drainage to the heart is captured and returned to the CPB circuit and subsequently to the patient. In lesions of the ascending aorta (Fig. 9.10e), arterial cannulation for return of oxygenated blood to the patient can be obtained in the distal ascending aorta, aortic arch, or femoral artery. This arrangement allows cerebral perfusion to be maintained. Venous cannulation usually is obtained via the right atrium.

If the aortic arch is involved, the great vessels to the head and upper extremities must be excluded (Fig. 9.10f). In this arrangement, there is no source of cerebral blood flow. As a result, some modifications must exist to provide either cerebral blood flow or to minimize the effects of cerebral ischemia during the cross-clamp period. In the absence of cerebral perfusion, mitigation of the effects of cerebral ischemia can be accomplished through the use of DHCA. Combining DHCA with continuous retrograde cerebral perfusion (CRCP) may extend the safe arrest limit to between 65 and 90 minutes and reduce the risk of neurologic injury during the surgical procedure. Continuous retrograde cerebral perfusion is accomplished by low pressure delivery (20–30 mmHg) of hypothermic (20°C), oxygenated blood from the CPB circuit to the superior vena cava with venting of the effluent via the aortic arch. This approach has many advantages, including its technical ease, ability to easily visualize blood returning from the great vessels, and the removal of particulate material from arterial sites.

Anesthetic technique for aortic surgery

Goals

1 Obtain a thorough understanding of the type and location of the lesion. Review the operative plan and prepare for use of OLV and adjuvant methods to provide distal perfusion when indicated.
2 Prepare for potential blood loss, including pharmacologic measures to reduce bleeding.
3 Determine necessary invasive and noninvasive monitoring.
4 Minimize hemodynamic perturbations during induction and maintenance of general anesthesia.

Evaluation

Review of the patient's medical history and prior radiographic, echocardiographic, and angiographic studies is critical for the anesthesiologist's understanding of preexisting conditions and current status. Information regarding the patient's prior lung status may provide insight into his ability to tolerate OLV for long periods. Evaluation of existing radiological studies will help determine the surgical approach, which will dictate monitoring and the need for OLV.

Control of both blood pressure and ejection velocity are the mainstays of hemodynamic optimization of the patient with an aortic lesion. Increased blood pressure and ejection velocity are capable of extending an existing dissection or causing aneurysm rupture. Aggressive control of blood pressure with vasodilators is likely to cause a reflex tachycardia and an increase in left ventricular change in pressure over change in time LV (dp/dt), thereby increasing ejection velocity and the sheer forces on the aortic lesion. This scenario is particularly likely in otherwise healthy patient with trauma who may already have a hyperdynamic LV secondary to blood loss and high catecholamine levels. Simultaneous control of both blood pressure and ejection velocity is best obtained with a combination of beta-blockers and vasodilators.

Premedication

Patients who present for elective repair of lesions often are hemodynamically optimized before surgery. Oral antihypertensive agents may include beta-blockers, calcium channel blockers, diuretics, and ACE inhibitors. Calcium channel and beta-blocking agents may be advantageous in providing simultaneous blood pressure and heart rate control. It is essential to continue all preoperative vasoactive

medications. Rebound tachycardia or hypertension from medication withdrawal may be disastrous. Treatment with anxiolytic agents assist in controlling hypertension and tachycardia and, therefore, minimize aortic wall tension.

In contrast, patients presenting emergently for repair of an aortic lesion are often poorly controlled. In the absence of hypotension or shock, beta-blocking agents along with vasodilators are indicated. Esmolol, metoprolol, or other beta-blockers are commonly used intravenous β-receptor-blocking agents in this setting. The advantages of esmolol include its high specificity for the $β_1$-receptor and its short duration of action. Options for vasodilator therapy include nitroprusside, nitroglycerin, trimethaphan, and halogenated inhalational anesthetic agents. Nitroprusside is a potent arterial vasodilator and may induce coronary steal and subsequent myocardial ischemia. Additionally, distal organ and spinal cord perfusion may be further compromised in patients receiving nitroprusside during aortic cross-clamping. Nitroglycerin is primarily a venodilator. This medication generally is easier to titrate and provides dilation of the large coronary arteries. However, nitroglycerin may not provide adequate arterial relaxation and blood pressure reduction. Both drugs may compromise oxygenation during OLV by blunting hypoxic pulmonary vasoconstriction. The clinical use of trimethaphan is limited by its side effect profile and tachyphylaxis.

Preinduction

Preparation for massive blood loss is critical. Bilateral upper-extremity 14-guage or 16-gauge intravenous catheters should be placed. Large-bore central venous access is required. The location for arterial line placement will depend on the location of the lesion.

Distal aortic lesions (Stanford type B) will necessitate placement of a right upper extremity (radial) arterial line. In repairing this lesion, the proximal aortic cross-clamp will probably be placed distal to the innominate artery. Therefore, the patency of the right subclavian artery will be preserved throughout the procedure.

Proximal aortic lesions (Stanford type A) will necessitate placement of a left upper extremity arterial line. The left subclavian artery probably will be distal to the aortic clamp site and should be used.

Femoral artery cannulation is used in conjunction with right radial artery cannulation in patients undergoing repair of aortic arch or descending thoracic aortic lesions with distal perfusion. The femoral artery cannula is necessary to monitor the adequacy of distal perfusion. Communication with the surgeon is necessary to determine which femoral artery can be used for monitoring pressure when a femoral artery also is going to be used for perfusion.

All necessary vasopressor and vasodilatory agents and six units of typed and cross-matched blood should be available in the operating room before induction. Antifibrinolytics are often used to reduce bleeding. Epidural catheters often are used in nonanticoagulated patients undergoing elective procedures. Caution must be exercised as inadvertent vascular placement of the catheter may delay the procedure. A test dose with 3–5 mL of 1.5% lidocaine with 1:200 000 epinephrine is important to confirm correct placement of the catheter. Confirming normal coagulation status before epidural catheter removal is essential.

Induction

There is no one anesthetic technique recommended for aortic surgery. The overriding factor in choosing any agent is hemodynamic control. For elective procedures, a narcotic induction with fentanyl (15–25 μg/kg) or sufentanil (1–3 μg/kg) will minimize hemodynamic disturbances. An intermediate-acting, nondepolarizing neuromuscular blocker such as vecuronium (0.1 mg/kg), rocuronium (0.6 mg/kg), or cisatracurium (0.2 mg/kg) will provide adequate muscle relaxation. Providing small doses of muscle relaxant during the narcotic infusion will minimize opioid-induced chest wall rigidity. Amnesia must be accomplished with benzodiazepines and/or inhalational agents.

Patients undergoing emergent procedures often require a rapid sequence induction. A sedative hypnotic such as sodium thiopental (3–5 mg/kg),

propofol (2.0–2.5 mg/kg), or etomidate (0.2–0.3 mg/kg) in combination with a smaller narcotic dose (fentanyl 10 μg/kg or sufentanil 1.0 μg/kg) will blunt the hemodynamic effects of laryngoscopy and will provide rapid induction of general anesthesia. Succinylcholine 1–2 mg/kg is used for rapid muscle relaxation, although large doses of nondepolarizing agents are an alternative. Protection of the airway and the potential for aspiration must be weighed against the undesirable hemodynamic response to direct laryngoscopy. The addition of beta-blockade and vasodilator therapy before laryngoscopy will help attenuate this undesirable response. After the airway is secured, deepening the anesthetic with a supplemental narcotic dose will improve hemodynamic stability.

Lesions of the ascending and aortic arch are managed with a single-lumen endotracheal tube of appropriate size. As discussed previously, aortic lesions may cause both tracheal and bronchial compression and caution should be exercised in tube placement. Repair of lesions of the distal aortic arch and descending thoracic aorta are facilitated by OLV. The options available for providing OLV are discussed in detail elsewhere. Many prefer a left-sided double-lumen endotracheal tube (DLT) unless collapse of the left main-stem bronchus has occurred. In these instances, a right-sided DLT is used. Achieving and maintaining proper positioning of the right upper lobe bronchus lumen can be problematic. This is particularly true when surgical manipulation of the tracheal-bronchial tree is necessary to mobilize the aorta. The left-sided DLT is placed using fiberoptic bronchoscopy. This approach virtually guarantees proper tube position. This approach, although very useful for all patients requiring DLT placement, is particularly important for patients with thoracic aortic lesions in whom unsuspected compression of the left main stem bronchus may exist. Blind advancement of the left-sided DLT under these circumstances may result in bronchial or aortic disruption. If unsuspected left main-stem bronchus compression is diagnosed with fiberoptic visualization, a right-sided DLT may be chosen.

A rapid-sequence induction with cricoid pressure may be necessary for the usual indications. Placement of a DLT under these circumstances may be difficult because of the DLT's large size and the propensity of the tracheal cuff to catch and tear on the patient's teeth as the tip of the tube is maneuvered to align with the larynx. When a potentially difficult DLT placement is anticipated in a patient requiring a rapid sequence induction, placement of a Univent tube (a single lumen tube with bronchial blocker in place) may be considered. The bronchial blocker can be directed into either main-stem bronchus. In addition to being easier to place in the trachea than a DLT, this tube eliminates the need for exchanging a DLT to a single lumen endotracheal tube at the end of the surgical procedure for patients who require postoperative ventilation. Disadvantages of this device include high bronchial cuff occlusion pressures and compromised ability to actively deflate, apply continuous positive airway pressure (CPAP) or suction the nondependent lung.

Intraoperative management

After induction of general anesthesia, additional venous access and monitoring lines are placed. Monitoring includes a 5-lead electrocardiogram (a V_5 lead is not possible in left thoracotomy patients and a modified V_{5R} can be employed), as well as arterial and pulmonary artery catheters. Intraoperative TEE should be employed if not contraindicated. If a DLT is used, the tube position should be checked with the fiberoptic bronchoscope after the patient has been positioned laterally to ensure that the tube remains optimally positioned.

Preparation for massive transfusion and red cell salvage before incision is recommended. Six units of compatible blood should be present throughout the procedure. Immediate availability of platelets and fresh frozen plasma also is crucial. A rapid transfusion device can be indispensable, particularly when full or partial CPB is not used.

Ascending aortic and aortic arch repairs

These lesions require full CPB and may require DHCA. There may be associated acute aortic insufficiency with an aortic dissection or a dilated aortic root. There may be pericardial tamponade and

myocardial ischemia if the dissection involves the coronary ostia.

Distal aortic arch and descending thoracic aortic lesions

If the approach is cross-clamp without distal circulatory support, vigorous afterload control with an intravenous or inhalational agent will be necessary. Reduction of MAP to approximately 20% below baseline with nitroglycerin or nitroprusside before aortic cross-clamping will minimize wall tension in the proximal aortic segment after the clamp is placed. Isoflurane also has been advocated as a vasodilatory agent in this setting. Patients have received up to 2.5 ± 0.3% isoflurane for hemodynamic control during aortic cross-clamping without negative consequence. Blood pressure

manipulation must always consider the potential detrimental effects on end-organ perfusion.

After cross-clamp application, blood pressure is maintained. Placement of the cross-clamp causes an acute increase in LV afterload and reduction in cardiac output. However, the pulmonary artery occlusion pressure and central venous pressure usually will remain unchanged. Diastolic dysfunction is common after cross-clamp placement. If pulmonary capillary wedge pressure (PCWP) increases with cross-clamp application, three etiologies must be entertained:

1 LV afterload mismatch with LV failure and dilation. LV dilation may be accompanied by development of a new V wave on the PCWP trace, suggesting functional MR. TEE is valuable in assessing LV size and function during this period. Left

Table 9.4 Clinical scenarios and therapeutic interventions during left heart bypass.

PP	DP	PCWP	TEE	Intervention
↑	↓	↑	↑ LVEDA	Increase pump flow
↑	↓	↓	↓LVEDA	Increase pump flow, volume infusion
↑	↑	→	→LVEDA	Vasodilation in conjunction with
		←	← LVEDA	volume infusion
↑	↑	↑	↑ LVEDA	Vasodilator, maintain pump flow, allow venous drainage to temporarily exceed arterial outflow when using partial CPB circuit
↓	↓	↓	↓ LVEDA	Volume infusion, temporary vasopressor support
↓	↓	↑	↑ LVEDA	Increase pump flow, inotropic support if resolution of LV distention does not improve LV performance and proximal pressure
↓	↑	↑	↑ LVEDA	Institution of inotropic support followed by incremental decrease of pump flow to avoid further LV distention
↓	↑	↓	↓ LVEDA	Decrease pump flow, if proximal pressure is low after desired distal pressure is reached then volume infusion

CPB, cardiopulmonary bypass; DP, distal pressure; LV, left ventricle; LVEDA, left ventricular end-diastolic area; PCWP, pulmonary capillary wedge pressure; PP, proximal pressure; TEE, transesophageal echocardiography.

ventricle dilatation with or without functional MR is an indication for immediate intervention with vasodilators. If LV dilation persists despite afterload reduction, initiation of inotropic support is warranted.

2 Myocardial ischemia may be accompanied by ST segment changes, but monitoring of ischemia is hampered by the lack of a V_5 lead. TEE can diagnose new regional wall motion abnormalities. Aggressive treatment of myocardial ischemia is indicated.

3 Impaired LV diastolic function due to impaired relaxation. Determination of impaired relaxation requires TEE to obtain Doppler spectra of the mitral valve inflow, pulmonary venous flow and tissue Doppler. Afterload reduction may improve diastolic function.

Acidosis may be treated with aggressive ventilation and bolus administration of sodium bicarbonate. A continuous infusion of bicarbonate (0.05 mEq/kg/min) during cross-clamping may be more efficacious. Large doses of sodium bicarbonate administered immediately before cross-clamp release will cause a transient iatrogenic hypercarbia, which when combined with a metabolic acidosis, can result in profound acidemia.

The physiologic changes associated with cross-clamp removal include hypotension, pulmonary hypertension, and metabolic acidosis. Preparation for cross-clamp removal will help minimize or attenuate these undesirable consequences. Several minutes before cross-clamp removal, the patient should be volume loaded to a PCWP of 10–20 mmHg. TEE can adequately assist with LV volume assessment. All vasodilating agents are discontinued and the cross-clamp is removed over a several-minute period. Hyperventilation before cross-clamp removal will help minimize the acidosis and the pulmonary hypertension associated with clamp removal. Despite these measures, patients may require variable periods of vasopressor support after removal of the aortic cross-clamp. Intractable hypotension after cross-clamp removal is an indication for reapplication of the cross-clamp.

If a shunt or assisted circulatory method is used, attention to the proximal and distal perfusion pressures is critical. In the case of passive shunts, attention is focused on adequacy of flow and patency of the shunt. Little control of proximal and distal pressure is possible. Proximal hypertension with the shunt patent requires pharmacologic interventions as described for simple cross-clamping. Distal hypotension with a patent shunt is problematic. Interventions to elevate proximal blood pressure with vasopressors and volume infusion may elevate distal pressure; however, such interventions may produce unacceptably high proximal pressures.

Left heart bypass and partial CPB provide better proximal hemodynamic control and more predictable distal perfusion than a passive shunt. With left heart bypass and partial CPB, the easiest initial approach is to decide, in conjunction with the perfusionist, the amount of flow that will be diverted to the distal aorta after cross-clamp application. This depends on the size of the patient and the desired distal perfusion pressure. Usually, distal perfusion pressure is maintained at 40–60 mmHg. Remember, it is essential to ensure adequate LV volume for heart and great vessel perfusion.

After this has been established, the balance of proximal and distal pressure is fine-tuned and managed as shown in Table 9.4 using proximal pressure, distal pressure, PCWP, and TEE.

Suggested reading

Campos JH. An update on bronchial blockers during lung separation techniques in adults. *Anesth Analg* 2003;**97**:1266–74.

Hagan PG, Nienaber CA, Isselbacher EM *et al*. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. *JAMA* 2000;**283**:897–903.

Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. *Chest* 2002;**122**:311–28.

Management of Cardiopulmonary Bypass

The cardiac anesthesiologist is integrally involved with commencing, maintaining, and terminating cardiopulmonary bypass (CPB). It is essential for the anesthesiologist to have a working knowledge of the CPB circuit to aid the surgeon and perfusionist in diagnosing and treating the problems that may be associated with extracorporeal circulation.

The CPB circuit

The CPB circuit is intended to isolate the cardiopulmonary system so that optimal surgical exposure can be obtained for operations on the heart and great vessels. For this isolation to be effective, the CPB circuit must be able to perform the functions of the intact cardiopulmonary system. At a minimum, the circuit must be capable of adding oxygen and removing carbon dioxide from blood and of providing adequate perfusion of all organs with this blood. In addition, the circuit must be able to fulfill these requirements without doing permanent damage to the cardiopulmonary system, the blood, or any of the patient's end organs. Substantial differences exist between adult and pediatric CPB and these are summarized in Table 10.1 and are addressed through this chapter. The components of a typical CPB circuit are illustrated in Fig. 10.1. The components of the circuit are described in the following sections.

Venous drainage

For the cardiopulmonary system to be isolated, all venous return to the heart must be made

Table 10.1 Comparison of adult and pediatric cardiopulmonary bypass.

Parameter	Adult	Pediatric
Minimum CPB temperature	Rarely <25–32°C	Frequently 15–25°C
Use of DHCA or RLFP	Rarely	Frequently
Pump prime		
Dilution of blood volume	25–33%	100–200%
WB or PRBC added	Rarely	Usually
Perfusion pressure	50–80 mmHg	20–50 mmHg
pH-stat management	Rarely	Usually, at temperature below 28–30°C
Glucose management		
Hyperglycemia	Frequently, requires insulin	Occasionally
Hypoglycemia	Rarely	Occasionally

CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; PRBC, packed red blood cells; RLFP, regional low flow perfusion; WB, whole blood.

available to the CPB circuit. Blood is collected from the venous circulation and then drains by a siphon into a reservoir that lies on or near the floor well below the patient. The pressure gradient for venous drainage (cm H_2O) is the height difference between the RA and the venous reservoir. The flow rate of venous blood (venous return) is determined
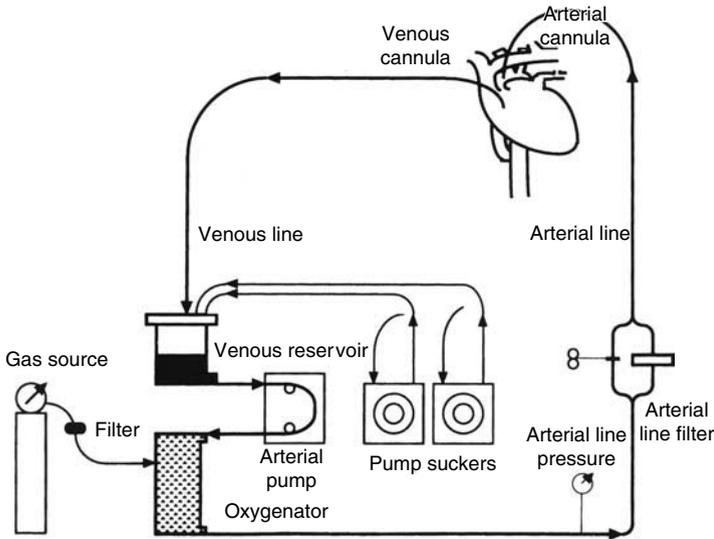
Fig. 10.1 A typical cardiopulmonary bypass (CPB) circuit.

by this pressure difference and by the resistance in the venous drainage system (cannula and tubing). For a given mean systemic venous pressure and venous resistance, maximum venous return is reached when the right atrial (RA) pressure falls to zero. When the RA pressure is less than zero the superior vena cava (SVC) and inferior vena cava (IVC) collapse and the heart acts as a Starling resistor.

Total (also complete or full) CPB

Total CPB exists when all of the systemic venous drainage to the heart is diverted to the CPB circuit. Total CPB is best accomplished with either direct cannulation of both the SVC and IVC or with use of two-stage single venous cannula in the RA.

● *Direct cannulation of the SVC and IVC.* This technique is necessary for all procedures that require opening of the RA or right ventricle (RV). It is also commonly used in procedures where retraction of a completely empty RA may facilitate surgical exposure (mitral valve exposure via the left atrium (LA)). Normally all systemic venous return can be captured via cannulation of both the SVC and IVC. In children with congenital heart disease, capturing all sources of systemic venous return may be problematic. Other sources of systemic venous return may exist such as a persistent left SVC draining

to the coronary sinus. In children with hetrotaxy syndrome there may be an interruption of the infrahepatic IVC with the hepatic veins draining directly to the floor of the right-sided atrium and azygous or hemi-azygous continuation of the IVC draining to a right- or left-sided SVC. For total CPB, once the cavae (and other sources of systemic venous return) are cannulated, surgical tourniquets or tapes are passed around the external circumference of the vessels. When these tourniquets are tightened around the cannulas the right heart can be isolated completely and subsequently opened without entrainment of air into the venous circuit or obscuration of the surgical field by venous blood. During delivery of antegrade cardioplegia, it is essential that at least one tourniquet be left un-tightened to allow egress of cardioplegia solution from the coronary sinus without distention of the right atrium. A larger cannula is used in the IVC as compared with the SVC, because a larger portion of systemic venous return (two-thirds) is from the IVC.

● *Two-stage venous cannula in the RA.* The single-cannula system is satisfactory for procedures that do not require opening the RA or RV, such as coronary artery bypass grafting or aortic valve replacement. Venous drainage is accomplished with one larger bore cannula with two orifices inserted via an incision in the RA appendage. One orifice

(32–36-French outer diameter) lies directly in the IVC and the other (40–51-French outer diameter) lies in the RA proximal to the SVC–RA junction. Coronary sinus and persistent left SVC return is collected continuously via the orifice that lies at the SVC–RA junction.

The vast majority of operative procedures in children require the use of either total CPB or deep hypothermic circulatory arrest (DHCA). Venous cannulation for DHCA is usually accomplished with a single large venous cannula in the right atrium. Once cooling is complete and circulatory arrest commences the cannula can be removed to allow maximum exposure.

Partial CPB

Partial CPB exists when only a portion of the systemic venous drainage to the heart is diverted to the CPB circuit. During partial CPB, the remaining portion of systemic venous return is to the RA. Ideally, this blood makes its way to the RV and pulmonary bed, where gas exchange occurs. The blood then returns to the LA and left ventricle (LV), where it is ejected into the systemic circulation. For partial CPB to be effective, two things must be true:

1 *The heart must be beating and ejecting.* If ejection is ineffective or nonexistent, distention of the heart will occur and systemic blood flow will be inadequate.

2 *The lungs must be ventilated.* In the absence of ventilation, systemic venous blood that enters the RA will ultimately reach the systemic circulation without gas exchange. This will result in hypercarbia and hypoxemia.

During partial CPB, the patient's systemic blood flow is provided in part by the CPB circuit and in part by the patient's heart. The patient's arterial pH, partial pressure of oxygen (P_{O_2}), and partial pressure of carbon dioxide (P_{CO_2}) are a reflection of the quantity and effectiveness of these two sources of blood. Therefore, during partial CPB, blood for blood gas analysis must be drawn from the patient and not from the CPB circuit.

Partial CPB can be accomplished with the cannulation techniques described for total CPB simply by partially impeding venous return to the CPB circuit with a clamp on the venous drainage line. More commonly, partial CPB is the result of cannulation of the right atrium directly with a small cannula or indirectly via the femoral venous system. A cannula is inserted retrograde up a femoral vein toward the heart into the IVC or RA. This system is much less effective than caval cannulation via the right atrium because the femoral vein limits the size of the cannula that can be inserted. This inhibits optimal systemic venous drainage because of the large pressure drop across the long, narrow cannula. This, in turn, elevates RA pressure, which for a given mean arterial pressure (MAP) and systemic venous resistance, further compromises venous return. For these reasons, with femoral venous cannulation, it is often impossible to divert all venous return to the CPB circuit. The major advantage of femoral venous cannulation is that it can be provided emergently and quickly without a sternotomy. Partial CPB is used under the following circumstances:

- During repair of thoracic aortic lesions.
- As temporary support for cardiogenic shock after interventional cardiac catheterization or electrophysiologic procedures.
- In patients undergoing reoperative procedures to provide elective or semi-emergent decompression of the heart or great vessels when they are adherent to the underside of the sternum.

Even with appropriate cannulation techniques, there may be compromise of venous return to the CPB circuit. An air lock may occur when large bubbles of air become lodged in the venous drainage lines. This air usually is entrained into the venous drainage lines from around loose cannulation sites. This can occur even when the right heart is not directly open to air. An air lock acutely disrupts the siphon effect. This causes RA pressure to rise above zero and venous return to the venous reservoir to fall. Malposition of the venous cannula is a constant risk particularly in infants and neonates. Even partial obstruction of IVC return can result in renal, hepatic, and gastrointestinal hypoperfusion and the development of ascites. Poor SVC drainage can result in engorgement and cyanosis of the head and neck. SVC obstruction can easily lead to cerebral ischemia particularly given the low cerebral perfusion pressure (CPP) that results from the low MAP

utilized during pediatric CPB. If poor SVC drainage is suspected, the surgeon should be alerted so that the cannula can be repositioned. Transducing the central venous pressure (CVP) catheter will allow measurement of the pressure in the SVC and is useful in detecting poor SVC drainage.

Venous reservoirs are either of the soft shell, collapsible type or the hard shell, noncollapsible type. Hard shell reservoirs are constructed of rigid plastic vented to atmosphere with the venous and cardiotomy reservoirs integrated in one unit. These reservoirs allow better visualization of the reservoir volume and easier removal of venous cannula air than soft shell reservoirs. Soft shell reservoirs also require a separate cardiotomy reservoir. These reservoirs generally have a smaller priming volume than their hard shell counterparts but can present a significant obstruction to venous return if they become distended.

Assisted venous drainage is a technique used in adult cardiac surgical patients to augment venous return while utilizing small venous cannulas primarily during minimally invasive procedures. Assisted venous drainage may be via a kinetic or vacuum assisted system. In the kinetic system, a centrifugal pump is interposed in the venous drainage system between the patient and the venous reservoir. Vacuum assisted venous drainage (VAVD) involves application of a vacuum ($-40\,cm$ H_2O) to a closed hard shell venous reservoir. Both methods serve to augment the pressure gradient for venous drainage. Both techniques have been applied to neonates and infants to allow use of smaller venous cannula and to reduce CPB prime volume. With use of 3/16-inch venous and arterial tubing, no arterial line filter, no prime in the venous line, and use of VAVD, the prime volume for a neonatal circuit can be as low 200 mL. Unfortunately, these techniques are not without risk. Using VAVD, arterial line emboli distal to the arterial filter is increased eight-to tenfold over that seen with conventional gravity venous drainage due to entrainment of air into the venous system. Arterial air embolism may also occur as the result of inadvertent positive pressurization of the venous circuit resulting in a paradoxic air embolus across an intracardiac communication.

Arterial inflow

Normally, arterial inflow is obtained via a cannula placed in the lesser curve of the ascending aorta proximal to the innominate artery. This arrangement allows perfusion of all vessels of the arch and distal aorta, as well as perfusion of the coronary ostia. Adult cannulas range from 19- to 24-French in outer diameter (6.3–8.0 mm). Pediatric cannulas range from 8.0- to 17.0-French in outer diameter (2.7–5.7 mm). Because the distal end of the arterial cannula is significantly smaller than the arterial inflow line, a large pressure drop exists across the arterial cannula. At normal bypass flows of $2.0\,L/min/m^2$, a gradient in excess of 120 mmHg may exist across an appropriate diameter cannula. This pressure drop is the result of a high velocity jet out the distal end of the cannula. It is essential that this jet be directed into the center of the aorta and not up into the innominate artery so that a cerebral overperfusion injury does not occur.

As with venous cannulation, arterial cannulation particularly in infants and neonates can be technically challenging. In circumstances where the ascending aorta and aortic arch are hypoplastic and systemic blood flow is ductal dependant (as in hypoplastic left heart syndrome) it may be necessary to obtain systemic perfusion through the ductus arterious by cannulating the pulmonary artery (PA). When the aortic arch is interrupted, cannulation of the aorta both proximal and distal to the interruption is necessary. Because the arterial cannula is relatively large as compared to the aorta in infants and neonates, complete or partial obstruction of the aorta by the cannula itself is possible. If dampening of the arterial trace, distension of the systemic ventricle, or an increase in CPB line pressure occurs with placement or manipulation of the arterial cannula, the surgeon should immediately be made aware of the situation so the cannula can be repositioned. Some centers utilize near infrared spectroscopy (NIRS) and transcranial Doppler (TCD) technology as adjunctive methods to assess cerebral blood flow during CPB.

In patients undergoing re-operative procedures it may be necessary to obtain arterial inflow via a femoral artery when the heart or great vessels are adherent to the underside of the sternum.

Placement of the cannula in the femoral artery provides retrograde perfusion to the proximal aorta and coronary ostia. This route has several limitations. The smaller caliber of the femoral vessel limits the size of the arterial cannula that can be used without risk of damage to the artery. The smaller the cannula, the larger will be the pressure drop across it. If the pressure drop is severe, flow will be limited after the safe maximum arterial perfusion line pressure (about 300 mmHg) has been reached. Perfusion to the leg in which the cannula is placed is limited by the fact that the cannula occupies the entire lumen of the femoral artery and is directed proximally. This may result in an ischemic leg and a persistent metabolic acidosis. When the cannula is removed, there is often a washout of lactic acid resulting in a metabolic acidosis that may require treatment with sodium bicarbonate and alveolar hyperventilation.

Pumps

There currently are two types of pumps used on modern CPB machines to provide nonpulsatile flow: the double-headed nonocclusive roller pump (Fig. 10.2) and the centrifugal blood pump (Fig. 10.3).

Double-headed roller pump

The double-headed roller pump is the most commonly used. The double-headed roller pump is a positive volume displacement pump. At least one

head is in contact with the pump boot at all times to push blood forward and ensure continuous forward flow. The pump boot is the piece of tubing in contact with the pump heads. It generally is thicker and more durable than the other sections of tubing in the CPB circuit. Roller pumps are driven by a load-independent electric motor. After the pump speed has been set, the pump will continue the forward displacement of the same volume of blood, even if the resistance to flow is increased by kinking or clamping the arterial line. This will result in a large pressure increase in the arterial inflow line, which can result in the rupture of connections between sections of tubing. To avoid this type of disaster pressure gauges are placed on the arterial inflow line. If arterial line pressure rises to dangerous levels (300 mmHg) pump flow can be reduced to allow line pressure to fall until the problem is identified and corrected.

Centrifugal pump

The centrifugal pump is a kinetic pump. It operates on the constrained vortex principle. Blood is driven through the pump by centrifugal forces generated by a vortex in the pump. It has been suggested that this causes less trauma to blood components than the roller pump. Although the pump is driven by a load-independent electric motor, this pump does not behave like the roller pump. When line

Fig. 10.2 A typical double headed nonocclusive roller pump. One head of the pump will be in contact with the pump boot at all times as is shown here.
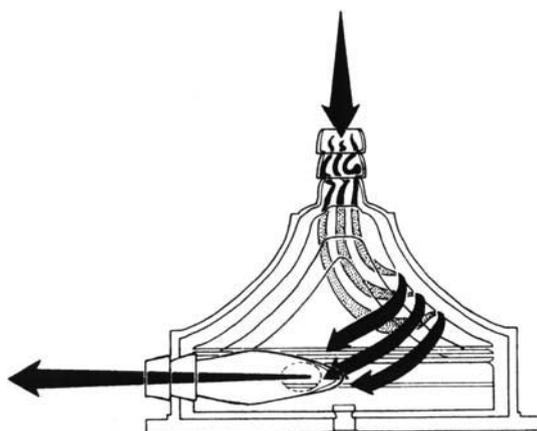
Fig. 10.3 A typical centrifugal pump. Entrained air will be drawn to the apex of the pump away from the outlet at the base of the pump.

resistance is increased, blood flow falls as the shear forces between the layers of blood are increased and less forward displacement of blood occurs. This resistance dependence prevents increases in arterial line pressure when clamping or kinking occurs. The pump is said to be inflow responsive as well. If a large quantity of air is introduced into this pump, cohesive forces will no longer exist between layers of blood and pumping will cease. In addition, the risk of micro air embolization is reduced because small, low-density air bubbles become trapped in the center of the vortex.

Oxygenators

Oxygenators perform the gas exchange functions of the lung in the CPB circuit. Despite the fact that oxygenators are incorporated in a system in which blood is pumped under pressure, all gas exchange occurs at atmospheric pressure because the oxygenators are vented to the atmosphere. There currently are two types of oxygenators available: bubble oxygenators and membrane oxygenators. Membrane oxygenators are the primary type of oxygenator currently used.

Bubble oxygenators

Bubble oxygenators provide oxygen delivery to and carbon dioxide removal from blood via a gas bubble-blood interface (Fig. 10.4). The venous blood from the venous drainage line and the blood from the cardiotomy lines drain passively to the bottom portion of a bubble column. The bottom portion of the bubble column is separated from the gas entry chamber by a dispersion or diffusor plate. The dispersion plate breaks up the bulk gas (100% oxygen or an oxygen/carbon dioxide mixture) into bubbles of appropriate size for gas exchange. This gas is bubbled through blood and gas exchange occurs as the bubble-blood mixture rises upward to the top of the bubble chamber. Heat exchange also occurs as the gas mixture rises. At the top of the bubble chamber the bubble-blood mixture passes through a debubbler/defoamer chamber. This chamber has a large surface area of polyurethane mesh sponge that is coated with a silicone antifoaming agent and covered with polyester mesh fabric. The antifoaming agent causes bubbles to collapse by reducing
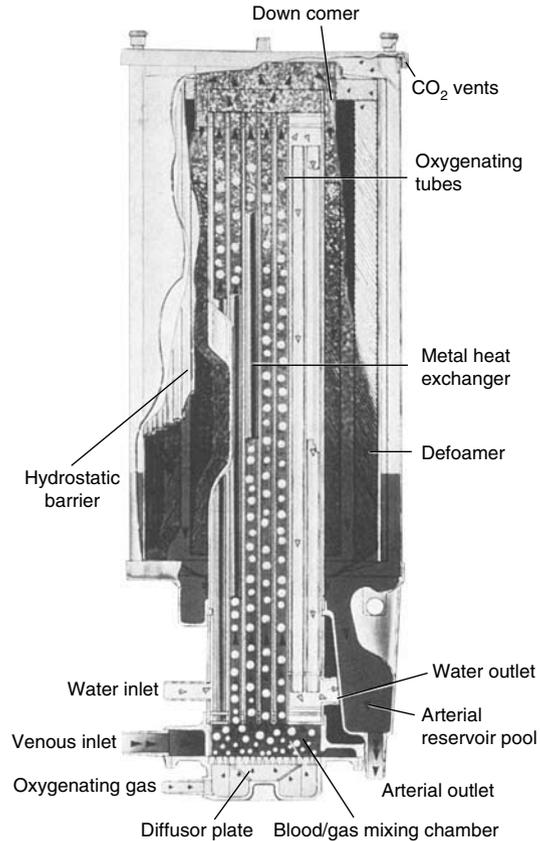
Fig. 10.4 Cutaway view of a typical bubble oxygenator. Water inlet and outlet for heat exchange coils are located at the bottom of the oxygenator. Oxygen inflow is also located at the bottom. Venous blood passively enters the bottom of the oxygenator via venous cannulas and venous drainage line. Oxygen (O_2), carbon dioxide (CO_2), and heat exchange all occur as bubble-blood mixture is carried to the top of the oxygenator. Bubble-blood mixture then passes into a debubbler/defoamer chamber before spilling over into the arterial reservoir. From the arterial reservoir, blood is pumped to the patient via arterial inflow line and arterial cannula.

surface tension and the other components mechanically disrupt the bubbles. This arrangement serves to eliminate the majority of gaseous microemboli. From here, the blood spills over into an arterial reservoir. The reservoir provides an area for further elimination of microbubbles by allowing them to rise to the top of the blood. Blood in the arterial reservoir is then pumped to the patient. The volume

in the reservoir provides a volume buffer that allows the perfusionist to react to changes in venous return without pumping the reservoir dry and then pumping air into the patient.

Oxygen is relatively less soluble and diffusible in blood than carbon dioxide (ratio of 1:25). Therefore, oxygen delivery is enhanced by the presence of small bubbles where the surface area available for gas exchange is large. Carbon dioxide removal, on the other hand, is enhanced by the presence of large bubbles where the volume of the gas bubbles is large. In reality, the bubble size is somewhere between these two extremes (3–7 μm). For a given bubble size, an increase in the flow of bubbles through blood results in enhanced carbon dioxide removal. Therefore, arterial partial pressure of carbon dioxide (Pa_{CO_2}) is controlled by the gas to blood flow ratio (GBFR). Some additional control of Pa_{CO_2} can be obtained by using an oxygen/carbon dioxide mixture instead of 100% oxygen as the bulk gas. Independent control of arterial partial pressure of oxygen (Pa_{O_2}) is difficult as the fraction of inspired oxygen (Fi_{O_2}) is fixed (100% oxygen) or very nearly fixed (oxygen/carbon dioxide). Removal of nitrogen bubbles is difficult and, therefore, oxygen/nitrogen mixtures are not used.

The bubble-blood interface is not physiologic due to the constantly changing blood-gas interface. This results in traumatization of the blood. Increasing gas flow to enhance gas exchange results in further traumatization of the blood. In addition, increasing gas flow increases the number and decreases the size of the bubbles generated. This increases the risk that gaseous microemboli will reach the arterial circulation.

Membrane oxygenators

Membrane oxygenators allow oxygen delivery to and carbon dioxide removal from blood across a thin membrane, eliminating any direct blood gas contact. The high resistance inherent in the membrane oxygenators does not allow gravity flow of venous blood through the membrane into an arterial reservoir. As a result, the venous drainage and cardiotomy lines empty into a venous reservoir and are pumped through the membrane and then out to the patient via the arterial line. As would be expected, the pressure drop across the membrane increases linearly with increasing flow.

Membrane oxygenators generally are of two types: microporous membranes and solid membranes.

● *Microporous membranes*. Microporous membranes are made of polypropylene with small, hydrophobic pores (0.03–0.07 μm in diameter) impermeable to blood and gas. These pores cover at least 50% of the membrane surface. Upon exposure to blood, these pores become covered with a thin proteinacous layer through which gas exchange occurs without blood and gas coming in direct contact. These microporous membranes offer little or no limitation to the diffusion of carbon dioxide or oxygen. Eventually, over the course of several hours the gas exchange capacity of these membranes deteriorates as serum evaporates and plugs the micropores.

There are two types of microporous membranes: hollow fiber and parallel plate or pleated sheet. Hollow fiber membranes are composed of a large bundle of polypropylene microporous capillary tubes 200–300 μm in diameter knitted together in a mesh, wrapped around a solid core and inserted into a cylindrical shell. Gas flows on the inside of the fibers and blood flows on the outside of the fibers; a design known as extra luminal flow (ELF). This allows air in the blood path to be recognized during priming. In addition, in the event of fiber rupture, blood will contaminate only the fibers affected with little effect on the gas exchange capacity of the membrane. Counter-current flow of gas and blood is induced by introducing gas into the fibers at one end of the cylinder and introducing blood around the fibers at the other end. In addition, the path of blood around the knitted mesh of fibers induces crosscurrent flow with blood flowing perpendicular to the fibers. A hollow fiber membrane oxygenation system is illustrated in Figs 10.5–10.7. The performance characteristics of this membrane are summarized in Fig. 10.8.

In the pleated sheet design a continuous microporous sheet is folded and compressed like a collapsible fan. Gas flows on one side of the sheet and blood flows on the other side with flow distribution promoted by polypropylene screens. The pleated design induces counter-current flow of

1. Venous reservoir
2. Cardiotomy reservoir
3. Connection key
4. Venous return connector: 3/16-1/4" I.D.
5. Turrets
6. Arterial blood outlet: 3/16-1/4" I.D.
7. Venous reservoir outlet: 3/16/1/4" I.D.
8. Venous blood inlet: 3/16-1/4 I.D.
9. Scavenging connector
10. Sampling connector
11. Arterial temperature probe site
12. Venous temperature probe site
13. Recirculation line clamp
14. Gas inlet
15. Gas escape
16. Sample port luer
17. Drug port luer
18. Cardiotomy bypass port

Fig. 10.5 Cutaway view of a Dideco Lilliput 1 hollow fiber microporous membrane oxygenator. The venous reservoir (1) is located at the top of the device and incorporates a cardiotomy reservoir (2), whereas the membrane oxygenator is located at the bottom. Cardiotomy suction blood enters at 9. Venous return blood passively enters the venous reservoir at 4. Venous return and filtered cardiotomy blood exit at 7. From there blood is delivered to a pump (roller or centrifugal) and is pumped into the membrane oxygenator at 8. After undergoing gas and heat exchange within the oxygenator blood exits at 6 and is delivered to the arterial cannula by the same pump which pumped blood into the membrane oxygenator. Fresh gas (sweep gas) enters the membrane oxygenator at 14 and exits at 15. If an inhalation agent were added to the sweep gas it would be scavenged at 15.

blood and gas. These types of membranes provide less gas exchange surface area per unit volume of blood than hollow fiber membranes. As a result they require a larger blood priming volume than hollow fiber membranes to provide comparable gas exchange. Both hollow fiber and pleated sheet arrangements of microporous material allow a large surface area (up to $4.5\,m^2$) for gas exchange to be contained in a relatively small space. However, neonate and infant membrane oxygenators are of the hollow fiber type to minimize prime volume.

• *Solid (nonporous) membranes.* These membranes are constructed of methyl silicon rubber that is thin enough ($<25\,\mu m$) to permit diffusion of gas. These membranes do offer some limitation to the diffusion of carbon dioxide and oxygen with carbon dioxide diffusing five times as easily as oxygen. As a result, these membranes require a greater gas exchange surface area and thus a greater priming volume than microporous membranes to provide comparable gas exchange. These membranes have

greater longevity (days verses hours) than microporous membranes and are reserved for use in extracorporeal membrane oxygenation (ECMO) circuits.

Although modern membranes themselves offer little impedance to the diffusion of gas, there are other characteristics of membrane oxygenators that limit gas exchange. The primary determinants of oxygen and carbon dioxide exchange across a membrane are the solubility and diffusibility of oxygen and carbon dioxide in blood and their partial pressure gradient across the membrane. Because oxygen is relatively less soluble and diffusible in blood than carbon dioxide, oxygen exchange is dependent on the thickness of the blood film and the pressure gradient for oxygen across the membrane. The vast majority (90%) of the resistance to oxygen diffusion in a membrane oxygenator system is diffusion of oxygen into blood and not diffusion across the membrane. The pressure gradient for oxygen can be increased by increasing the oxygen content of
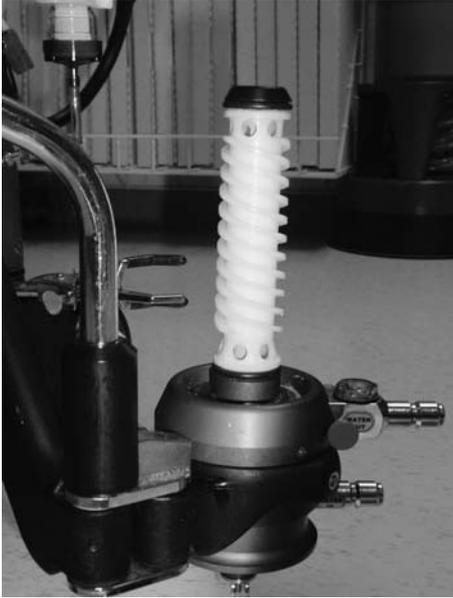
Fig. 10.6 Photo of the heat exchange unit of the Dideco Lilliput 1 with the rest of the system removed. Water outlet (upper) and inlet (lower) ports are clearly seen at the lower right.

Fig. 10.7 Photo of an assembled Dideco Lilliput 1 system mounted on the heat exchanger. The heat exchange unit is inserted into the core of the membrane oxygenator. Water inlet and outlet ports are seen as in Fig. 10.5.
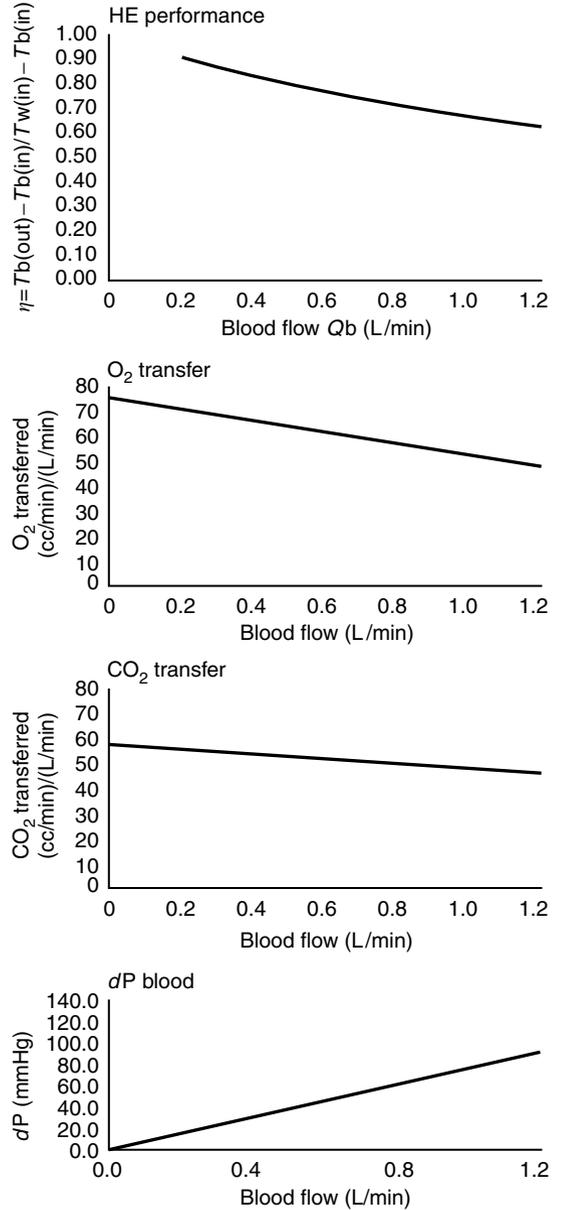
Fig. 10.8 Performance characteristics of the Dideco Lilliput 1 oxygenator and heat exchanger over a typical range of blood flows through the membrane. As the upper limits of blood flow are reached gas (oxygen (O_2) and carbon dioxide (CO_2)) transfer diminishes as does the performance factor (η) of the heat exchange unit. The pressure drop across the membrane also increases as blood flow increases. HE, heat exchange; dP, pressure change.

Oxygenator	Patient weight (kg)	Oxygenator prime (mL)	Total circuit prime including oxygenator (mL)	Manufacturer reference flow rate (mL/min)
Dideco Liliput 1	<8	60	Neonate 300 Infant 320	800
Dideco Liliput 2	<20	105	Infant 425 Toddler 575	2300
Cobe Optimin	<40	170	Toddler 790 Small adult 1110	5000
Cobe Optima	>40	260	Adult 1300	8000

Table 10.2 Comparison of membrane oxygenators.

the fresh gas flow. However, because of the low diffusibility of oxygen in blood, a thick blood film or boundary layer will result in poor oxygen delivery to the cells most distant from the membrane, even when the pressure gradient for oxygen is high. Modern membranes have design features to induce eddy currents or static mixing which serves to disrupt the boundary layer and enhance diffusion of oxygen into blood.

Because carbon dioxide is relatively more soluble than oxygen, carbon dioxide exchange is dependent only on the pressure gradient for carbon dioxide across the membrane. Normally, fresh gas flow to the membrane oxygenator contains no carbon dioxide, and thus the gradient for carbon dioxide removal will not be improved by lowering the carbon dioxide content of the fresh gas. The rate of carbon dioxide removal can be increased by increasing the rate of fresh gas flow or sweep rate to the oxygenator; this is analogous to increasing alveolar ventilation.

An important measure of oxygenator performance is reference flow rates as defined by the manufacturer and the Association for the Advancement of Medical Instrumentation (AAMI). Carbon dioxide reference flow is defined as the maximum flow of blood with a hemoglobin of 12 g/dL, zero base deficit, and an oxygen saturation of 65% at a temperature of 37°C that can enter an oxygenator and subsequently leave the oxygenator with the carbon dioxide content decreased by 38 mL/L. Oxygen reference flow is defined as the maximum flow

Table 10.3 Comparison of membrane oxygenator heat exchange capacity.

Oxygenator	Membrane surface area (m^2)	Heat exchange surface area (m^2)
Dideco Liliput 1	0.34	0.02
Dideco Liliput 2	0.64	0.02
Cobe Optimin	1.0	13.74
Cobe Optima	1.9	13.74

of blood with a hemoglobin of 12 g/dL, zero base deficit, and an oxygen saturation of 65% at a temperature of 37°C that can enter an oxygenator and subsequently leave the oxygenator with the oxygen content increased by 45 mL/L. The recommended reference flow rate is the lesser of these two values. The performance characteristics of a range of membrane oxygenation systems typically utilized are summarized in Tables 10.2 and 10.3.

Heat exchangers

Heat exchangers are necessary to produce the active cooling and rewarming of the patient's blood required for systemic hypothermia on CPB. Heat exchange is accomplished by a countercurrent flow of water and the patient's blood. Water of a predetermined temperature is pumped into a spiral stainless steel coil as blood flows in the opposite direction over the coil. The countercurrent flow arrangement provides the most efficient method of

heat exchange. Water input temperature is determined by mixing various proportions of hot and cold water before its introduction into the coil. A device capable of accurately producing water of the appropriate temperature and pumping it to the heat exchange coils is a necessary component of the CPB circuit.

Heat exchange coils are inserted into the core of the membrane oxygenator in some systems (see Fig. 10.6) or are located prior to blood entry into the membrane in others. They are generally not located in the CPB circuit after the oxygenator in order to minimize the risk of systemic gaseous microemboli that may be produced during rewarming as the solubility of gases in blood is reduced. As the temperature gradient between the venous blood input and water input decreases, heat exchange slows exponentially. Nonetheless, the temperature gradient between venous blood input and water input is kept between 8°C and 10°C to avoid large changes in gas solubility. During warming, the heated water input temperature never exceeds 40°C to avoid heat damage to blood and tissue.

Heat exchangers are rated according to the performance factor (PF). The PF is the amount of heat actually transmitted to blood divided by the maximal amount of heat that could theoretically be transferred. The PF of heat exchangers varies from 0 to 1 with a PF of 1 (100% efficiency) being unobtainable. The performance characteristics of a typical infant and neonatal heat exchanger are illustrated in Fig. 10.8. The heating and cooling efficacy of the Dideco Lilliput 2 system would be expected to be inferior to that of the Lilliput 1 given that the two systems have the same heat exchange surface area and the Lilliput 2 is utilized for larger patients at almost three-times the reference flow rate of the Lilliput 1 (see Table 10.3).

Cardiotomy suction

Cardiotomy or pump suction is incorporated into most CPB circuits, where it serves as an important source of blood conservation. Most systems use a roller pump to provide the necessary suction. The collected blood goes either to a filtered cardiotomy reservoir and then to the venous reservoir or directly to a venous reservoir that contains a filter. Often, the cardiotomy suction is used before initiation of CPB during cannula placement. It is essential that adequate heparinization be obtained before use of cardiotomy suction so that clot is not introduced into the cardiotomy or venous reservoir.

Blood from the pericardial collected by cardiotomy suction and returned to the venous reservoir is know to activate the extrinsic coagulation pathway during CPB. In fact it has been demonstrated that aspirated pericardial blood returned to the venous reservoir is the most important activator of the coagulation system during CPB. In addition to bone and fat fragments, pericardial aspirate is rich in tissue factor (TF) and procoagulant cellular (primarily platelet) derived microparticles. It has also been demonstrated that elimination of pericardial cardiotomy suction return to the venous reservoir or washing of pericardial cardiotomy blood prior to return reduces inflammatory mediator generation and thrombin, neutrophil, and platelet activation.

Cardiotomy suction is also the major source of blood trauma and hemolysis during CPB due to the simultaneous aspiration of air and blood. For this reason, it is important that the pump head on the cardiotomy suction turns only fast enough to allow aspiration of blood. If a sucking sound is heard from the cardiotomy, sucker aspiration of air is occurring and the pump head rotation should be slowed.

Vent line

Venting is intended to prevent blood from collecting in the ventricles during CPB. When blood collects in the ventricles, distension of the ventricles and warming of the heart may occur. Distension causes mechanical damage to the heart from subendocardial compression and also compromises surgical exposure. The risk of distension is greatest when the blood return to the right or left heart is high and when the ventricles are no longer effectively ejecting blood. As CPB commences, bradycardia, ventricular fibrillation, or asystole may occur and prevent effective ventricular ejection. Myocardial hypothermia during cardioplegic arrest will be compromised by warm blood collecting in the ventricles during aortic cross-clamping in the unvented heart.

Figure 10.9 illustrates the most common causes of continued blood return to the right and left
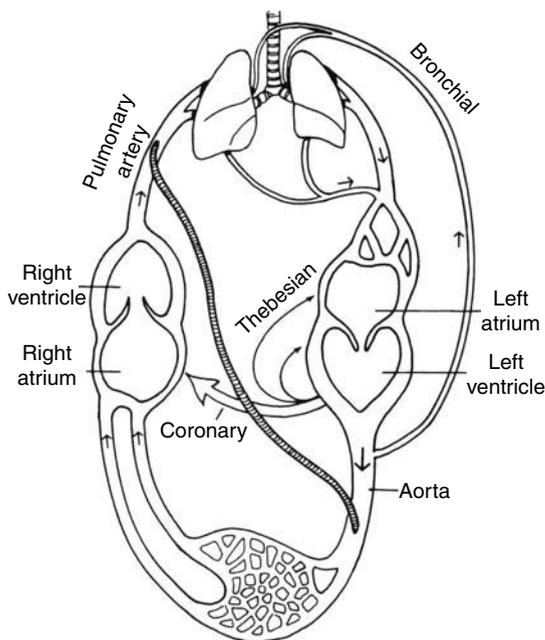
Fig. 10.9 Potential sources of continued blood flow to right and left heart during cardiopulmonary bypass (CPB). Bronchial flow is derived from aorta and returns to left atrium. Coronary blood flow returns to the right atrium via coronary sinus but variable proportions may return to the left atrium and ventricle via thebesian veins. Shunt is seen between the aorta and pulmonary artery. This shunt may be anatomical (patent ductus arterious) or surgical (Blalock–Taussig, Potts, Waterston). Finally, aortic regurgitation may be responsible for blood flow into left ventricle on CPB before aortic cross-clamping.

ventricles after institution of CPB with all IVC and SVC return diverted to the circuit. Blood flow to the right heart during CPB usually is the result of coronary blood flow. Most coronary blood flow comes from coronary arteries and their collaterals. A small portion comes from noncoronary collaterals, usually of pericardial and mediastinal origin. Coronary venous blood returns to the coronary sinus, which is located near the junction of the IVC and the RA. Coronary sinus return can be captured by a properly positioned single cannula or with separate IVC and SVC cannulas with the tourniquets loosened. For procedures in which the right heart is opened, coronary sinus blood can be captured with the cardiotomy suction. Coronary sinus blood flow (except

that contributed by noncoronary collaterals) will cease when the aortic cross-clamp is applied and coronary arterial blood flow ceases.

Blood flow to the left heart during CPB arises from several sources. The Thebesian veins drain a very small portion of the coronary circulation into the LA and ventricle. This flow will cease when the aortic cross-clamp terminates coronary blood flow. The bronchial veins drain into the pulmonary veins and subsequently into the LA and ventricle. The bronchial circulation may be very large in patients with cyanotic heart disease. In patients with congenital heart disease, a large portion of pulmonary blood flow may be supplied by anatomic (patent ductus arteriosus, aortopulmonary collaterals) or surgical (Blalock–Taussig, Waterston, Potts, central shunts) systemic-to-pulmonary artery communications. If these communications are not ligated or controlled before institution of CPB, the blood return to the PA, and subsequently to the LA and LV, may be very large. In this circumstance venting will relieve left heart distention. However, unless CPB flow rate is increased by an amount equal to the vented blood systemic oxygen delivery to the patient will be compromised. Flow return to the LV also may result from an incompetent aortic valve. In this instance, retrograde filling of the LV with blood from the aortic cannula will occur until the aortic cross-clamp is applied.

Normally, right ventricular venting is unnecessary because coronary sinus flow is captured by the venous drainage system. Several sites are available for left ventricular venting. The right superior pulmonary vein provides relatively easy retrograde access to the LA and the ventricle via the mitral valve. The insertion site subsequently can be used for placement of a transthoracic LA pressure line. Direct venting of the left ventricular apex is possible, but this route requires careful repair and may result in damage to the LV. Direct venting via the LA is also possible. The PA can be used to vent both the right heart and the left heart. A competent mitral valve will limit effective venting of the LV via this route.

The vent line returns blood either to the filtered cardiotomy reservoir and then to the venous reservoir or directly to a venous reservoir that contains a filter. The vent line may be either active or passive.

The risk of active venting is that after the ventricle has been emptied of blood, continued active venting may result in entrainment of air into the ventricular cavity. In procedures in which the heart is not opened (such as coronary artery bypass grafting), this entrainment of air will require the additional step of evacuating air from the heart before termination of bypass. Close communication between surgeon and perfusionist are necessary to avoid this complication.

Micropore filters

Most CPB circuits are equipped with both cardiotomy and arterial microporous filters. These filters remove particulate contaminants such as bone, tissue, and fat fragments from blood and prevent micro- and macro- air emboli. Screen filters are made of a woven polyester mesh. These filters have a 30–40 μm pore size and a large working surface area. This pore size makes these filters useful for trapping both air and particulate microemboli without high resistance to flow or damage to cellular blood elements. Depth filters are composed of packed fibers of Dacron and filter by impaction of particles on their wetted surface. These filters tend to lose their air-filtering capabilities over time, cause more hemolysis, and are more damaging to platelets.

Screen filters commonly are used on the arterial side of the circuit. The vent at the top of the filter allows air to be vented directly back to the venous reservoir so that it is not trapped in the filter. This is important in cases of massive air emboli, in which the presence of trapped air will greatly reduce the filter surface area and allow the pressure in the filter to become high enough to translocate air across the filter and into the arterial circulation of the patient. The arterial filter also has a bypass line so that it can be excluded from the circuit if it becomes clogged with debris. A combination of depth and screen filters is used in most cardiotomy reservoirs.

Ultrafiltrators

Ultrafiltrators are devices commonly added to the CPB circuit to remove excess fluid and produce hemoconcentration. When used in conjunction with CPB, these devices produce an ultrafiltrate that

occurs as the result of a hydrostatic pressure gradient across a semipermeable membrane. These are the same devices that can be used for hemodialysis when they are used in conjunction with a dialysate. When used during CPB, they are commonly called hemoconcentrators as they produce an increase in hematocrit by removing excess fluid.

These devices consist of a core of microporous hollow fibers made of polysulfone, polyamide, or polyacrylonitrile material arranged in a bundle. The pore size generally is 0.30–0.40 μm. Due to the pressure drop across the device, blood inflow must be obtained from the arterial side of the CPB circuit while blood outflow is diverted to the cardiotomy reservoir or venous reservoir. The ultrafiltrate is collected in a container connected to a vacuum source.

The ultrafiltrate is discarded and has the composition of glomerular filtrate. The rate at which ultrafiltrate is produced is dependent on the trans-membrane pressure gradient (TMP). TMP is determined by the arterial inlet pressure (P_a), the venous outlet pressure (P_v), the absolute value of applied suction at the outlet (P_n), the oncotic pressure at the inlet (P_i), and the oncotic pressure at the outlet (P_o):

$$\text{TMP} = \frac{P_a + P_v}{2} + P_n - \frac{P_i + P_o}{2}$$

is increased by using the regulated vacuum source connected to the outlet of the device. TMP should not exceed 500 mmHg.

A number of different ultrafiltration techniques exist.

Continuous ultrafiltration

Continuous ultrafiltration (CUF) refers to ultrafiltration occurring throughout CPB or during those intervals when venous reservoir volume is sufficient to allow it. This system would be expected to produce hemoconcentration (Fig. 10.10).

Modified ultrafiltration

Modified ultrafiltration (MUF) allows ultrafiltration to continue after weaning from CPB. MUF allows the CPB circuit to remain primed while both the patient's blood volume and the CPB circuit contents are hemoconcentrated. MUF may be performed
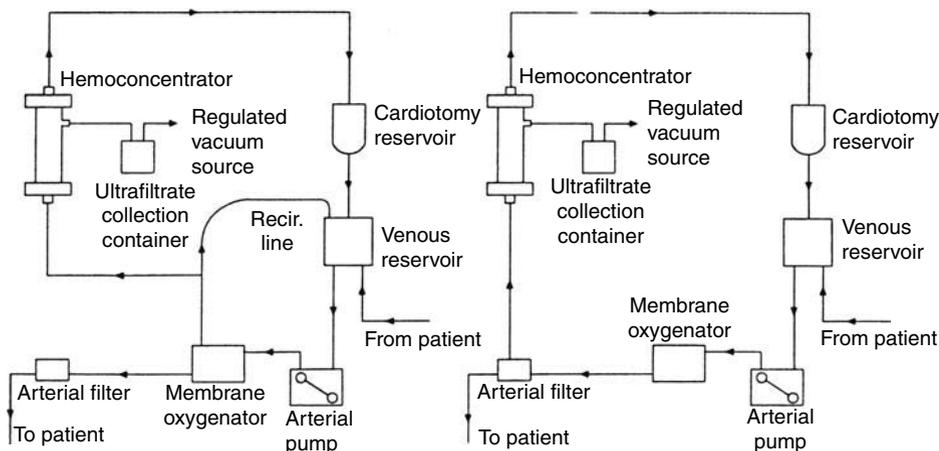
Fig. 10.10 Two arrangements that allow continuous ultrafiltration (CUF), dilutional ultrafiltration (DUF), and zero-balance ultrafiltration (ZBUF) to be performed during cardiopulmonary bypass (CPB).

utilizing either an arteriovenous or veno-venous system. In the arteriovenous system inflow to the ultrafiltrator during MUF is directly from the aortic cannula. Outflow from the ultrafiltrator is to the right atrium. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the right atrium (Fig. 10.11). In the veno-venous system, the IVC cannula provides inflow to the ultrafiltrator with the aid of a roller pump while outflow from the ultrafiltrator is returned to the SVC cannula. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the SVC. The end point for termination of MUF following CPB varies from institution to institution and may depend on either a set time interval (15–20 minutes), a set hematocrit (40%) or a set volume removed (750 mL/m^2). Heparin anticoagulation must be maintained during MUF with protamine reversal of heparin initiated after termination of MUF.

The major advantage of MUF over CUF is that it allows hemoconcentration to continue once CPB has been terminated. As a result MUF normally allows a greater degree of hemoconcentration than can be obtained with CUF alone particularly in small children. Some institutions utilize both CUF and MUF, as the techniques are not mutually exclusive.

Use of MUF is not without potential problems. MUF use has been associated with air cavitating into the circuit potentially increasing the risk of iatrogenic air embolism. MUF has been demonstrated to increase plasma heparin concentrations that may require reevaluation of the protamine dose. MUF has also been demonstrated to cause reductions in plasma aprotinin, opioid, and benzodiazepine levels. While the reductions in anesthetic agents are generally clinically insignificant, the clinical significance of plasma aprotinin level reductions is unknown. Patient hypothermia is a potential complication of MUF if the system is not modified to allow warming of re-infused filtrate.

Dilutional ultrafiltration and zero-balance ultrafiltration

Dilutional ultrafiltration (DUF) and zero-balance ultrafiltration (ZBUF) utilize the same system as CUF but involve high-volume ultrafiltration during CPB in which crystalloid solution is continuously used to replace the ultrafiltrate in order to maintain reservoir volume. ZBUF utilities ultrafiltration rates of 200 mL/kg/min while DUF utilizes rates of 40–80 mL/kg/min. These methods do not result in hemoconcentration but may be beneficial in removing inflammatory mediators. MUF is usually
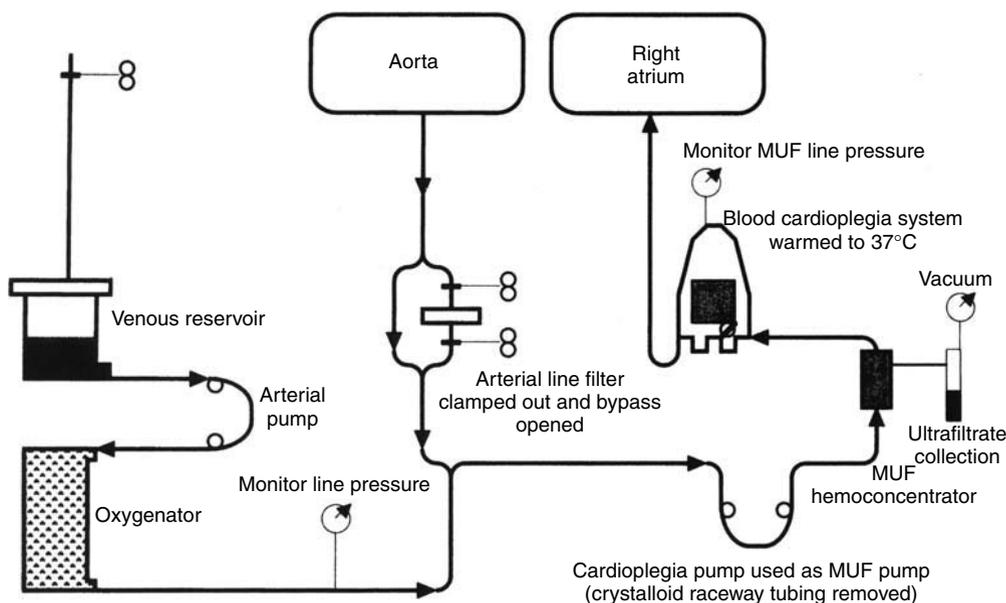
Fig. 10.11 A typical arteriovenous modified ultrafiltration (MUF) circuit. Input to the ultrafiltrator is via the aortic cannula with warmed, hemoconcentrated blood returned to the patient via the venous cannula. Blood from the venous reservoir can also be hemoconcentrated and returned to the patient.

used in conjunction with these techniques to obtain hemoconcentration.

Circuit prime

Basic prime solutions in adults are usually isotonic crystalloid solutions (lactated Ringer's lactate or Plasmalyte). Some institutions add albumin to the CPB prime to increase the oncotic pressure of a crystalloid prime and to precoat the membrane oxygenator so as to delay absorption of fibrinogen with subsequent platelet activation. It has been consistently demonstrated that albumin and crystalloid primes reduce the CPB positive fluid balance, postoperative weight gain, and provide better preservation of platelet counts as compared to pure crystalloid primes. No clear clinical outcome advantage associated with these differences has been demonstrated. Enthusiasm for increasing the oncotic pressure of the CPB prime with hydroxyethyl starch is tempered by the fact that its use compromises post-CPB hemostasis.

The volume and composition of the CPB circuit prime for pediatric patients has more important physiologic consequences than in adult patients. In order to keep prime volumes, exposure of the patient's blood to artificial surfaces, and hemodilution to a minimum, the appropriate size circuit is essential in the pediatric population. The smallest membrane oxygenator with a reference flow rate capable of meeting the anticipated CPB flow rates is selected. In addition, the smallest diameter venous and arterial tubing that will not impede anticipated flow due to high resistance is selected. The tubing is kept as short as possible by positioning the CPB close to the OR table. The volumes of various tubing diameters per 1 foot of length are: 3/16 inch – 5 mL; 1/4 inch – 9.7 mL; 3/8 inch – 21.7 mL; and 1/2 inch – 38.6 mL. For infants and neonates 3/16 inch arterial and 1/4 inch venous tubing is used. With currently available technology, the smallest CPB prime volume for neonatal use is approximately 300 mL. Given that the blood volume of a 4.0 kg neonate is approximately 340 mL, 100% dilution of the patient's blood volume is expected upon initiation of CPB (Table 10.4).

Both Ringer's lactate solution and Plasmalyte contribute to the development of a metabolic acidosis with initiation of CPB. Ringer's lactate solution

Table 10.4 Estimated blood volume (EBV) comparison.

Patient weight (kg)	Estimated blood volume (mL/kg)
<10	85
10–20	80
20–30	75
30–40	70
>40	65

does this via hyperchloremia and Plasmalyte via an increase in unmeasured anions, most probably acetate and gluconate. Hemofiltration of the circuit prime prior to initiation of CPB is an effective method to normalize electrolyte balance (particularly potassium and pH) and reduce inflammatory mediator concentrations. Additional components commonly added to the CPB prime are sodium bicarbonate, mannitol, calcium chloride, and magnesium.

The circuit prime volume to patient blood volume ratio would be expected to decrease plasma unfractionated heparin (UFH) levels with initiation of CPB unless an appropriate quantity of heparin is added to the CPB prime. Most institutions add UFH to the CPB prime (3–4 unit/mL of prime) to reach a CPB target UFH concentration similar to the patient's plasma UFH concentration.

Blood is often added to the prime to reach a target CPB hematocrit. Whole blood can be used to prevent dilution of coagulation factors in pediatric patients. The target CPB hematocrit and the degree of coagulation factor dilution that is tolerated vary from institution to institution. Hemodilution during hypothermic CPB may be advantageous because it offsets the increase in blood viscosity induced by hypothermia and promotes microvascular flow. In addition, systemic hypothermia reduces whole-body and cerebral oxygen consumption 5% for each 1°C decrease in body temperature allowing the reduction in oxygen delivery which accompanies reduction of red cell mass and oxygen-carrying capacity to be tolerated. The hematocrit (Hct) on CPB can be accurately predicted in the following manner

when the pump is primed with an asanguineous solution:

- Estimated blood volume (EBV) is calculated using the patient's weight and Table 10.4.
- Patient red cell mass (RCM_P) = patient hematocrit (Hct) × EBV.
- Hct on CPB = RCM_P/(EBV + prime volume).

In a 4.0 kg neonate with a hematocrit of 45%, the expected CPB hematocrit would be 24% using a 300 mL asanguineous circuit prime.

The CPB red cell mass (RCM_{CPB}) necessary to obtain a target hematocrit on CPB can be determined as follows:

$$RCM_{CPB} = [(\text{desired Hct on CPB})$$
$$\times (EBV_P + \text{prime volume})] - RCM_P$$

The volume of blood prime necessary to obtain the desired RCM_{CPB} will depend on whether whole blood or packed cells are used in the prime. The RCM of a blood product is determined by multiplying the hematocrit of the blood product by its volume. Therefore, the RCM of a unit of packed cells might be (0.7 × 350 mL) or 245 mL, whereas that of whole blood will be (0.4 × 350 mL) or 140 mL. The 4.0 kg neonate described would have to the have the CPB circuit primed with 98 mL of whole blood to reach a target CPB hematocrit of 30%.

An ancillary method of limiting the hemodilution induced by the CPB prime is the technique of retrograde autologous priming (RAP). This technique is initiated in the 5–10 minutes just prior to commencing CPB. A 1000 mL blood collection bag is connected to the CPB circuit and is suspended at a level 20 cm higher than the patient's right atrium. The technique involves three steps. First, blood from the patient's aorta is permitted to flow retrograde through the arterial filter displacing approximately 300 mL of semi-sanguineous pump prime into the collection bag. It is often necessary to use phenylephrine to maintain a systemic systolic blood pressure >100 mmHg during this phase. Next, volume in the venous reservoir is pumped forward through the membrane oxygenator into the collection bag until the reservoir volume is reduced to 200 mL. At this point, additional blood from the arterial cannula is allowed to fill the venous reservoir retrograde via the arterial filter purge line.

The added venous reservoir volume is then pumped forward into the collection bag until sanguineous fluid leaves the oxygenator. This displaces approximately 300 mL of semi-sanguineous prime. Finally, the collection bag in lowered and as CPB commences the prime solution from the venous line is drained into the collection bag yielding an additional 300 mL of prime solution. In a typical adult patient approximately 800–1000 mL of a 1500 mL asanguineous CPB prime can be removed with this method. The semi-sanguineous solution in the collection bag can be processed via a cell-saver system and re-infused.

Circuit coating

Recent attempts to attenuate the deleterious effects of blood contact with nonphysiologic surfaces have focused on modification of CPB tubing and membrane surfaces. A number of CPB coating substances are currently under investigation. These include a phosphorylcholine coating, a poly 2-methoxyethylacrylate coating, a siloxane/caprolactone oligomer coating and covalent heparin binding via the terminal amine. To date there is conflicting evidence as to whether these surface modifications reliably reduce thrombin formation and the associated consumption of platelets, fibrinogen, and antithrombin, allow reduced doses of heparin to be utilized, or attenuate complement activation and initiation of systemic inflammation.

Preparation for CPB

The anesthesiologist has several important responsibilities in ensuring safe preparation for CPB. These are described in the following sections.

Assess anticoagulation

Before use of cardiotomy suction, cannulation, and commencing bypass, it is essential that adequate anticoagulation be obtained. Inadequate anticoagulation will result in thrombus formation on the cannulas during cannulation and on the oxygenator once CPB commences. UFH currently is the primary anticoagulant used for CPB. UFH is an animal tissue (bovine lung, porcine intestinal mucosa) derived mucopolysaccharide (glycosaminoglycan) that has an antithrombin (AT)-III dependant anticoagulant mechanism of action. AT-III is responsible for binding to and inactivating the serine proteases thrombin (factor IIa), factor Xa, factor IXa, factor XIa, and factor XIIa. AT-III is 10–20 times more efficient in inactivating thrombin and factor Xa than it is in inactivating factors IXa, and XIa, and XIIa. Binding of AT-III to a specific pentasaccharide induces a conformation change in AT-III that enhances binding to and subsequent inhibition of these serine proteases by a factor of 1000–10 000. This pentasaccharide is present in about a third of the 10–90 mucopolysaccharide chains that comprise UFH. In combination with AT-III, any mucopolysaccharide chain containing the specific pentasaccharide (UFH, low molecular weight heparin (LMWH), fondaparinux) can inhibit factor Xa while only mucopolysaccharides with the specific pentasaccharide *and* a chain length ≥18 can inhibit factor IIa. This is due to the fact that a chain length of at least 18 monosaccharides is necessary to link factor IIa (thrombin) to AT-III. As a result, the anti-factor Xa/anti-factor IIa ratio of these mucopolysaccharides is solely dependent on their chain lengths. Essentially all the mucopolysaccharide chains in UFH contain >18 monosaccharide units.

It generally is acknowledged that an activated clotting time (ACT) in excess of 480 seconds is necessary to ensure adequate anticoagulation for the safe conduct of CPB. An UFH dose does not reliably result in a predictable plasma UFH concentration and that the plasma UFH concentration does not necessarily correlate with the anticoagulant effect of UFH. For this reason, a test such as the ACT, which quantitates the functional anticoagulant effect of UFH in a dose responsive fashion, must be used prior to CPB. Hypothermia, hemodilution, platelet dysfunction, and low coagulation factor levels also prolong the ACT. When any of these conditions are present the ACT will overestimate the anti-factor IIa and anti-factor Xa effects of heparin. These conditions are commonly present during CPB in infants and children.

Automated ACT determination is used in most institutions. Kaolin or celite, both potent activators

of the contact phase of coagulation, is used to initiate clot formation in whole blood. The two most common devices automated ACT devices are the Hemochron® (International Technidyne Corp.) and the Hemotec® (Medtronic).

• The Hemochron device requires placement of 2 mL of whole blood into a test tube containing either kaolin or celite and a small iron cylinder. A timer is started and the test tube is placed in the device where it is rotated in a nearly horizontal position within a magnetic field and heat block. The iron cylinder rolls along the bottom side of the tube until enough clot forms to entrain it. Once the cylinder is entrained and is longer detected by the magnetic field the timer stops signaling the clotting time.

• The Hemotec device requires placement of 0.4 mL of blood into each of two chambers that contain kaolin or celite. Each chamber contains a flag like plunger that can be raised vertically and allowed to fall passively. The chambers are placed in the device containing a heating block. A timer is started and the device raises the plungers in each chamber and allows them to fall. As clot forms the passive descent of the plunger is progressively inhibited. A photo-optical sensor detects descent of the plunger. When the velocity of the decent of the plunger falls to a predetermined value the timer stops signaling the clotting time. The ACT is the average of the two separate determinations.

• The Hemochron® and Hemotec® ACT determinations are not interchangeable. The Hemochron® determinations are typically longer than the Hemotec® determinations for a given heparin level. This difference is particularly pronounced in infants and children.

UFH is dosed in USP units not milligrams because UFH preparations vary in the number of USP units per milligram. Generally speaking UFH is prepared as 100 USP unit/mg and packaged as 1000 USP unit/mL. UFH can be dosed in two ways as follows:

• *Empirically*. Many institutions use an age or weight based empiric protocol to determine the initial pre-CPB dose of heparin. A typical adult dose of UFH would be 300–400 unit/kg. The large circuit prime volume to blood volume ratio (particularly in infants and children) would be expected to decrease plasma heparin levels with initiation of CPB unless an appropriate quantity of heparin is added to the CPB prime. Most institutions add heparin to the CPB prime in a quantity sufficient (3–4 unit/mL) to give the prime volume an UFH concentration similar to that of the patient. As a result, 5000–10 000 units are added to a 1500 mL adult prime. A typical UFH dose in children is as follows: patients <30 kg − 200 unit/kg; patients >30 kg−300 unit/kg. UFH is added to the CPB prime as follows: patients <30 kg − 2.5 unit/mL of CPB prime; patients >30 kg − 3.0 unit/mL of CPB prime.

• *Individualized heparin dose response.* Some institutions make use of technology that allows the patient UFH dose response to be determined and the individualized UFH dose to achieve a target ACT to be administered. The two most commonly used commercially available tests are the heparin response test (HRT, Hemochron®) and the heparin dose-response test (HDR, Medtronic Hemotec®). These monitors will allow detection of patients with an altered UFH dose response (those requiring a larger or smaller dose of UFH per kilogram to achieve a target ACT than the "average" empirically dosed patient).

If a baseline ACT is drawn, the following factors must be taken into consideration:

• An ACT drawn after incision will be shorter than one drawn before incision presumably due to the procoagulant state induced by surgical stress.

• Patients on preoperative UFH infusions and those with factor deficiencies that impair the intrinsic and common coagulation pathways will have prolonged ACT.

UFH should always be given into a central line or directly into the heart (usually the right atrium) by the surgeon. This is necessary to ensure that the UFH dose has reached the central circulation. The CVP port of a PA catheter or a central venous catheter works well in this regard. The ACT should be measured after UFH administration. The clinical onset of UFH is rapid with peak arterial ACT prolongation occurring within 30 seconds and peak venous ACT prolongation occurring within 60 seconds.

Heparin resistance, more properly called altered heparin dose responsiveness may occur in some patients. It is generally defined as an ACT <480

seconds following administration of 500 unit/kg of UFH. Generally, a 400 unit/kg dose of UFH is effective in prolonging the ACT to more than 400 seconds. Approximately 50% of patients who have been receiving preoperative intravenous (IV) UFH therapy will have an ACT of less than 400 seconds after a 400 unit/kg dose of UFH. The etiology of this resistance is unknown, and doses of UFH as high as 1000 unit/kg may be needed for these patients. UFH resistance has been observed in elderly patients due to decreased AT-III levels and in patients with thrombocytosis. Platelet factor 4 (which neutralizes heparin) may be released in excess in patients with thrombocytosis after UFH administration. Other causes of UFH resistance include AT-III deficiency; infective endocarditis, intracardiac thrombus, shock, and low-grade disseminated intravascular coagulation. Fresh frozen plasma (FFP) (a source of AT-III) and recombinant AT-III administration have been used as a method of improving UFH response in patients with documented AT-III deficiency. They have also has been used to reduce the UFH requirement in cases in which the source of UFH resistance is unknown.

Administration of UFH for CPB may result in hypotension due to calcium binding and can be treated with calcium administration (1–2 mg/kg). If UFH is administered over 1–2 minutes and adequate intravascular volume is maintained, calcium administration usually is unnecessary.

If the ACT is more than 480 seconds, no additional UFH is necessary. The ACT should be checked every 20 minutes until CPB commences. Additional UFH may be necessary if an extended period of time elapses. If the ACT is less than 480 seconds after the initial UFH dose, additional UFH will be necessary. By constructing a UFH dose–response curve, the required UFH dose can be determined. Most centers no longer use this cumbersome method; instead, an additional 100 unit/kg of UFH is administered and the ACT is checked 5 minutes later. This process should be repeated until an ACT level greater than 480 seconds is reached or until the total UFH dose equals 600 unit/kg. Before reaching the 600 unit/kg dose it may be prudent to make certain that the UFH is reaching the central circulation, that the UFH is

really UFH and is not outdated, and to try a different lot of UFH.

When the UFH dose reaches 600 unit/kg without an ACT of more than 480 seconds one of the following interventions should be undertaken to increase plasma AT-III levels and improve heparin dose responsiveness: 0.015–0.03 unit/kg of FFP (1–2 units in an adult) should be administered and the ACT should be rechecked, or 75 unit/kg of recombinant AT-III should be administered. In either case the possibility that enhanced heparin dose responsiveness will exacerbate heparin rebound (described later) and contribute to post-CPB bleeding must be kept in mind.

If the ACT is still less than 480 seconds, additional UFH in 100 unit/kg increments should be administered. In patients deemed to be at high risk for UFH resistance, it is best to begin the heparinization process as early as possible so that the commencement of CPB will not be unduly delayed.

Arterial cannulation

Arterial cannulation generally occurs before venous cannulation. Prior placement of the arterial cannula allows prompt commencement of CPB if severe hemodynamic compromise occurs with venous cannulation. The arterial cannula usually is placed in the ascending aorta via an aortotomy encircled by two purse-string sutures after adequate heparinization has been obtained. Transesophageal echocardiography (TEE) may be useful in guiding cannula placement. Arterial blood pressure and aortic wall tension must be carefully controlled to avoid a hematoma or intimal dissection at the cannulation site. Generally, a systolic blood pressure less than 100 mmHg or a mean blood pressure less than 60–70 mmHg is satisfactory. It may be necessary to use vasodilator therapy to accomplish this. The anesthesiologist should aid the surgeon in visually examining the arterial cannula and arterial inflow line for air bubbles after they are connected and before bypass commences. These bubbles must be eliminated before bypass starts by disconnecting the cannula and the inflow line, holding them upright, and tapping them with clamps. This allows the bubbles to float upward, where they can be

flushed out before the inflow line and cannula are reconnected.

Obstruction of the lumen of the aorta may occur if the cannula is introduced too far into the aorta. Because the arterial cannula is relatively large as compared to the aorta in infants and neonates, complete or partial obstruction of the aorta by the cannula itself is possible. Constant vigilance is necessary to avoid this problem. If dampening of the arterial trace, distension of the systemic ventricle, or an increase in CPB line pressure occurs with placement or manipulation of the arterial cannula, the surgeon should immediately be made aware of the situation so the cannula can be repositioned.

Venous cannulation

Placement of the venous cannula requires that the surgeon manipulate the right atrium and potentially the IVC and SVC. This manipulation may result in compromise of venous return to the heart as well as a variety of atrial dysrhythmias such as atrial premature beats, atrial fibrillation, or atrial flutter. These perturbations may result in hemodynamic compromise. For this reason, it is essential that the internal cardioversion paddles be on the surgical field, ready to be synchronized before atrial cannulation commences. Placement of the venous cannula also may result in rapid blood loss. This blood can be collected with the cardiotomy suction and rapid transfusion of prime solution can occur via the arterial cannula.

Temperature

Various sites are available for monitoring body temperature. The core is considered to be the well-perfused organs; the shell is an intermediate area that consists mainly of less well-perfused muscle and fat. Shell temperature will lag behind core temperature during cooling and rewarming. Homogenous cooling and rewarming should result in a minimal temperature gradient between core and shell temperature.

Tympanic membrane

This is a core temperature site. These probes provide close correlation to the temperature at the base of the brain during cooling and rewarming and to actual brain temperature during stable hypothermia. These probes are associated with minimal risk of tympanic membrane damage.

Esophagus

This is a core temperature site. During rapid cooling and rewarming and during CPB, temperature measurements in the esophagus must be interpreted with caution. Because of their proximity to the mediastinum, probes in the esophagus will reflect changes in the CPB perfusate temperature and the temperature of blood or fluid in the pericardial space not detected in other core sites. Esophageal temperatures will fall quickly during cooling and rise rapidly during rewarming and may not accurately reflect the patient's temperature in other core sites. The blood temperature, as measured by the PA catheter, closely approximates esophageal temperature. The reliability of PA catheter temperature monitoring on CPB is limited because there is little or no pulmonary blood flow at this time.

Nasopharyngeal

These probes, like tympanic membrane probes, provide close correlation to the temperature at the base of the brain during cooling and rewarming and to actual brain temperature during stable hypothermia. There is little risk associated with placement of these probes and, as a result, this site is preferred by many institutions to the tympanic membrane. This site is not influenced by acute changes in mediastinal temperature changes and will more closely reflect actual core temperature changes.

Rectum and urinary bladder

Rectal temperature is not a core temperature but a measure of shell temperature. Bladder temperature and rectal temperature correlate closely. High urine output creates closer correlation between bladder temperature and core temperature. Temperature changes in the rectum and bladder will lag behind temperature changes in the core sites. These probes are therefore very useful in determining whether the core and shell temperatures have equilibrated after cooling and rewarming.

Temperature monitoring in association with CPB and particularly DHCA is of paramount importance given that hypothermia prior to and during CPB and DHCA and the avoidance of hyperthermia after CPB and DHCA are the mainstays of cerebral protection. It has been demonstrated clinically in association with DHCA that core temperature monitoring sites (esophagus, tympanic membrane, nasopharyngeal, and PA) track brain temperature. However, temperature at these sites differs from true brain temperature by several degrees, sometimes overestimating and sometimes underestimating true brain temperature. None of these sites consistently and accurately measures brain temperature. Shell sites, such as rectum and bladder, may be useful in assuring homogenous somatic rewarming but perform poorly as measures of brain temperature. It is prudent then to use temperature readings from multiple sites (both core and shell) during cooling and rewarming.

Baseline assessment of the pupils

The pupils should be checked for symmetry, and any asymmetry due to iridectomies or the like should be noted.

Commencing CPB

The anesthesiologist must work in concert with the perfusionist and the surgeon to ensure that CPB commences smoothly. The anesthesiologist must remain alert to help solve problems.

Assess venous drainage

When the clamps are taken off the venous line, there should be continuous flow of venous blood from the venous cannula(s) into the pump reservoir. If this does not occur, the venous line must be examined for air lock, residual clamps, or mechanical obstruction of the cannula due to malposition. The surgeon and perfusionist must be alerted if they are not aware of the situation. The head and neck should be assessed for adequate venous drainage, and the pupils should be rechecked for symmetry. Poor SVC drainage will result in engorgement and cyanosis of the head and neck. If poor SVC drainage is suspected, the surgeon should be alerted so that the cannula can be repositioned. Measurement of the pressure in the SVC (not the RA) is useful in detecting poor SVC drainage. The monitoring site must be cephalad to the SVC lumen of a two-stage venous cannula or cephalad to the tourniquet around the SVC cannula when the SVC is cannulated separately. This can be accomplished by transducing the side port of the PA catheter introducer or a catheter in the SVC. PA catheters migrate further out into the pulmonary arterial system during CPB and ventricular apical retraction. The PA catheter should be pulled back 5 cm as CPB commences to prevent it from lodging in the wedge position.

Assess arterial inflow

When the pump head begins to turn, there should be continuous flow of the crystalloid prime followed by oxygenated blood into the aorta. The arterial waveform will take on a nearly nonpulsatile flat line form punctuated by intermittent small pulsations as the LV ejects its small residual volume. When an extremely low (<30 mmHg) or nonexistent pressure is observed as CPB commences, dissection at the site of aortic cannulation must be excluded immediately. It is heralded by dilation and bluish discoloration of the cannulated vessel, a reduction in arterial pressure, and an increase in the pump line pressure. An aortic dissection requires immediate attention. The dissection site must be repaired and an alternate cannulation site must be found.

Misdirection of the aortic cannula into one of the arch vessels should be assessed as CPB commences. A high arterial perfusion line pressure is likely to result but is not uniformly observed. If the subclavian or innominate artery is cannulated, the blood pressure measured in the ipsilateral radial artery will be abnormally high with wider-than-normal pulsations, whereas that measured in the contralateral radial artery will be abnormally low (below 30 mmHg). Cannulation of either carotid artery will result in an abnormally low pressure, regardless of which radial artery pressure is being monitored. Unilateral otorrhea, rhinorrhea, conjunctival edema, facial edema, and facial coldness are later signs of arch vessel cannulation and are the result of cerebral overperfusion. Misdirection has been reported into the innominate artery;

left subclavian artery, and left carotid artery. If misdirection is suspected, immediate action to correct the placement is necessary.

The risk of misdirection of the arterial cannula into one of the arch vessels is higher in reoperative procedures because the surgeon may need to cannulate the aorta higher to avoid the previous cannulation site. TEE is not reliable in visualizing the ascending aortic cannulation site due to the blind spot created by the trachea and bronchus. However, longitudinal plane imaging reliably allows visualization of the left subclavian and left carotid arteries. In conjunction with color flow Doppler imaging, it is possible to detect preferential direction of the jet of blood out of the cannula into one of these arteries. Some centers utilize NIRS and TCD technology as adjunctive methods to assess cerebral blood flow during CPB.

Assess oxygenator function

After CPB has commenced the oxygenator function must be rapidly assessed. There should be immediate visual assessment of bright red blood leaving the oxygenator. Infrared oxygen saturation monitors on the venous and arterial lines will verify that the blood leaving the oxygenator is saturated with oxygen. Optical fluorescence technology allows on-line monitoring of both venous and arterial Po_2, Pco_2, and pH. Blood gas analysis is routine and will provide information on oxygenation, carbon dioxide elimination, and acid-base status. If arterialized blood does not leave the oxygenator, it must be assessed immediately for malfunction. The most likely cause of failure is an inadequate supply of fresh gas to the oxygenator from a flow meter malfunction, gas line switch or gas line leak.

Inadequate arterial oxygenation also may occur if the maximum flow capacity of the oxygenator is exceeded. Inadequate arterial oxygenation may occur at flow rates less than the maximal flow capacity if a very low mixed venous saturation exists as bypass commences. The most common causes of a low mixed venous oxygen saturation as CPB commences are as follows:
- Low pre-bypass cardiac output.
- Oxygen consumption that is abnormally high due to shivering, light anesthesia, or hyperthermia.

- The surface area of the oxygenator is too small to meet the metabolic demands of a large patient.

Discontinue ventilation

Ventilation should be discontinued after bypass has commenced unless partial CPB is initiated and a significant volume of blood continues to flow through the pulmonary arteries. Complete collapse of the lungs provides optimal surgical exposure, whereas continuous positive airway pressure potentially inhibits exposure and has no proven benefit in the post-CPB period.

Assess need for venting

The anesthesiologist can aid the surgeon in the decision to vent by observing the right and left heart for dilation with TEE and by examining the RA and pulmonary artery pressure traces on CPB. An elevation of the RA pressure suggests continued blood return and dilation of the right heart. An elevation of the PA pressure suggests left ventricular distension with mitral valve incompetence and retrograde flow of blood into the PA.

Supplement neuromuscular blockade

It is important to administer a muscle relaxant as CPB commences to prevent the large increases in systemic oxygen consumption that accompany shivering and to prevent the diaphragmatic movement that compromises surgical exposure during the operative procedure. The effect of hypothermic CPB on nondepolarizing neuromuscular blockade is complex. Hypothermic CPB in the absence of neuromuscular blockade enhances electrochemical neuromuscular transmission, assessed by electromyogram (EMG) but attenuates mechanical function, assessed by twitch tension development. Clinically, the goal is attenuation of the mechanical response with neuromuscular blocking agents. Vecuronium neuromuscular blockade as assessed by twitch tension is enhanced and prolonged by hypothermic CPB, whereas pancuronium neuromuscular blockade as assessed by twitch tension is unaltered.

From a practical point of view, any of the nondepolarizing muscle relaxants can be utilized

to ensure muscle relaxation during CPB. It has been demonstrated that pancuronium requirements are increased at the initiation of CPB and during rewarming. Presumably, hemodilution at the onset of CPB reduces the plasma concentration of neuromuscular blocking agents, whereas rewarming reverses hypothermia-induced depression of twitch tension development. Pancuronium 0.05 mg/kg at the start of CPB, followed by pancuronium 0.01 mg/kg/h while on CPB, is sufficient. When DHCA is used, a large enough dose of relaxant to last the entire arrest period must be administered at the outset.

Conduct of CPB

After CPB has commenced, the perfusionist assumes primary responsibility for its safe conduct with the cooperation of the surgeon and anesthesiologist. It is necessary to be familiar with the effects of CPB on various organ systems to make rational management decisions.

Temperature

CPB is most commonly conducted in conjunction with systemic hypothermia. Systemic hypothermia reduces systemic oxygen consumption and reduces cerebral oxygen consumption. Q_{10} defines the ratio of oxygen consumption at a defined temperature to the oxygen consumption at temperature $10°C$ lower. Systemic Q_{10} is approximately 2.5, whereas cerebral Q_{10} is approximately 2.1–3.5. Reductions in oxygen consumption permit reductions in oxygen supply to be tolerated. Levels of hypothermia have been defined as follows: mild (32–35°C), moderate (26–31°C), deep (20–25°C), and profound (<20°C). Unfortunately, not all authors adhere to this classification and care must be taken when comparing data from studies. For instance, it is not uncommon for temperatures <20°C used in conjunction with pediatric cardiac surgery to be called "deep hypothermia".

Normothermic CPB for CABG surgery is utilized in some institutions. When normothermic CPB is conducted so as to avoid inadvertent cerebral hyperthermia there is no difference in cognitive outcome as compared to hypothermic CPB in CABG patients.

Systemic blood flow

Systemic blood flow on CPB can be varied instantaneously and is determined by the rate of arterial pump head rotation. In the steady state, systemic blood flow and venous return must be equal, just as they are in the intact circulatory system. If venous return is compromised for any reason, then systemic blood flow may transiently exceed venous return and the volume of blood in the venous reservoir will diminish. As the volume of blood in the venous reservoir falls, the perfusionist must decrease systemic blood flow by decreasing the speed of pump rotation. Simultaneously, volume is added to the venous reservoir while the source of compromised venous return is aggressively pursued and corrected. If the venous reservoir is inadvertently emptied, massive arterial air embolization may occur. This disastrous complication is preventable in several ways:

- Vigilance on the part of the perfusionist and anesthesiologist.
- Level sensors on the venous reservoir that sound and/or shut down the arterial pump head when a predetermined reservoir volume is reached.
- Bubble sensors on the arterial perfusion line that shut down the arterial pump head before massive transfusion of air occurs.

Optimal flow rates for CPB have yet to be defined clearly, although the goal is to maintain systemic and cerebral oxygen delivery. Flows of 2.0–2.4 L/min/m² are used for infants, children, and adults during mild to moderate systemic hypothermia. Due to age-related differences in the relationship of surface area to weight, these flow rates expressed in milliliters per kilograms per minute will be substantially higher in the neonate than in the adult. The recommended full flow rates for CPB are summarized in Table 10.5. Low flow CPB in neonates and infants conducted in conjunction with temperatures of 18–25°C is generally defined as 50–70 mL/kg/min or approximately 1.0–1.5 L/min/m². Flows as low as 1.2 L/min/m² will not compromise whole-body oxygen delivery when moderate systemic hypothermia is employed. At such low flow rates, with higher temperature, systemic oxygen delivery is maintained by increased peripheral extraction of oxygen. Because low mixed

Table 10.5 Full cardiopulmonary bypass (CPB) flow rates.

Patient weight (kg)	Full CPB flow rates (mL/kg/min)
<3	150–200
3–10	125–175
10–15	120–150
15–30	100–120
30–50	75–100
>50	50–75

venous oxygen saturations result, oxygen delivery reserve is compromised.

To improve surgical exposure during complex intracardiac repairs and arch reconstructions in neonates and children and during aortic arch repairs in adults, DHCA may be used. DHCA allows cessation of blood flow, cannula removal, and exsanguination of the patient into the venous reservoir. DHCA has been studied most extensively in pediatric patients.

Systemic blood pressure

Mean arterial pressure (MAP) on CPB is determined by the relationship between pump flow and systemic vascular resistance (SVR):

$$SVR = [(MAP - CVP) \times 80]/\text{pump flow rate}$$

Recall that the CVP on CPB with adequate venous drainage will be zero and that 80 is a conversion factor (Wood units to dynes s/cm^5). For a given SVR, the MAP can be instantaneously increased or decreased by increasing or decreasing pump flow. Likewise, the perfusionist is able to maintain MAP when acute increases or decreases in SVR occur by decreasing or increasing pump flow. It is not uncommon for MAP to decrease to 30–50 mmHg as CPB commences despite pump flow rates of 2.0–2.4 L/min/m^2 or approximately 4 L/min in a 70-kg patient.

This is due, in part, to the enormous decrease in viscosity that occurs when the patient's blood volume and the asanguineous prime first mix. Viscosity, as discussed previously, is a major determinant

of SVR. Several other factors have been identified which influence SVR on CPB:

- *Temperature.* The incidence of low SVR is significantly higher during normothermic compared with hypothermic CPB. This may be caused by vasoconstriction induced by hypothermia or release of vasodilator substances during normothermia. Long periods of rewarming during reperfusion also seem to contribute to low SVR.
- *Age and peripheral vascular disease.* Older patients and patients with peripheral vascular disease are less likely to exhibit low SVR during CPB secondary to a less compliant arterial system.
- *Diabetes mellitus.* Diabetics are less likely to exhibit low SVR during CPB secondary to coexisting vascular disease, sympathetic neuropathy with near maximum vasodilation at rest, and reduced baroreceptor sensitivity.
- *Left ventricular function.* Patients with LV ejection fraction (EF) < 40% are less likely to exhibit low SVR during CPB. These patients tend to be receiving vasodilator therapy to improve systolic function and may have near-maximal vasodilation at rest.

Cerebral blood flow

The control of cerebral blood flow on CPB is dependent on several factors, as described in the following sections.

Cerebral autoregulation

Cerebral blood flow autoregulation is altered by hypothermic nonpulsatile CPB. Cerebral blood flow is autoregulated between MAP values of 30 and 110 mmHg during CPB in patients without cerebrovascular disease or preexisting hypertension. In contrast, in the intact circulation of normal, nonhypertensive patients, cerebral blood flow is autoregulated between MAP values of 50 and 150 mmHg. Unfortunately, there are no data on the lower limit of cerebral autoregulation on CPB in patients with coexisting cerebrovascular disease. It may be prudent to maintain a slightly higher MAP (higher than 50 mmHg) on CPB in patients with known cerebrovascular disease although there is no evidence to support or refute this recommendation.

Aging has not been shown to have an effect on cerebral autoregulation during CPB. Diabetics

appear to have impaired cerebral autoregulation during CPB. Cerebral autoregulation is lost and cerebral vascular responses to $Paco_2$ are attenuated under conditions of deep (18–20°C) hypothermia CPB in infants and children. This is felt to be due to cold induced vasoparesis.

Acid-base management

Electrochemical neutrality is important in preservation of cellular protein and enzyme structure and maintenance of the constant transcellular hydrogen (H^+) ion gradient necessary for many cellular processes. In addition, optimal functioning of the imidazole buffering system is dependent on maintenance of cellular electrochemical neutrality. The imidazole group of the amino acid histidine is present on many blood and cellular proteins and is an important buffer. Electrochemical neutrality occurs when there are equal concentrations of hydroxyl (OH^-) and hydrogen (H^+) ions. As temperature decreases, the dissociation constant (pK) of aqueous systems such as those found in cells increases. This process results in a reduction in the concentrations of OH^- and H^+ ions as temperature decreases. If there are equal concentrations of OH^- and H^+, then electrochemical neutrality will be maintained. Recall that pH is the inverse log of the H^+ ion concentrations; as the H^+ ion concentration decreases, pH increases. Thus, for electrochemical neutrality to be maintained, pH must increase as temperature decreases. In an electrochemically neutral cell at 37°C, the measured pH will be 7.40, whereas in an electrochemically neutral cell at 20°C, the measured pH will be 7.80.

Changes in cellular pH during hypothermia are mediated through $Paco_2$ homeostasis. As temperature decreases, the solubility of carbon dioxide in blood increases. If the total carbon dioxide content of blood is held constant, this increase in carbon dioxide solubility will result in a reduction in $Paco_2$. For example, if the total carbon dioxide content is held constant and the measured $Paco_2$ at 37°C is 40 mmHg, then the measured $Paco_2$ at 20°C will be 16 mmHg. This situation causes pH to increase as temperature decreases and electrochemical neutrality to be maintained.

pH-Stat and α-stat regulation are acid-base management methods that directly influence blood flow to the brain and other organs. Although pH-stat and α-stat acid-base management commonly are mentioned in association with temperature-corrected and temperature–uncorrected blood gases, it must be emphasized that these are entirely different concepts. The method of blood gas interpretation (corrected or uncorrected) does not dictate the method of acid-base management (pH-stat or α-stat). In fact with the use of Table 10.6, α-stat or pH-stat management is possible with use of both temperature-corrected and uncorrected blood gases. In addition, is important to point out that at a patient temperature of 37°C there is no difference between pH-stat and α-stat management. The difference between these two strategies becomes

Table 10.6 Alpha-stat versus pH-stat acid-base management.

Patient temp. (°C)	Temperature uncorrected (reported at 37°C)				Temperature corrected (reported at patient temperature)			
	α-stat pH	pH-stat pH	α-stat Pco_2	pH-stat Pco_2	α-stat pH	pH-stat pH	α-stat Pco_2	pH-stat Pco_2
37	7.40	7.40	40	40	7.40	7.40	40	40
33	7.40	7.34	40	47	7.44	7.40	35	40
30	7.40	7.30	40	54	7.50	7.40	29	40
27	7.40	7.26	40	62	7.55	7.40	26	40
23	7.40	7.21	40	74	7.60	7.40	22	40
20	7.40	7.18	40	84	7.65	7.40	19	40
17	7.40	7.14	40	96	7.69	7.40	17	40

more marked as patient temperature progressively decreases below 37°C and is not clinically relevant until patient temperature <30°C (see Table 10.6).

When a blood gas sample is drawn from a patient at 25°C and sent to the blood gas laboratory, the sample is warmed to 37°C before measurement. The values obtained at 37°C are called the temperature-uncorrected values. These values are converted to temperature-corrected values using a nomogram. The nomogram accounts for temperature-induced changes in pH, oxygen solubility, and carbon dioxide solubility in a closed-blood system. When pH and $Paco_2$ are measured at 37°C and then corrected to a lower temperature, the electrochemically neutral pH will be higher and the corrected $Paco_2$ will be lower than the normal values at 37°C. Therefore, electrochemical neutrality is maintained by keeping pH alkalotic in temperature-corrected blood gases and normal in temperature-uncorrected gases. This is known as α-stat regulation. For practical purposes, it is easier to use uncorrected gases and keep pH and $Paco_2$ in the range considered normal at 37°C. Cerebral blood flow and oxygen consumption are appropriately coupled when α-stat regulation is used. Deep hypothermia in the presence of α-stat regulation produces loss of cerebral autoregulation such that cerebral blood flow varies directly with arterial pressure.

pH-Stat regulation refers to maintaining pH and $Paco_2$ at normal values for 37°C when temperature-corrected gases are used and at acidotic values when temperature-uncorrected gases are used. pH stat is maintained by adding carbon dioxide to the ventilating gas during hypothermic CPB to increase $Paco_2$ and decrease the pH. In contrast to α-stat regulation, in which total carbon dioxide content is kept constant, pH stat regulation results in an increase in total carbon dioxide content. The cerebral vasculature maintains vasomotor responses to varying $Paco_2$ during hypothermic CPB. This response is maintained during moderate hypothermia and is attenuated during deep hypothermia despite the fact that deep hypothermia induces loss of cerebral blood flow autoregulation. When pH-stat regulation is used with moderate hypothermic CPB, there is uncoupling of cerebral blood flow and metabolism and loss of cerebral autoregulation.

As a result, cerebral blood flow varies linearly with arterial blood pressure and cerebral hyperperfusion exists with cerebral blood flow far in excess of that dictated by cerebral metabolic rate. This hyperperfusion state is the result of reduced cerebral oxygen consumption induced by hypothermia and cerebral vasodilation resulting from a disproportionately high $Paco_2$ for the degree of hypothermia present. The potential danger of the hyper-perfused state is increased delivery of microemboli into the cerebral circulation.

Clinical trials in adults suggest that use of α-stat management during normothermic or hypothermic CPB results in improved cognitive outcome following cardiac surgical procedures. The question as to whether pH-stat or α-stat management should be utilized during DHCA in adults is a source of debate. In infants and children, pH-stat management is generally initiated once the perfusate temperature <28–30°C.

Pump flow rates

Cerebral blood flow and oxygen delivery are maintained with flow rates as low as $1.0 \, L/min/m^2$ and perhaps as low as $0.5 \, L/min/m^2$ when moderately hypothermic CPB (26–29°C) and α-stat regulation are used. There is preferential distribution of blood flow to the brain when low pump flows are used. Despite this, cerebral oxygen delivery at these flows is maintained at the expense of increased cerebral extraction of oxygen and decreased jugular venous oxygen saturation. In addition, despite the fact that somatosensory neural transmission remains intact when moderate systemic hypothermia is used and pump flow is reduced to $0.5 \, L/min/m^2$, significant cerebral lactate accumulation develops after 15 minutes.

Low flow rates are used most commonly in conjunction with pediatric open-heart procedures to improve surgical exposure. In neonates, infants, and children, cerebral blood flow and cerebral metabolism are unaffected by reductions in conventional pump flow rates less than 45%. When conventional flow rates (150 mL/kg/min for neonates and 100 mL/kg/min for infants and children) are reduced 45–70% at moderate hypothermia (26–29°C) with α-stat acid-base management,

cerebral blood flow and metabolic rate decrease with a compensatory increase in oxygen extraction. Similar reductions during deep hypothermia (18–22°C) do not produce increased oxygen extraction. Minimal acceptable low flows on CPB for pediatric patients are not yet clearly defined, but cellular oxygen debt occurs at 5–30 mL/kg/min at 18°C and at 30–35 mL/kg/min at 28°C. In neonates cooled to 18°C, cerebral blood is detectable in the middle cerebral artery by TCD as long as CPB flow rate is at least 30 mL/kg/min.

Myocardial blood flow

On CPB, the coronary ostia are provided with hemodiluted, nonpulsatile blood flow until the aortic cross clamp is applied. Aortic cross-clamping for cardiac surgery involves placing a completely occlusive clamp across the ascending aorta between the aortic cannula and the aortic valve, such that the coronary circulation is excluded from the CPB circulation. Aortic cross-clamping has evolved as the method of choice for providing an immobile, bloodless field for the cardiac surgeon. Depending on the operative procedure and technique, variable periods of time may pass from the onset of CPB until placement of the aortic cross-clamp. It is therefore necessary to be familiar with the effects of CPB, hemodilution, and hypothermia on myocardial oxygen delivery and demand.

Myocardial oxygen delivery

Myocardial oxygen delivery is the product of coronary blood flow and the oxygen-carrying capacity of the blood. Coronary blood flow in turn is dependent on the pressure gradient between the aorta and the myocardial tissue. For the subendocardium, the tissue most likely to be hypoperfused, this gradient is equal to the MAP minus the right or left ventricular intracavitary pressure. The factors described in the following sections play a major role in determining oxygen and substrate delivery to the myocardium, particularly the subendocardium, during CPB.

• *Coronary stenoses.* Due to the pressure drop across stenoses, perfusion to the area supplied by the stenosed artery will be compromised if

MAP is reduced. Therefore, whereas cerebral blood flow can be maintained with perfusion pressures as low as 30 mmHg, myocardium supplied by stenosed arteries is poorly perfused at this pressure. Such low perfusion pressures should not be tolerated for more than a few minutes in patients with critical stenoses. Subendocardial ischemia in the distribution of a critical coronary stenosis is avoided if MAP is maintained at 80 mmHg in the beating empty heart. However, subendocardial ischemia is inevitable in the distribution of a critical coronary stenosis when ventricular fibrillation exists despite maintenance of MAP. This ischemia is seen to develop after as little as 15 minutes of ventricular fibrillation with MAP values as high as 80 mmHg.

• *Ventricular distension.* Ventricular distention markedly elevates intracavitary pressure and compromises subendocardial perfusion for a given MAP. The causes of ventricular distension have been discussed previously. If ventricular distension is likely to persist, then ventricular venting is necessary. Ventricular distension can be terminated promptly when aortic insufficiency exists by placing the aortic cross-clamp.

• *Ventricular fibrillation.* As systemic cooling on CPB progresses, the heart becomes progressively more bradycardic. When the temperature of the heart reaches approximately 28°C, coarse ventricular fibrillation ensues and myocardial wall tension increases. As the temperature of the heart continues to drop, the ventricular fibrillation becomes finer, myocardial oxygen consumption decreases, and ventricular wall tension diminishes. Ventricular fibrillation, particularly in hypertrophied myocardium, results in poor perfusion of the subendocardium due to increased myocardial wall tension and a reduced perfusion gradient. When the MAP is less than 50–60 mmHg, subendocardial perfusion will be compromised when ventricular fibrillation exists.

• *Hemodilution.* In the presence of adequate perfusion pressures, myocardial oxygen delivery is potentially compromised by the reduced oxygen-carrying capacity of the hemodiluted systemic perfusate despite the fact that the decreased temperature allows more oxygen to be carried in solution.

Oxygen delivery to the nonhypertrophied ejecting myocardium is unlikely to be compromised unless the Hct is less than 15%. In the presence of coronary stenoses or concentric hypertrophy, Hct values in the 20–30% range may be needed to prevent ischemia during normothermic CPB.

● *Hypothermia.* Hypothermia reduces coronary vasodilator reserve capacity and potentially limits myocardial oxygen delivery. Therefore, despite the fact that hypothermia reduces myocardial oxygen consumption (described later), subendocardial ischemia develops in the beating, empty heart when MAP is lower than 50 mmHg at 28°C due to attenuated coronary vasodilator reserve.

Myocardial oxygen demand

CPB provides a state of hypothermic, hemodiluted, nonpulsatile flow during which the heart is called upon to do little or no mechanical work in the form of generating pulsatile flow. The two major determinants of myocardial oxygen consumption on CPB are temperature and the functional status of the myocardium.

● *Temperature.* As Fig. 10.12 illustrates, the lower the temperature of the heart, the less oxygen it
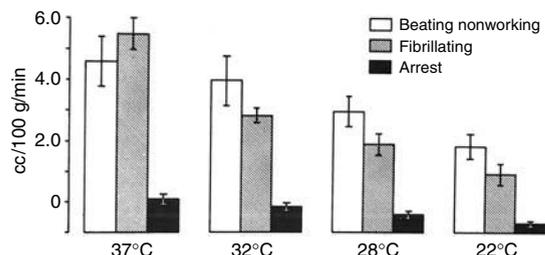
Fig. 10.12 Left ventricular oxygen consumption during three functional states (beating empty, fibrillating, and arrested) and at four temperatures. Hypothermia clearly reduces myocardial oxygen consumption for any functional state. Below 37°C, the beating empty heart consumes the most oxygen, followed in decreasing order by the fibrillating and arrested heart. (From Buckberg GO, *et al.* Studies on the effects of hypothermia on regional myocardial blood flow and metabolism during cardiopulmonary bypass I. The adequately perfused beating, fibrillating, and arrested heart. *J Thorac Cardiovasc Surg* 1977;**73**:89, with permission.)

consumes per minute for a given functional state. For the beating empty heart, oxygen consumption per beat increases as temperature decreases due to the positive inotropic effect of hypothermia on the myocardium. However, this increase in oxygen consumption per beat is overshadowed by the larger relative decrease in heart rate induced by cold, such that oxygen consumption per minute falls.

● *Functional status.* The functional status of the myocardium whether beating and empty, fibrillating, or arrested plays an important role in determining myocardial oxygen consumption (see Fig. 10.12). Below 37°C, the heart consumes less oxygen fibrillating than it does beating and empty. Recall, however, that subendocardial perfusion is compromised by fibrillation due to increased wall tension. Subendocardial perfusion will be further compromised in the un-vented fibrillating, heart.

Renal function

Normally, renal blood flow is autoregulated between renal artery pressures of 80 and 180 mmHg. Despite this, systemic flows as low as 1.6–1.8 L/m^2/min and sustained MAP as low as 50 mmHg during hypothermic, hemodiluted, nonpulsatile CPB do not result in a deterioration of post-CPB renal function. In addition, pH management, pulsatile versus nonpulsatile flow, and CPB temperature do not influence renal function during or after CPB. The quantity of urine output on CPB is not a reliable predictor of post-CPB renal dysfunction. The presence of preexisting renal dysfunction, post-CPB ventricular dysfunction and low cardiac output, use of intra-aortic balloon pump (IABP), emergency operative procedures, DHCA, prolonged CPB time, valve surgery, diabetes mellitus, and advanced age have all been identified as independent predictors of post-CPB renal dysfunction and acute renal failure. In fact, the presence of post-CPB ventricular dysfunction and low cardiac output is a major risk factor in the development of post-CPB renal dysfunction and failure.

Generally, a urine output of 1 mL/kg/h is considered adequate while on CPB. Although urine output on CPB has not consistently been correlated

with post-CPB renal function, oliguria (urine output <0.5 mL/kg/h) must be considered a harbinger of renal hypoperfusion and ischemia.

Recommendations for conduct of CPB

Lower limits of MAP

The safe lower limits of MAP on CPB must be determined with all organ systems in mind. If the aortic cross-clamp is applied within 1–2 minutes after the start of CPB, a MAP greater than 30 mmHg with a pump flow of 2.0–2.4 L/min/m^2 is acceptable for patients without cerebrovascular disease. For patients with known cerebrovascular disease, a MAP in excess of 50 mmHg may be more prudent. If there is a delay in placing the aortic cross-clamp, then attention should be directed toward optimal perfusion of the myocardium. A MAP of at least 50 mmHg should be maintained for perfusion of the beating, empty heart. If ventricular fibrillation develops and is likely to persist for more than a few minutes, then MAP must be elevated to at least 60–80 mmHg to ensure subendocardial perfusion. Likewise, if ventricular fibrillation is likely to persist, myocardial temperature should be decreased to reduce oxygen consumption and improve perfusion by lowering wall tension. A vent must be placed if left ventricular distension occurs. If coronary stenosis or ventricular hypertrophy also exists, MAP must be elevated to 80–100 mmHg and the cross-clamp should be applied as soon as possible.

If high pump flows are needed to maintain the desired MAP, the maximal flow capacity of the oxygenator may be exceeded. If this is likely, then SVR can be increased and pump flow can be decreased to maintain MAP. SVR can be increased by transfusion of blood into the venous reservoir to increase viscosity. Generally, this strategy is reserved for those instances in which the Hct is less than 20%. SVR can also be increased by increasing arteriolar tone. The simplest way to accomplish this is by infusing an α-agonist such as phenylephrine into the pump. As a rule, as CPB progresses, arteriolar tone will increase and the phenylephrine can be stopped.

Upper limits of MAP

Generally, a mean arterial blood pressure less than 70 mmHg is maintained to remain within the limits of cerebral autoregulation and to reduce noncoronary collateral blood flow after the aortic cross-clamp has been applied. Because the noncoronary collaterals originate from the mediastinum and pericardium, the blood they deliver to the heart will be at the same temperature as the patient (25–30°C). While the aortic cross-clamp is in place and the heart is arrested with cardioplegia, optimal myocardial temperature is usually between 8°C and 15°C. Excessive noncoronary collateral flow will cause the heart to rewarm and compromise myocardial preservation. Excessive noncoronary collateral flow also will compromise surgical exposure by causing bleeding from the incised coronary artery. There are several strategies available to reduce MAP and each has its own advantages and disadvantages:

- Reduction of pump flow is useful as a temporizing maneuver, but a prolonged reduction may result in systemic and cerebral hypoperfusion.
- Sodium nitroprusside is a very effective arteriolar dilator and thus very useful in reducing SVR. It is easily titratable, has no negative inotropic properties, and has a short half-life. It has, however, been implicated in causing reversible platelet dysfunction. Nitroglycerin does not cause platelet dysfunction, is easily titratable, and has a short half-life and no negative inotropic properties but is much less effective than nitroprusside. This decreased effectiveness is because nitroglycerin is primarily a venodilator and actively adheres to the plastic components of the CPB circuit.
- Volatile anesthetic agents such as sevoflurane, desflurane, and isoflurane are very effective, easily titratable arteriolar dilators. The vaporizer must be spliced into the fresh gas flow line of the oxygenator. Caution must be exercised when CPB vaporizers are filled with inhalation agent because the plastic components of the oxygenator may crack if agent is accidentally spilled on them. During CPB with a membrane oxygenator, inhalational anesthetic agents are completely eliminated from the circulation 10–15 minutes after they are discontinued. Nonetheless, it is prudent to discontinue these agents before removal of the aortic cross-clamp to

allow adequate time for their elimination before coronary blood flow resumes if there is a concern.

Urine output

A urine output of at least 1.0 mL/kg/min is desirable on CPB. Urine output should be assessed every 15 minutes while on CPB. If urine output falls below 0.1 mL/kg/15 min (0.5 mL/kg/h), action is necessary. Aortic perfusion pressure should be increased to at least 50 mmHg. If this fails to increase urine output or if aortic perfusion pressure is already optimized consideration should be given to improving hematocrit to at least 25%. Induction of diuresis with furosemide 0.5–1.0 mg/kg or mannitol 0.5–1.0 g/kg is of no proven utility but can be considered in circumstances where extensive use of cardiotomy suction leads to hemolysis and hemoglobinuria. In this circumstance alkalization of the urine with sodium bicarbonate should also be considered. Prophylactic administration of dopamine or fenoldopam during CPB is of no proven benefit in improving renal function during or after CPB.

Monitoring of anticoagulation

Maintenance of anticoagulation must continue on CPB. The anticoagulant effect of UFH is prolonged by the presence of hemodilution, the anticoagulant effect of hypothermia, and the prolonged half-life of UFH associated with hypothermia. Nonetheless, the anticoagulation status of the patient should be monitored at least every 30 minutes with an ACT. More frequent ACT assessment is necessary during periods of cooling and rewarming. Care must be taken to ensure adequate anticoagulation during rewarming.

Preparation for termination of CPB

It is essential that an organized approach be taken to preparing for the termination of CPB so that a smooth transition is ensured. The anesthesiologist has a number of responsibilities as outlined below.

Ensure rewarming

After induced systemic hypothermia, it is necessary to ensure that adequate core rewarming has

occurred before termination of CPB. The perfusionist will assume responsibility for using the heat exchanger to rewarm the patient when instructed to do so by the surgeon. Generally, rewarming will take place for 30–60 minutes before termination of CPB, depending on the degree of the hypothermic state and its length. As with cooling, the site of temperature measurement is important in assessing homogeneous core rewarming. Equilibration of the bladder or rectal temperature and the nasopharyngeal temperature at 36–37°C is desired.

The rate of rewarming is important, as increased cerebral oxygen extraction has been noted in adults during rapid rewarming. In the setting of constant cerebral oxygen delivery this increase in oxygen extraction results in a wider cerebral AVO_2 saturation difference (a lower jugular venous oxygen saturation). This increase in cerebral oxygen extraction during rewarming is associated with subsequent cognitive defects, particularly in elderly patients. Better cognitive outcome is achieved following coronary artery bypass surgery in adults when slow rewarming (2°C difference between nasopharyngeal and CPB perfusate temperature) is compared to more standard rewarming (4–6°C difference between nasopharyngeal and CPB perfusate temperature).

Enthusiasm for homogenous somatic rewarming should also be tempered by the fact that brain temperature continues to increase for at least 6 hours following CPB procedures. Postoperatively, actual brain temperature is underestimated by esophageal, tympanic and rectal temperatures and may rise to levels that exacerbate neuronal injury. The maximum postoperative temperature as measured by a PA catheter in the first 24 hours is weakly associated with a greater amount of cognitive dysfunction after cardiac surgery in adults.

Despite homogeneous core rewarming, it is not uncommon for the patient's core temperature to drop 2–3°C in the hour after termination of CPB. This is due to reperfusion of the cold extremities, which results in a re-equilibration of the patient's temperature at a lower core temperature. The greater the difference between the nasopharyngeal and the rectal or urinary bladder temperature

when CPB is terminated, the greater will be the expected temperature afterdrop. This temperature afterdrop may result in arterial vasoconstriction and shivering, which will increase myocardial oxygen consumption. Infusing sodium nitroprusside or providing vasodilatation with an inhalational anesthetic while maintaining MAP greater than or equal to 50–70 mmHg by increasing pump flow has been advocated as a method of decreasing afterdrop. This method allows the poorly perfused cold extremities to be perfused with warmed blood before termination of CPB. Therefore, the caloric load of peripheral rewarming is in large part assumed by the heat exchanger and not the patient. Warmed, humidified airway gases have not been found to be beneficial in decreasing afterdrop in adults because humidifiers contribute relatively little heat to the large heat deficit that exists at the termination of CPB. The use of heat exchange systems utilizing circulating water in pads in direct contact with the have been found to be beneficial in preventing afterdrop in adults, infants, and children. In infants and children, convection systems utilizing forced warm air are useful as well due to the larger surface-area-to-volume ratio in these patients.

Ensure adequate anesthesia and muscle relaxation

Awareness is unlikely to exist during systemic hypothermia but may occur during rewarming. Unfortunately, this has not been well studied. Appropriate care dictates that some provision for amnesia be made as rewarming occurs. Volatile anesthetic agents may be continued during this interval to assure amnesia. A benzodiazepine such as midazolam 0.05–0.15 mg/kg, or lorazepam 0.025–0.05 mg/kg, administered as rewarming commences, can be used. Alternatively, a propofol infusion can be initiated. A muscle relaxant should be titrated to ensure adequate relaxation as the hypothermic attenuation of mechanical muscle function is reversed.

Perform an air drill

After procedures in which the heart chambers are opened, or in closed procedures in which air may have entered a heart chamber, it is necessary to evacuate all intracardiac air before termination of CPB to avoid systemic air embolism. In some centers, the surgeon floods the field with carbon dioxide during open procedures to reduce entrainment of air. It is felt that the higher solubility of carbon dioxide in blood and tissue (25 times > air) may reduce the risk of air embolic mediated neurologic events.

TEE is invaluable during deairing as it allows the effectiveness of the previously described procedures to be monitored on line. Air is particularly likely to be retained in the LV apex, LA, right coronary sinus, and the pulmonary veins. The right upper pulmonary veins in particular tend to entrain air given their more vertical entry into the LA. Removal of retained air requires flow through the pulmonary circulation and the heart. TEE surveillance, combined with the joint efforts of the surgeon, anesthesiologist, and perfusionist, are necessary to prevent systemic air emboli during evacuation procedures. Ejected air will tend to track along the anterior aspect of the aorta (air rises). The first manifestation of small amounts of ejected air may be ST segments elevations in the territory of the anterior right coronary artery (leads II, II, aV_F). In the cases of anteriorly placed coronary artery bypass grafts the distribution will tend to be more global.

To remove detected air, the following steps are useful:

• The patient is placed in the head-down position.
• The lungs are ventilated and the table is rolled from side to side to help remove sequestered air from the pulmonary veins.
• With the open atrium under a pool of blood, the venous line is partially clamped and the lungs are ventilated so that the ventricle becomes filled with blood. The ventricle is then freed of air either by aspiration on a vent line or by apical needle aspiration while the heart is elevated and massaged.
• The atriotomy or vent insertion site is closed under a pool of blood or fluid.
• The proximal aorta is evacuated of air either through the cardioplegia cannula or through a needle placed in the aorta.
• The aortic cross-clamp is not removed until the heart and aorta are free of air so that no air is ejected systemically.

● The LV may be vented directly through the apex with an 18-gauge needle by the surgeon. After venting, the puncture site is sutured closed.

Determine factors that may make termination of CPB difficult

Communication with the surgeon is essential here. It is best to know about the possibility of residual defects or incomplete revascularization before termination of CPB. Such information will affect the management of the patient if termination of CPB is difficult or impossible. Factors that increase the likelihood of a need for inotropic support to terminate CPB include: poor preoperative systolic function, a history of congestive heart failure, pre- or intraoperative inotropic support, poor myocardial preservation, a long cross-clamp time, incomplete revascularization, advanced age, female gender all increase the likelihood that post-CPB inotropic support will be needed.

Defibrillation

After rewarming and removal of the aortic cross-clamp, it may be necessary to defibrillate the heart. Several factors have been shown to be important in determining the ease of defibrillation after aortic cross-clamp removal:

● A serum potassium level of approximately 5 mEq/L decreases the defibrillation threshold compared with levels approximately 0.5 mEq/L lower. In many institutions where potassium cardioplegia solution is used, serum potassium levels are in the 5 mEq/L range at the time of aortic cross-clamp removal. If defibrillation is unsuccessful in the presence of a low serum potassium, infusion of potassium should be considered.

● Aortic perfusion pressure and the duration of reperfusion after aortic cross-clamp removal are important. Recall that subendocardial perfusion is compromised during ventricular fibrillation on CPB. A longer reperfusion period after aortic cross-clamp removal allows for washout of the products of anaerobic metabolism and for replenishment of energy stores. For these reasons, a mean aortic blood pressure of at least 50 mmHg for greater than 5 minutes is likely to increase the success of defibrillation.

● Myocardial temperature at the time of defibrillation should be greater than 30°C. Recall that spontaneous fibrillation occurs at a myocardial temperature of 28°C.

● Patients with valvular heart disease are more likely to need multiple defibrillation attempts compared with patients without valvular disease. This does not appear to be due to the increased heart weight and size often associated with valvular heart disease.

● Lidocaine reduces the number and the energy dose of DC shocks required for ventricular defibrillation. Lidocaine 1 mg/kg is given 5 minutes before aortic cross-clamp removal. Prophylactic lidocaine infusions are unnecessary. Lidocaine infusions initiated after CPB in coronary artery bypass patients have been shown to slightly decrease the incidence of nonsustained ventricular tachycardia with no apparent clinical benefit. Infusions of lidocaine are warranted for treatment of high grade ventricular ectopy.

● Hypomagnesemia occurs in up to 70% of patients after CPB and may predispose ventricular and supraventricular tachyarrhythmias. As a result, some centers supplement magnesium (2.0–4.0 g or 100 mg/kg in children) before or immediately after termination of CPB.

After optimization of conditions as described above, ventricular defibrillation is accomplished by the use of internal paddles. Much lower energy levels are required than for transthoracic defibrillation; 2.5–20.0 J or watt-seconds using internal paddles is sufficient to defibrillate most hearts. Defibrillation energy is started at 2.5 J and increased in 2.5–5.0-J increments. Inability to defibrillate a heart of a patient in whom conditions have been optimized suggests ongoing myocardial ischemia from poor revascularization or from coronary air or particulate emboli. Coronary air embolus is particularly common in procedures in which the left heart has been opened. When coronary air embolus is suspected, efforts should be made to increase perfusion pressure to break up bubbles and move them through to the venous side of the circulation. Increasing MAP on CPB will increase coronary

perfusion pressure. This in combination with nitroglycerine administration to dilate the epicardial coronary arteries and phenylephrine administration to further elevate MAP may be helpful in this situation.

Potassium and acid-base balance

Hypokalemia will compromise defibrillation and has been discussed. Hyperkalemia presents other problems. As the serum potassium level climbs greater than 5 mEq/L, the PR and QT intervals shorten and the T waves become peaked. A serum potassium level greater than 6 mEq/L will increase the incidence of dysrhythmias and conduction abnormalities due to a reduction in the threshold for membrane depolarization. This may predispose the patient to pacemaker-induced dysrhythmias. Pacing may not be possible as the serum potassium approaches 7 mEq/L. As levels reach 9–10 mEq/L idioventricular rhythm progresses to ventricular asystole and fibrillation.

Immediate treatment of elevated serum potassium with electrocardiogram (ECG) changes is indicated. IV calcium chloride 10 mg/kg or calcium gluconate 50 mg/kg, sodium bicarbonate 0.5–1.0 mEq/kg, or 1 mL/kg of 50% dextrose and 0.1 unit/kg of regular insulin all work immediately to reduce serum potassium by shifting it intracellularly. Where severe hyperkalemia exists, diuretic therapy will be necessary to increase the excretion of potassium as well. Alpha-stat pH management should continue as the patient is warmed. Total carbon dioxide, $Paco_2$, and pH should be corrected if necessary before termination of CPB. It may be necessary to give sodium bicarbonate to treat a metabolic acidosis or to adjust oxygenator gas flow to correct $Paco_2$.

In patients with compromised renal function, efforts must be made to avoid hyperkalemia resulting from use of potassium cardioplegia. It is possible to scavenge the cardioplegic solution from the coronary sinus so that it does not end up in the pump and elevate the serum potassium. In addition, it also is possible to use cold crystalloid cardioplegia without potassium in these patients. ZBUF may also be used to reduce serum potassium prior to termination of CPB in these patients.

Obtain pacing

After the aortic cross-clamp has been removed, the heart has been defibrillated, and potassium and acid-base status has been corrected, it may be necessary to obtain pacing. Although many patients will be in sinus rhythm, slow rates may compromise cardiac output, and therefore pacing is beneficial. In other patients, sinus rhythm is not immediately present at CPB termination. Pacing is initiated with use of epicardial pacing wires. Epicardial pacing can be bipolar (two wires on the heart) or unipolar (one wire on the heart, one through the skin of the epigastric area). Atrial, ventricular, or atrial and ventricular wires may be placed. Atrial wires usually are placed at or near the RA appendage. Ventricular wires are placed on the free wall of the RV. The wires are brought out through the skin in the epigastric area and can be removed easily postoperatively. By convention, the atrial wires are brought out on the right side of the epigastric area and the ventricular wires are brought out on the left side. The combination of atrial and ventricular wires allows atrial, ventricular, or atrial ventricular sequential pacing when used in combination with a dual output (atrial and ventricular) sequential external pacemaker.

An additional set of leads placed on the LV allows biventricular pacing. Pacing of the RV alone produces septal wall dyskinesis and asynchronous delayed activation of the LV. Biventricular pacing improves septal wall motion and produces simultaneous activation of the right and left ventricles. Biventricular pacing improves global systolic function in patients with low ejection fraction.

Because electrocautery is used extensively in the post-CPB period, the sensing threshold (millivolts) of the pacemaker may have to be increased toward the nonsensing or asynchronous mode to prevent inhibition of the pacemaker by electrocautery radiofrequency current. In general asynchronous (nonsensing) pacing is used post-CPB to avoid electromagnetic interference (EMI) from electrocautery. If the SA node rate is slow and AV node conduction is intact atrial pacing (AOO) should be provided as activation of ventricular contraction via the native conduction system provides optimal ventricular synchrony. When both SA and AV node dysfunction exist AV sequential pacing (DOO)

will be necessary and the optimal AV interval to provide AV synchrony will need to be determined. Generally, an interval of 150 ms is chosen to start in adults and then varied within the 120–200-ms range as needed to optimize ventricular filling and cardiac output. Infants will need a shorter PR interval. At pacing rates of 150–170 b/min this interval will likely be 100–120 ms in duration.

An alternative to DOO pacing when AV nodal block or a very prolonged AV interval exists in the presence of normal SA node function is DDD pacing. This mode will allow tracking (sensing) of the atrial rate with subsequent ventricular sensing and pacing to a set maximum rate at which point the pacemaker will produce Wenchebach type block. The disadvantage of this mode of pacing is that it is susceptible to EMI interference.

The current output (milliamperes) of the pacemaker is increased slowly until the desired cardiac chamber is captured. Each pacemaker spike must result in appropriate atrial and/or ventricular capture and contraction. There also must be appropriate sequential contraction of the atria and ventricles when atrial ventricular sequential pacing is desired. It is necessary to look at both the ECG trace and the heart to ensure capture. After the minimum current output necessary for capture has been determined (usually 5–10 mA), the current output is increased by 5 more milliamperes to ensure continued capture. In patients having undergone previous cardiac surgery (redos), atrial and ventricular scarring may necessitate higher current outputs than normal to obtain capture. In some instances, capture may not be possible until the epicardial pacer wire is moved to a site with less scarring.

Arterial pressure and pump flow

After the aortic cross-clamp has been removed, the MAP should be maintained in the 60–80 mmHg range to allow adequate reperfusion of the heart to replenish adenosine 5-triphosphate (ATP) stores and remove anaerobic metabolites. In preparation for termination of CPB, it is best to accomplish this by maintaining a calculated SVR in the range of 1000–1500 dynes s/cm^5 and adjusting pump flows accordingly. SVR can be varied with the use of either phenylephrine or nitroprusside as needed.

Hematocrit

Generally, a hematocrit greater than 25% is sought as CPB terminates. Advance planning is needed to achieve this goal. Reduction of the prime volume may be needed for some patients, as described previously. Vigorous diuresis during CPB may result in hemoconcentration; likewise, the use of an ultrafiltration device during CPB will achieve the same end. Transfusion of red blood cells may be necessary if these methods fail or are not appropriate due to low venous reservoir levels on CPB. Low hematocrit levels (<22%) as CPB terminates at 37°C may result in low SVR due to decreased viscosity.

Resume ventilation

Before terminating CPB, it is necessary to be certain that the lungs are easily reinflated, that if the pleural cavity is not opened that no pneumothorax exists, and that all fluid is removed from open chest cavities. Caution should be exercised when reinflating the lungs of patients with internal mammary artery (IMA) grafts to avoid stretching or avulsing the grafts. It also is necessary to resume ventilation at minute ventilation that will prevent hypercarbia after CPB terminates. Large increases in pulmonary vascular resistance (PVR) are seen with small elevations in arterial carbon dioxide after cardiac surgery. Such elevations in PVR may cause RV failure in patients with compromised RV systolic function. It should be remembered that carbon dioxide production is likely to be higher at the termination of CPB than it was before initiation of CPB due to the differences in body temperature.

For infants and children, it may be desirable to maintain mild hypercarbia in certain instances. In patients undergoing systemic to PA shunt procedures, pulmonary overperfusion (recirculation of pulmonary venous blood into the pulmonary circulation) may occur if the shunt is large and PVR is low. Hypercarbia may provide protection from overperfusion by increasing PVR. Conversely, high pulmonary vascular resistance and high airway pressures will compromise pulmonary blood flow in children having undergone the Fontan procedure (total cavopulmonary connection) due to the low driving pressure for pulmonary blood flow.

Termination of CPB

Termination of CPB is accomplished after the heart has been de-aired, ventilation has been resumed, electrolyte (particularly calcium and potassium) homeostasis has been achieved, and adequate myocardial contractility, rate and rhythm have been established. A coordinated effort between surgeon, perfusionist, and anesthesiologist is then directed toward allowing the heart to fill and eject as venous drainage into the CPB reservoir is reduced and finally terminated.

Volume infusion following termination of CPB is guided by both direct and TEE visualization of heart size and by analysis of intracardiac pressures and systemic blood pressure. Because volume can initially be delivered intravenously or via the arterial cannula, communication between the surgeon, anesthesiologist, and perfusionist is necessary. The range of filling pressures expected to provide optimal preload for a particular patient should be discussed before termination of CPB. Visual inspection of the heart will provide information on distension and wall motion but it must be remembered that it is primarily the free wall of the RV that is visible through a median sternotomy. The functional status of the RV is not necessarily the same as that of the LV. TEE allows visualization of the LV.

The endpoint of volume infusion is optimization of preload recruitable stroke work. If preload recruitable stroke work exists then volume infusion should induce an increase in blood pressure with little or no elevation in ventricular end-diastolic pressure as measured by atrial pressures. If further infusion of volume results in an increase in heart size and elevation of pulmonary artery occlusion pressure (PAOP) or left atrial pressure (LAP) and/or right atrial pressure (RAP) with no increase in blood pressure than it can be assumed that preload is optimized. Further volume infusion at this point will not improve arterial blood pressure and will likely distend the heart, elevate ventricular end-diastolic pressure and wall stress, and compromise subendocardial perfusion leading to a decrease in arterial blood pressure.

If inotropic support is anticipated to be necessary for termination of CPB, it should be started 5 minutes before termination of CPB. Starting the infusion of inotropic agents too soon increases myocardial oxygen consumption while the heart is being reperfused on CPB. This compromises the replenishment of energy stores and serves no useful purpose.

CPB should be terminated at a pump flow and SVR that are reasonable for the patient. If the perfusionist is pumping 5 L/min with a MAP of 50 mmHg, then the patient will have to have a cardiac output greater than 5 L/min to maintain a MAP of 70 mmHg after CPB has been terminated. If such an output is an unreasonable expectation, then efforts must be made to increase SVR to a normal range before termination of CPB. This will allow termination of CPB at the desired MAP with a cardiac output that the patient can realistically produce. Recall that on CPB, SVR = (MAP × 80)/pump flow, with the normal range 1000–1500 dynes s/cm^5.

CPB is terminated by gradually clamping the venous line so that venous return to the reservoir is impeded. Simultaneously, the perfusionist slows the rate of the arterial pump head. This results in gradual transfusion of blood to the patient via the arterial cannula. The volume of blood in the venous reservoir will slowly drop as the process continues. When adequate preload is obtained as assessed by PAOP, RAP, visual inspection of the heart, and TEE the transfusion is terminated.

As the heart fills with blood, ejection is noted. The simplest way to assess this is by observing the arterial waveform. Elevation of filling pressures with evidence of poor ejection is indicative of contractility/afterload mismatch. There is either poor systolic function or a level of afterload that is excessive for the inotropic state of the heart. If SVR has been normalized before termination of CPB, efforts can be directed toward increasing the contractile state of the heart with inotropes.

Administration of calcium salts at this time is controversial. In some institutions, calcium chloride 5–10 mg/kg or calcium gluconate 25–50 mg/kg is used as the first intervention in this setting. Calcium chloride increases the inotropic state of the myocardium and induces an increase in SVR that outlasts the inotropic effects. Often, this intervention is all that is required to complete

termination of CPB. There is evidence, however, that calcium chloride administration is contraindicated at this time because of the compromised calcium homeostasis that accompanies the insult of aortic cross-clamping. Administration of calcium may exacerbate ischemic damage by causing accumulation of intracellular calcium. Beta-adrenergic agents, on the other hand, increase intracellular calcium but also promote its reuptake into the sarcoplasmic reticulum and may be more appropriate in this setting.

Before therapy for low arterial pressure is initiated, the possibility that a discrepancy exists between the intra-arterial radial arterial pressure and the central aortic or femoral artery pressure should be investigated. This can be determined by simultaneous observation of the central aortic and radial artery pressures and will prevent unnecessary therapeutic interventions. Central aortic pressure can be monitored easily by having the surgeon place a small needle in the ascending aorta or aortic cannula attached to a length of pressure tubing that is passed over the drapes to a transducer. After CPB, intra-arterial radial arterial systolic pressure may underestimate central aortic, brachial, or femoral artery systolic pressure by as much as 40–50 mmHg in a significant number of both children and adults. This effect is most pronounced following periods of DHCA. It has been demonstrated that the gradient develops upon initiation of CPB and is not affected by vasodilators or vasopressors. Because this discrepancy may persist for up to 90 minutes after the termination of CPB, it may be necessary to place a femoral arterial line for continued monitoring. The etiology of this discrepancy appears to be a reduction in pulse wave velocity implying an acute reduction in radial arterial elastance leading to reduced pulsatility in the peripheral arteries. Both arterial-to-venous shunting in forearm blood vessels and peripheral vasospasm have been implicated as well.

If the patient separates from CPB with high filling pressures, ventricular distension, low cardiac index (below $2 \, L/min/m^2$), and low MAP (under 40 mmHg), prolonged efforts to correct the hemodynamics of CPB should not be made. Reinstitution of CPB will prevent the downward spiral induced by subendocardial ischemia and elevated wall tension. In addition, it will allow reperfusion of the heart during a low energy consumption state. After CPB has been reinstituted several questions must be addressed:

- Was the ventricular failure biventricular or was only one ventricle involved?
- Was there PA hypertension and RV failure?
- Was there RV or LV ischemia?
- Is the prosthetic valve working properly?
- Is all of the monitoring equipment functioning properly and giving accurate information?
- Are there other unsuspected lesions such as previously clinically insignificant mitral regurgitation (MR)?
- Is the repair of the congenital lesion complete and successful? Is there a residual defect that requires repair?
- Is the heart rate and rhythm optimized?
- Is the appropriate type of pacing being performed and is the pacemaker capturing the desired chambers?

Having addressed these questions, therapy directed toward specific problems can be instituted, and another attempt can be made to terminate CPB.

Post-CPB management

After termination of CPB, it is necessary to stabilize the patient and to reverse heparinization to allow decannulation and chest closure.

Protamine administration

Protamine is a polyvalent cation derived from salmon sperm that is currently used to neutralize systemic UFH. Protamine is given after stable hemodynamics are maintained after termination of CPB. It should not be administered until the likelihood that having to reinstitute CPB is small. After protamine neutralization of UFH begins, the cardiotomy suction should not be used and removal of the arterial and venous cannulas should proceed. This prevents contamination of the heparinized CPB circuit with protamine should prompt reinstitution of CPB be necessary and prevents thrombus formation on the cannulas.

There are several approaches to the neutralization of UFH with protamine:

- *Reverse extrapolation.* Some centers use 1.0 mg of protamine for each 100 USP units of UFH determined to exist at the termination of CPB. This ratio is based on the *in vitro* protamine to UFH neutralization ratio of 1:1. Some institutions believe this ratio to be more like 1.3:1.0. An ACT is obtained when CPB terminates and reverse extrapolation of the patient's UFH dose response curve is used to correlate the ACT with the amount of UFH present. This method has been criticized because the ACT obtained at the termination of CPB is prolonged by factors other than UFH, such as CPB-induced platelet dysfunction and hemodilution. This may result in an overestimation of the UFH present at the termination of CPB and a larger than necessary protamine dose.
- *Empiric dosing.* Some centers simply administer a fixed dose. This method does not rely on any post-CPB assessment of residual UFH effect such as ACT to determine the protamine dose. Nonetheless, these methods have been shown to result in adequate UFH reversal. In the case of the fixed dose regimen, UFH reversal is obtained at much lower protamine doses than predicted by the reverse extrapolation method. The dose of protamine is based on either the patient's weight (3–4 mg/kg) regardless of the UFH dose, or 1.0 mg of protamine for each 100 USP units of UFH administered at the onset of CPB.
- *Anti-factor Xa assay.* This UFH assay is used to calculate the protamine dose based on the patient's blood volume and a neutralization ratio of 1:1. Despite the fact that not all UFH present in blood exerts an anticoagulant effect and need be neutralized, this method has been shown to provide adequate UFH reversal with low doses of protamine.
- In vitro *protamine titration.* This method requires ACT tubes (celite or kaolin) containing protamine. Assuming a protamine to heparin neutralization ratio of 1:1 this method allows determination of the whole blood heparin level. Typically the results of this test are used in combination with an estimate of the patient's blood volume to determine the appropriate protamine dose to neutralize circulating UFH.

Both the protamine response test (PRT, Hemochron®) and the heparin/protamine titration test (HPT, Medtronic Hemotec®) provide *in vitro* protamine titration. The HPT method measures clotting times enhanced by addition of thromboplastin in several channels that contain varying quantities of protamine. The first channel to clot is the channel in which the protamine to heparin ratio is closest to neutralization. The absolute clotting time is not important; only the determination of the channel with the appropriate ratio. Therefore, the determination should be independent of non-UFH factors that prolong the ACT. This method results in adequate UFH reversal at lower doses of protamine than predicted by the reverse extrapolation using only a post-CPB ACT.

The PRT uses two channels. One channel is the native ACT (post-CPB) the other channel is an ACT (post-CPB) with either 20 or 40 μg of added protamine. The results of the clotting times in these two tubes are used to construct a linear protamine dose–response relationship extrapolated back to a baseline (pre-CPB) ACT. In combination with an estimate of the patient's blood volume the neutralizing dose of protamine can be determined with reverse extrapolation. This determination will not be independent of non-UFH factors that prolong the ACT.

The ACT should be checked after administration of the selected protamine dose. The goal is to return the ACT to a normal value. Excess protamine is clearly detrimental to platelet function by nature of its inhibitory effects on the platelet receptor GPIb/IX/V interaction with vWF that is a critical component of platelet adhesion and aggregation. Administration of additional protamine is not benign and tends to delay detection and treatment of thrombocytopenia, platelet dysfunction, and coagulation factor deficiencies.

There are several potential adverse reactions associated with protamine administration. These protamine reactions occur in both children and adults. The incidence of protamine reactions in children following cardiac surgery is lower than in adults (approximately 10%); on the order of 1.76–2.88% depending on the stringency of criteria linking the episode to protamine administration. Risk factors

for these reactions (NPH insulin use, previous drug reaction, or an allergy to protamine or fish) may exist in up to 40% of cardiac surgical patients.

Reactions to protamine (defined as arterial hypotension, pulmonary hypertension, or both) are associated with increased mortality following coronary artery bypass surgery. It is unclear whether intervention to treat these events reduces mortality or whether there is a cause and effect relationship between the hemodynamic events and mortality. It is possible that the hemodynamic events are a surrogate marker for the ultimate cause such as an enhanced pro-inflammatory response.

The reactions associated with protamine administration are described in the sections that follow.

Systemic hypotension

This is the most common reaction to protamine administration and it is more common in patients with poor ventricular function. The decrease in systemic blood pressure is multifactorial. A decrease in SVR mediated via a nitric oxide/cyclic guanosine monophosphate (NO/cGMP) dependent and endothelial-mediated mechanism has been implicated, as has pulmonary histamine release. Protamine-induced platelet aggregation and release of vasoactive substances also may produce systemic hypotension, particularly when platelet concentrates are infused in association with protamine. Protamine induced reduction in myocardial contractility has also been implicated.

The incidence of this reaction appears to be related to the speed of infusion. Regardless of the infusion site (right atrium, LA, aorta, peripheral vein) this reaction can be avoided or at least decreased in severity when a slow infusion (over more than 3 minutes) of protamine is used. Some centers advocate prophylactic administration of calcium chloride/gluconate or H_1 and H_2 blockers to attenuate this reaction. These interventions are of unproven benefit.

Pulmonary hypertension

Pulmonary hypertension after protamine may be so profound as to result in RV failure and circulatory collapse. This reaction is idiosyncratic and is associated with high levels of thromboxanes and C5a anaphylatoxins, which result in broncho-constriction and pulmonary vasoconstriction in susceptible patients after protamine administration. Heparin-protamine complexes are the likely initiating mechanism. This reaction seems to occur in susceptible patients regardless of whether the protamine is infused into the right or LA, administered as a bolus, or given as a slow infusion. Patients with pre-existing pulmonary hypertension are not at greater risk for this reaction. Fortunately, this reaction is rare, occurring in less than 3% of cases. Pulmonary hypertensive episodes in children following protamine administration are very rare.

True allergic (anaphylactic and anaphylactoid) reactions

True allergic reactions require the presence of immunoglobulin E (IgE) or immunoglobulin G (IgG) antibodies to the substance in question. Typical manifestations of this type of reaction include hypotension, flushing, urticaria, bronchospasm, and pulmonary edema secondary to capillary leak. IgE-mediated reactions are the result of IgE-antigen complex causing mast cells degranulation. IgG mediated reactions are the result of activation of the complement cascade by the IgG-antigen complex.

Formation of these antibodies is enhanced in patients who have been exposed previously to the allergen or to a substance that is similar to the allergen. An increased incidence of protamine reactions has been reported to occur in:

- *Patients taking NPH insulin.* These patients are presumed to be pre-sensitized to protamine from the insulin preparation. An incidence of reactions as high as 27% has been reported, but prospective studies suggest an incidence of approximately 0.6%.
- *Patients with fish (not shellfish) allergies.* These patients are believed to be at higher risk due to several case reports but prospective analysis does not support this contention.
- *Vasectomized men.* IgG (antisperm) antibodies to protamine are found in 29% of vasectomized men but they are present in low titers and prospective analysis does not support the contention that these patients are at higher risk.

● *Previous protamine reaction.* These are the highest risk patients.

The risk of an adverse response to protamine is 25 times higher in patients with protamine-specific IgG antibody and 95 times higher in patients with protamine-specific IgE antibody. However, the percentage of patients exposed to protamine or protamine-like substances that go on to develop IgG or IgE antibodies is low. Furthermore, not all patients with IgG antibodies to protamine develop reactions to protamine. Therefore, the overall risk of true allergic reactions in patients who were previously sensitized to protamine seems to be low.

Efforts have been made to identify patients suspected to be at risk for protamine may be tested for IgE and IgG antibodies. Skin testing commonly is used to test for IgE-mediated hypersensitivity. Enzyme-linked immunosorbent assays (ELISAs) and radioallergosorbent tests (RASTs) are used to detect minute quantities of circulating IgG and IgE to an allergen. Both skin testing and ELISA in patients at risk for protamine reactions have been shown to have a high false-positive rate and poor specificity. In other words, many patients with a positive test for protamine antibodies do not go on to develop a reaction. This severely limits the value of this type of testing.

Noncardiogenic pulmonary edema

This reaction has been reported to occur as both an immediate and a delayed reaction (more than 20 minutes after administration) to protamine in a small number of case reports. It is not entirely clear that protamine alone is responsible for this reaction, as concomitant blood product administration also has been implicated.

Heparin rebound

Heparin rebound may occur after protamine administration. This phenomenon is defined as a re-prolongation of the ACT occurring 1–8 hours after adequate UFH neutralization. The elevated ACT renormalizes with additional protamine. Several etiologies have been suggested. A large quantity of UFH remains bound to plasma proteins for up to 6 hours after clinically adequate neutralization of UFH with protamine. As protamine is cleared, the protein-bound UFH dissociates slowly and binds to AT-III to produce an anticoagulant effect. It is not surprising, then, that the incidence of heparin rebound is reduced when a heparinization protocol that uses lower UFH doses is compared with one that uses higher doses. Concurrent protamine metabolism also may be a factor. Heparin rebound also may be due to enhancement of residual UFH by infusion of blood components such as FFP that elevate AT-III levels.

Recommendations for protamine administration

● Slow administration (25–50 mg/min) of the chosen protamine dose into the right atrium via a central venous catheter. The central venous route is chosen over peripheral venous administration to ensure that the drug reaches the central circulation just as with UFH administration.

● If systemic hypotension due to a decrease in SVR occurs, the protamine infusion should be stopped. The SVR should be elevated with an α-agonist (phenylephrine, norepinephrine) and preload should be optimized with volume infusion. The protamine infusion can then be restarted slowly while SVR and preload are maintained.

● If pulmonary hypertension occurs, immediate action is necessary. The protamine should be stopped in an effort to reduce pulmonary vascular resistance while the circulation is supported. Infusion of epinephrine may be necessary to provide inotropic support of the RV. If pulmonary hypertension persists, infusion of nitroglycerin, or prostaglandin E_1 (started at 0.01–0.05 μg/kg/min) into the right atrium will help reduce PVR and improve RV function. Inhaled NO may be a better alternative, as it will not exacerbate systemic hypotension. In either case, simultaneous infusion of norepinephrine into a left atrial catheter provides treatment for both elevated PVR and reduced SVR. Protamine infusion may have to continue with continued vasopressor vasodilator therapy. In severe cases, reinstitution of CPB may be necessary to provide cardiopulmonary support. Following subsequent discontinuation of CPB protamine administration may have to be avoided.

- If an anaphylactic or anaphylactoid reaction occurs in association with protamine administration, therapy with epinephrine, steroids, H_2 blockers, and bronchodilators is warranted.
- An ACT should be repeated after protamine infusion. If the ACT remains elevated above normal (120 ± 40), an additional 0.25–0.50 mg/kg of protamine can be administered and the ACT rechecked (essentially *in vivo* protamine titration). No change in the ACT will essentially eliminate excess protamine as the source of ACT elevation.

Alternatively, a heparinase ACT test can be performed. Two-chamber cartridges are available (Medtronic Hemotec®). Both chambers contain kaolin and calcium chloride. One chamber contains highly purified heparinase capable of rapidly neutralizing 6 USP unit/mL of UFH. A >10–15% elevation of the native ACT relative to the heparinase ACT is indicative of the need for additional protamine regardless of the absolute ACT values as follows:

a If the heparinase ACT is normal and the nonheparinase ACT is within 10–15% of this value, then the UFH has been neutralized and no additional protamine is necessary.

b If the heparinase ACT is normal and the nonheparinase ACT is elevated, then UFH is present and more protamine is warranted.

c If both the heparinase ACT and the nonheparinase ACT are elevated above normal and are within 10–15% of each other, the patient should be evaluated for other causes of an elevated ACT besides UFH such as factor deficiencies (intrinsic and common pathway). No further protamine is necessary.

d If both the heparinase ACT and the nonheparinase ACT are elevated above normal and the nonheparinase ACT is elevated more than 10–15% above the value of the heparinase ACT, the patient has both UFH and other factors as a cause. Additional protamine and evaluation for factor deficiencies both are warranted.

In vitro protamine dose assay (PDAO, Hemochron®) can be done as well. This test uses a two-channel system in which one channel is the native ACT and the other has 10 µg protamine added. Reverse extrapolation of the two results back to a baseline ACT in combination with the patient's blood volume yields the supplemental protamine dose. Administration of additional protamine is not benign and tends to delay detection and treatment of thrombocytopenia, platelet dysfunction, and coagulation factor deficiencies by the surgical team.

- If heparin rebound is suspected, the ACT should be rechecked and use of the one of the methods to detect residual UFH described above considered. Additional protamine 0.25–0.50 mg/kg should then be administered. This usually is adequate to treat heparin rebound.

Causes of impaired hemostasis following protamine administration

Hemostasis following termination of CPB and protamine administration can be problematic for a number of reasons.

Surgical bleeding

The surgical field must be assessed carefully for bleeding sites. This inspection must include the cut sternal edges, the harvest site of the mammary artery, and the back of the heart. Many of the surgical procedures involve long suture lines in vessels with systemic pressures. In addition portions of the suture line such as the posterior aortic wall may be concealed making detection and control of the bleeding site challenging.

Platelet function defects

In adults, this is the most common cause of bleeding after CPB once heparin has been reversed and surgical bleeding has been controlled. Platelet dysfunction may be secondary to CPB, particularly if the CPB time >2 hours or to preoperative antiplatelet therapy with aspirin, nonselective nonsteroidal anti-inflammatory drugs (NSAID), platelet GPIIb/IIIa-receptor antagonists, or ATP receptor ($P2Y_{12}$) blockers (thienopyridines). Platelet functional defects tend to compound hemostasis problems from all other causes.

Transient defects in platelet plug formation and aggregation are seen in all patients after CPB. Generally, platelet function returns to near normal status 2–4 hours after CPB. This transient dysfunction is caused by platelet surface glycoprotein (GP)

receptors that are redistributed internally into platelets during CPB. The presence of plasmin is responsible for this inactivation or redistribution of GP receptors. These GP receptors are essential for platelet adhesion and aggregation. Tethering, translocation and stable arrest of platelets leading to platelet adhesion and aggregation in arterioles requires at least four platelet GP receptors (GPVI, GPIb/IX/V, GPIa/IIa, GPIIb/IIIa) and three ligands (von Willebrand factor (vWF), collagen, fibrinogen).

Platelet GPIIb/IIIa receptors are the final common pathway in platelet aggregation. They bind with high affinity to fibrinogen and mediate platelet-to-platelet aggregation via a fibrinogen bridge. The GPIIb/IIIa antagonists abciximab (Reopro®), eptifibatide (Integrilin®) and tirofiban (Aggrastat®) inhibit this aggregation irrespective of the platelet-activating stimulus. These agents are commonly used in patients who present for surgery following percutaneous interventional coronary arterial procedures such as angioplasty and stent placement. Both eptifibatide and tirofiban bind competitively and have short (2 hours) half-lives. As a result they generally do not cause bleeding problems. Abciximab is a large monoclonal antibody that binds irreversibly and sterically blocks the receptor for the life of the platelet. Patients presenting for surgery following administration of this agent within a 1–2 week time frame usually require aggressive replacement of platelets following CPB.

Aspirin (acetylsalicylic acid) ingestion irreversibly inhibits platelet cyclo-oxygenase 1 (COX-1) for the 10–15 day life span of the platelet. This results in inhibition of platelet thromboxane A_2 production. Thromboxane A_2 is potent vasoconstrictor and stimulant for platelet activation and aggregation. Preoperative aspirin ingestion has been shown to increase blood loss after CPB by exacerbating CPB-induced platelet dysfunction. Additionally, 15–20% of patients who ingest aspirin are hyper-responders, which further contributes to platelet dysfunction. Nonselective NSAID have similar effects to aspirin lastly only as long as significant blood levels are maintained.

Thienopyridines (clopidogrel, ticlopidine) are agents that selectively and irreversibly block platelet adenosine diphosphate (ADP) receptors $P2Y_1$ and $P2Y_{12}$. These receptors are responsible for ADP-induced platelet activation and aggregation. Both receptor pathways must be intact for normal platelet responses to occur. $P2Y_1$ linked to the G_q pathway is responsible for platelet shape change and transient aggregation triggered via an increase in intracellular calcium. $P2Y_{12}$ linked to the G_i pathway is responsible for completion and amplification of the aggregation response via inhibition of adenylyl cyclase. Clopidogrel is used almost exclusively as ticlopidine use is associated with an unacceptable incidence of neutropenia.

The anti-platelet effects of aspirin and clopidogrel are synergistic. Ideally, aspirin and clopidogrel would have to be discontinued for 10–15 days prior to surgery for termination of their clinical effect. There may reluctance to discontinue these medications prior to surgery, as discontinuation has been associated with acute coronary syndrome and coronary stent thrombosis.

Desmopressin acetate (DDAVP) in a dose of 0.3 μg/kg increases levels of factor VIII and vWF. Von Willebrand's factor is known to mediate platelet aggregation and adherence on thrombogenic surfaces. The increased levels of vWF that result from DDAVP infusion may be responsible for improving platelet function post-CPB. Despite this, DDAVP is not consistently effective in reducing blood loss or homologous transfusion requirements in pediatric and adult cardiac surgical patients when given after CPB and protamine administration. Of particular importance DDAVP is not consistently been effective in the subset of adult CABG patients taking preoperative aspirin.

Thromboelastography may be useful in identifying patients who will benefit from DDAVP after CPB and protamine reversal of UFH. Patients with an maximal amplitude (MA) < 50 mm indicative of reduced platelet function demonstrate less blood loss and a reduction in homologous transfusion requirements after CABG surgery with DDAVP compared with placebo.

DDAVP relaxes vascular smooth muscle and should be administered slowly (over 20–30 minutes) to avoid reductions in SVR with subsequent hypotension.

Thrombocytopenia

Platelet counts decrease during CPB, but generally they do not fall below 100 000 in adults. In general, the fall in platelet counts on CPB is slightly greater than what would be expected with hemodilution, with the difference being due to platelet adherence to synthetic surfaces, platelet destruction, platelet sequestration in the lungs, and platelet consumption in wounds. Because platelet function defects are so prevalent, thrombocytopenia, when it does exist, is an important cause of altered hemostasis.

In infants and children, platelet functional defects induced by CPB are overshadowed by the presence of CPB-induced dilutional thrombocytopenia. Dilutional thrombocytopenia is a problem in neonates and infants given the relatively large CPB pump prime volumes and the absence of platelets in all prime solutions except fresh, unrefrigerated whole blood. Whole blood stored for more than 48 hours using ACD or CPD at 4°C is devoid of platelets.

In centers where refrigerated whole blood (<1 week old) is used to prime a 300 mL CPB circuit for infants and neonates (2–5 kg) there is a 50–80% immediate post-CPB reduction in preoperative platelet count. The largest reductions are seen in the smallest patients undergoing the longest procedures.

Prophylactic platelet transfusion after CPB is not warranted; however, when there is post-CPB bleeding unrelated to residual heparin or surgical bleeding, platelets should always be administered as a first-line treatment. A unit of platelets contains 5.5×10^{10} platelets; 0.1 unit/kg generally will raise the platelet count by 50 000–80 000. In most cases, this will control the bleeding. For cases in which other deficiencies exist, platelet therapy will prevent platelet defects from compounding the problem.

Platelet transfusions of 0.5–1.0 unit/kg may be necessary to normalize the post CPB platelet count (250–600 K/μL) in neonates and infants. Thrombocytopenia just prior to termination of CPB or following protamine administration consistently correlates with excessive postoperative blood loss in children. Since platelets are suspended in FFP, platelet transfusions in these patients also provide a substantial FFP transfusion. The minimum volume of FFP suspension for 1 unit of platelets is 20 mL (concentrated platelets) while the usual volume is 40 mL. Therefore, a 2-unit platelet transfusion would provide a 4-kg patient with a 10–20 mL/kg FFP transfusion.

Dilution of clotting factors

The extent to which dilution of coagulation factors is present depends on the size of the patient, the extent of pre-existing factor deficiencies, and the volume and composition of the CPB pump prime.

In adults, factor levels rarely fall below the 30% level, leaving the coagulation system intact. Likewise, the fibrinogen level is reduced by dilution during and after CPB but rarely falls below the critical 100 mg/dL level. It is not surprising, then, that the prophylactic administration of FFP has not been shown to reduce bleeding after routine CPB procedures in adult patients without preexisting coagulopathies.

Dilution of coagulation factors in neonates and infants is less likely if the CPB pump prime consists of whole blood or reconstituted whole blood (packed red blood cells and FFP). Dilution of coagulation factors is particularly likely to occur when the patient is polycythemic (reduced plasma volume). Significant dilution of coagulation factors is likely if an asangeous colloid or crystalloid prime is used. Dilution of coagulation factors and red cells can be mitigated by use of conventional or MUF. Children whose transfusion requirements in the immediate post-CPB period are met with whole blood that is less than 48 hours old have total transfusion requirements 85% less than those treated with component therapy.

Cryoprecipitate may be indicated in some circumstances. Both hypofibrinogenemia and reduced factor XIII are correlated with postoperative blood loss. Cryoprecipitate contains fibrinogen, factor VIII/vWF, and factor XIII. One unit of cryoprecipitate (20–30 mL) contains 150 mg of fibrinogen and 80–120 units of factor VIII/vWF. This quantity of fibrinogen is comparable to what would be found in 75 mL of FFP. This quantity of factor VIII/vWF is comparable to what would be found in 80–120 mL of FFP. In small patients, where volume constraints limit transfusion, cryoprecipitate

is a much more efficient source of fibrinogen, factor XIII and factor VIII/vWF. In children cryoprecipitate 0.5–1.0 unit/kg is transfused for bleeding that persists following normalization of platelet count. In adults, cryoprecipitate is usually transfused at 0.25–0.50 unit/kg.

Fibrinolysis

The continued generation of thrombin during CPB despite heparinization is largely responsible for induction of ongoing fibrinolysis. Adjuvant therapy to improve hemostasis post-CPB is directed toward use of anti-fibrinolytic agents. Sequential cleavage of fibrin by the serine protease plasmin is responsible for fibrinolysis. Plasmin is the activated form of plasminogen. Plasminogen contains 5-lysine binding domains or kringles that allow it to bind to the lysine residues on partially lysed fibrin. Fibrin bound plasminogen is subsequently cleaved to plasmin by tissue plasminogen activator (t-PA). t-PA also contains lysine binding domains that allows binding to fibrin. Free t-PA is capable of converting fibrin bound plasminogen to plasmin but t-PA bound to fibrin lysine residues stimulates activation of plasminogen to plasmin by two orders of magnitude.

Antifibrinolytic agents

Three antifibrinolytic agents currently are in use. Each improves hemostasis after CPB. Ideally, these agents are administered before CPB and before stimulation of the coagulation and fibrinolytic processes. The three agents epsilon (ε)-aminocaproic acid (EACA), tranexamic acid (TXA), and aprotinin are summarized below.

Lysine analogs

The lysine analogs TXA and EACA inhibit fibrinolysis by: (i) binding to plasminogen thus rendering it incapable of binding to the lysine residues on fibrin; and (ii) inhibiting the proteolytic action of plasmin. The reduction in plasmin generation is also beneficial in that plasmin is a potent platelet activator. Subsequent to plasmin induced platelet activation the platelet adhesion molecule GPIb/IX/V undergoes proteolysis or translocation away from the platelet surface. TXA is 6–10 times more potent than EACA.

Aprotinin

Aprotinin is naturally occurring (bovine lung) 59-amino-acid polypeptide that is a serine protease inhibitor. Aprotinin is a potent inhibitor of fibrinolysis and prevents plasmin activation of platelets even at low doses. Plasma concentrations of aprotinin inhibit the action of plasmin and kallikrein by reversible binding to the active serine sites of these enzymes. Because aprotinin binds 30 times more avidly to plasmin than kallikrein, a higher plasma concentration of aprotinin is needed to inhibit kallikrein as compared with plasmin. Concentrations of aprotinin high enough to inhibit kallikrein are not maintained throughout CPB, even when high doses are used. Therefore, inhibition of the contact activation system probably is not as important to the action of aprotinin as inhibition of plasmin induced fibrinolysis. Administration of aprotinin to patients undergoing CPB results in reduced formation of fibrin degradation products, increased α-antiplasmin (an inhibitor of plasmin) and plasminogen activator inhibitor activities, and decreased tissue plasminogen activator release.

In addition to its effects on plasmin, aprotinin has direct effects on platelets that serve to reduce platelet activation. Thrombin, a serine protease, is the main effector protease of the coagulation cascade and arguably the most important physiologic platelet agonist. It has now been established that thrombin activation of platelets occurs via G-protein coupled protease activated receptors (PAR). Human platelets express PAR-1 and PAR-4. PARs are essentially receptors that carry their own tethered ligand. Thrombin recognizes and binds to the NH_2-terminal extracellular domain of PAR-1 and PAR-4. Subsequent proteolysis by thrombin results in exposure of a new NH_2-terminus that binds intramolecularly to the body of the receptor producing transmembrane signaling. This PAR-1 ligand-receptor coupling mediates platelet activation at physiologic thrombin concentrations. Aprotinin blocks thrombin proteolysis of PAR-1 and as a result prevents thrombin induced platelet activation. Aprotinin does not however inhibit platelet activation via epinephrine, ADP, or collagen.

Aprotinin is also capable of inhibiting monocyte expression of TF induced by CPB. TF production during CPB results in thrombin generation via the TF-factor VIIa pathway. Aprotinin also counteracts heparin-induced reduction of platelet contractile force similar to that seen with protamine reversal of heparin. Aprotinin also blunts the inflammatory response induced by CPB and heart and lung reperfusion in a manner similar to that of methylprednisolone by inhibiting release of interleukins and tumor necrosis factor.

Dosage and administration of antifibrinolytic agents

Prophylactic administration of these agents (before commencement of CPB) is superior to administration following commencement of CPB.

ε-aminocaproic acid

This drug is typically given as 100–150 mg/kg IV after induction and 10–15 mg/kg/h, usually for 5–6 hours. Higher doses (as much as 40 g) have been used, but no dose-response data exist to support them. A smaller loading dose with a higher infusion rate may provide more stable plasma levels. In adults an ε-aminocaproic acid (EACA) loading infusion of 50 mg/kg given over 20 minutes and a maintenance infusion of 25 mg/kg/h maintains a constant therapeutic plasma concentration of EACA (>130 μg/mL). In children ranging in age from 5 months to 4 years, and in weight from 7.2 to 18.9 kg, with CPB prime volumes of 650–850 mL, a bolus of 75 mg/kg over 10 minutes, 75 mg/kg in the CPB prime, and a continuous infusion of 75 mg/kg/h following the bolus maintains the same therapeutic plasma concentration. The drug is renally concentrated and the infusion rate should probably be decreased in accordance with creatinine clearance.

Tranexamic acid

This drug can be given as a single bolus of 50–100 mg/kg IV following induction. More typically it is given as 10–20 mg/kg IV after induction and 1–2 mg/kg/h, usually for 5–6 hours. A smaller loading dose with a higher infusion rate may provide more stable plasma levels. In adults,

tranexamic acid (TXA) administered as a bolus dose of 12.5 mg/kg over 30 minutes, 1 mg/kg in the CPB prime, and a continuous infusion of 6.5 mg/kg/h results in a constant therapeutic plasma concentration of 53 μg/mL. Similarly, TXA administered as a bolus dose of 30 mg/kg over 30 minutes, 2 mg/kg in the CPB prime, and a continuous infusion of 16 mg/kg/h should result in a constant therapeutic plasma concentration of 126 μg/mL. In children undergoing re-operative procedures, TXA in a dose of 100 mg/kg as a bolus over 30 minutes, 100 mg/kg in the CPB prime, and as a continuous intra-operative infusion of 10 mg/kg/h is superior to placebo in reducing blood loss, total transfusion requirements and total donor unit exposure. The drug is renally concentrated and the infusion rate should be decreased in accordance with creatinine clearance.

Aprotinin

Aprotinin is dosed in kallikrein inhibition units (KIU). A KIU is defined as the quantity of aprotinin that produces 50% inhibition of 2 kallikrein units. Aprotinin is packaged to contain 10 000 KIU/mL that is equivalent to 1.4 mg/mL. Aprotinin is administered to adults on a fixed dose protocol. The high dose or Hammersmith regimen consists of:

- 2 million KIU (280 mg) as an IV loading dose over 30 minutes after induction.
- 500 000 KIU/h (70 mg/h) as an intraoperative infusion.
- 2 million KIU (280 mg) in the pump prime.

Recent evidence suggests that dosing on a per kilogram basis provides more consistent plasma aprotinin levels than a fixed dose regimen. In infants and children dosing on a per kilogram basis is more common. Given the discrepancy between weight and body surface area (BSA) in infants and neonates and small children it has been suggested that dosing on a per meter squared basis in this patient population will produce more consistent aprotinin concentrations and less likelihood of sub- and supra-therapeutic aprotinin levels than dosing on a per kilogram basis. In addition, more consistent plasma levels are achieved if the CPB prime dose is not based on patient weight or BSA but on the actual volume of the CPB circuit relative to either of these

two variables. Nonetheless, two commonly used aprotinin dosing regimens for infants and children are as follows:

- 30 000 KIU/kg as bolus to the patient and added to the CPB prime in addition to a continuous infusion of 10 000 KIU/kg/kg.
- 1.7×10^6 KIU/m^2 (240 mg/m^2) as a bolus to the patient and added to the CPB prime in addition to a continuous infusion of 4×10^5 KIU/m^2/h (56 mg/m^2/h).

The incidence of both mild and severe allergic reactions to aprotinin following initial exposure is similar in children and adults and is approximately 0.5–1.0%. The incidence of both mild and severe allergic reactions on re-exposure in adults and children is similar and is approximately 2.8%. Up to 9% of the re-exposure reactions may be fatal. The likelihood of a reaction on re-exposure is increased if the re-exposure occurs within 6 months of the initial exposure with 95% of all reported re-exposure events occurring within 6 months of initial exposure. Patients who are likely to have previous exposure are those who have undergone prior cardiac surgical procedures including children undergoing staged procedures. In particular, bridge to cardiac transplant patients are likely to have prior exposure. A second exposure is likely at the time of device explantation and cardiac transplantation. Aprotinin use also has been extended to noncardiac surgical procedures (orthopedics, ear, nose and throat (ENT)) and previously was used for treatment of pancreatitis.

Neither skin testing, nor antiaprotinin IgG nor IgE antibody testing is specific enough to be clinically useful for prediction of anaphylaxis on re-exposure. Very high levels of antiaprotinin IgG antibodies may help identify patients at risk. It is recommended that a test dose of aprotinin 0.5 or 1.0 mL be administered before both initial and subsequent administrations keeping in mind that test doses have been reported to trigger acute reactions. If there is no reaction after 10 minutes, the bolus dose can be given. Pre-treatment with H$_1$, H$_2$ antagonists and corticosteroids prior to re-exposure has been recommended but this practice has not been critically evaluated. In a patient with a history of prior exposure is probably prudent to delaying injection of the test dose until the surgeon is ready to commence CPB so that circulatory support can be initiated immediately in case of a reaction. In all patients, aprotinin should not be added to the CPB pump prime until it is certain that the patient has not reacted to the test dose or bolus dose.

Efficacy of antifibrinolytics agents

There are many studies examining the efficacy of EACA, TXA, and aprotinin in reducing blood loss and allogeneric transfusion requirements. Most studies compare these agents to placebo, but some head-to-head comparison studies exist. Comparisons are complicated by the fact that not all groups use comparable dosages of these agents. In children, such determinations are more complicated given the large variability in patient size, type of operative procedure, age-related distribution and elimination kinetics, CPB prime volume and the use of ultrafiltration. There are anecdotal reports of adverse thrombotic events such as shunt thrombosis and premature fenestration closure associated with use of lysine analogs and aprotinin in children. To date, there exists little objective evidence to accurately quantify the risk of such events with use of these agents.

Aprotinin

- Meta-analysis of trials of aprotinin compared to a placebo control group in adults demonstrates that high-dose aprotinin in effective in reducing the number of patients who require transfusion following CABG, redo-CABG, CABG/valve, and valve surgery. High-dose aprotinin also reduces the incidence of postoperative re-exploration for bleeding following surgery.
- High-dose aprotinin has been demonstrated to reduce blood loss and transfusion requirements in patients undergoing heart, heart-hung, and lung transplantation. In addition, aprotinin reduces blood loss and transfusion requirements in patients receiving mechanical circulatory assist devices.
- High-dose aprotinin has been demonstrated to reduce blood loss and transfusion requirements in patients taking perioperative aspirin. Similar efficacy of high-dose aprotinin has been demonstrated in patients taking perioperative clopidogrel discontinued <5 days prior to surgery.

- High-dose aprotinin has been demonstrated to reduce blood loss and transfusion requirements in patients undergoing off-pump coronary artery bypass (OBCAB).
- In children with congenital heart disease undergoing cardiac surgery, meta-analysis of appropriate trials indicates that while aprotinin use reduces the proportion of children of children receiving allogeneric transfusions it does not reduce chest tube drainage or the total volume of blood transfused. This analysis is plagued by the limitation that both intra-study and inter-study variability in a number of parameters involving the patient (age, weight, cyanotic versus noncyanotic, procedure type, redo versus primary surgery), the CPB circuit (prime volume and composition, ultrafiltration use), the aprotinin dose (fixed, per kg, per m^2), and the outcome variables (blood loss, transfusion requirement, cost analysis) make comparisons between studies difficult.

Lysine analogs

- At comparable doses, TXA and EACA have comparable efficacy.
- EACA and TXA are better than placebo in limiting the number of patients transfused after CABG.
- TXA and EACA are comparable to high-dose aprotinin in limiting the number of patients transfused following CABG.
- High-dose aprotinin may be superior to TXA or EACA in limiting transfusion following CABG/valve surgery or redos. A recent propensity score analysis suggests that TXA and aprotinin have comparable efficacy in this high-risk group.
- In pediatric patients undergoing primary and repeat surgery, TXA and EACA, as compared to placebo, reduce the number of patients being transfused, total blood product exposure and blood loss across a wide age range. A well-controlled trial comparing aprotinin to lysine analogs in children has not been conducted.

Special considerations regarding use of aprotinin

Activated clotting time

Kaolin ACT are used to measure Activated clotting time (ACT) in conjunction with aprotinin use. Celite ACT are prolonged in the presence of aprotinin due to aprotinin inhibition of contact activation as well as the ability of aprotinin to preferentially inhibit celite mediated activation *in vitro*. Concern exists as to whether this aprotinin induced *in vitro* prolongation is correlated with *in vivo* anticoagulation. Kaolin ACT is unaffected by aprotinin except at very high plasma levels (400 KIU/mL) because kaolin is a more potent contact activating agent than celite and kaolin binds aprotinin. While adequate heparinization for CPB has been demonstrated using celite ACT in conjunction with a lower heparin dose than would be used with a kaolin ACT, the majority of centers use the kaolin ACT in conjunction with aprotinin. Therapeutic plasma levels of aprotinin also prolong both the activated partial thromboplastin time (aPTT) and the R of the thromboelastograph (TEG) but not the prothrombin time (PT) as a result of aprotinin's effect on contact activation. This makes use of these parameters difficult in post-CPB bleeding treatment algorithms.

Renal function

Aprotinin is filtered; rapidly bound to the brush border of the proximal convoluted tubules and subsequently enters the cytoplasm of these tubules by pinocytosis. Ninety percent of the administered dose appears in the cytoplasm in a few hours and remains there for 12–14 hours until metabolized. Aprotinin compromises deep cortical and medullary perfusion and autoregulation via its tubule based effects on kallikrein–kinin pathways and via renal afferent arteriolar vasoconstriction. These effects are exacerbated by hypothermia.

High-dose aprotinin administration in adults is associated with tubular proteinuria and transient (1–7 days) mild plasma creatinine elevations (0.5 mg/dL). Similar creatinine elevations are seen with low-dose aprotinin (30 000 KIU/kg in the pump prime) in pediatric cardiac surgical patients. The vast majority of data to date indicates that aprotinin administration has minimal adverse clinical effect on renal function. However, recent investigations have associated aprotinin use with an increased risk of renal dysfunction (creatinine increase) and renal failure requiring dialysis. In addition, preoperative use of angiotensin-converting enzyme (ACE) inhibitors in

combination with intraoperative aprotinin use is associated with a higher incidence of acute renal failure. With these issues in mind, aprotinin should be used at a reduced dosage in patients with pre-existing renal dysfunction and should not be administered to patients taking ACE inhibitors at the time of surgery.

Coronary artery bypass graft patency

Concerns that aprotinin use may contribute to early graft occlusion or postoperative myocardial infarction have not been substantiated.

Deep hypothermic circulatory arrest

Concern has been raised regarding the use of aprotinin in association with Deep hypothermic circulatory arrest (DHCA) due to reports of increased mortality, renal failure, myocardial infarction, disseminated intravascular coagulation, and death. Others report significant reductions in homologous blood requirements and a trend toward improved outcome with aprotinin despite significant, transient renal dysfunction. It is unlikely that aprotinin alone can be implicated in the development of renal failure following DHCA. Previously it was thought that aprotinin use was associated with thrombosis in association with DHCA, however, this thrombosis was due to a failure to appreciate the aprotinin effect on celite ACT resulting in sub-therapeutic heparinization. More recent reports of thrombosis have occurred in the setting of adequate heparinization emphasizing that use of aprotinin during DHCA requires further elucidation.

Post-CPB bleeding and point of care testing

Transfusion algorithms utilizing Post-CPB bleeding and point of care testing (POCT) can reduce transfusions following cardiac surgery in adults by appropriately directing the use of nonerythrocyte blood products to deal with specific coagulation abnormalities. Two such protocols utilizing POCT including TEG are provided in Fig. 10.13.

It should be emphasized that use of these algorithms are complicated by the use of aprotinin, which prolongs the aPTT, the celite ACT (and to

a lesser extent the kaolin ACT), and the R of the TEG.

Decannulation

Generally, the venous cannula is removed first. With the arterial cannula in place, urgent reinstitution of CPB can be accomplished quickly. Hemodynamic compromise due to atrial dysrhythmias and volume loss may accompany removal of the atrial cannula. As long as only a small portion of the protamine has been infused, volume infusion via the arterial cannula can be undertaken safely.

To avoid undue stress on the aortotomy and to allow its easy closure, the aortic systolic blood pressure should be 100–120 mmHg in adults. Vasodilator therapy may be necessary to achieve this goal.

Pericardial and chest closure

The pericardium is not routinely closed after all cardiac surgical procedures. When a normal pericardium, small ventricular volumes, and low filling pressures exist, pericardial closure does not affect left ventricular diastolic or systolic function. For patients with distended ventricles, myocardial edema, and poor systolic function after CPB, pericardial closure may further compromise hemodynamics secondary to extrinsic reduction in diastolic filling. Chest closure may produce the same effects. In patients with severe post-CPB ventricular dysfunction, this compromise may prohibit pericardial and/or chest closure despite initiation or acceleration of inotropic and vasodilator therapy. In these patients, the chest is left open and covered with a piece of nonlatex rubber or an adhesive plastic drape, with closure accomplished 2–3 days after the procedure.

On occasion, one or both of the epicardial pacer wires may short out and become nonfunctional when the chest is closed. Therefore, atrial and ventricular epicardial pacing should be checked after the sternal edges are allowed to fall together but before chest closure. If the wires become nonfunctional, it may be necessary for the surgeon to move them to alternate sites on the atrium and ventricle before chest closure.
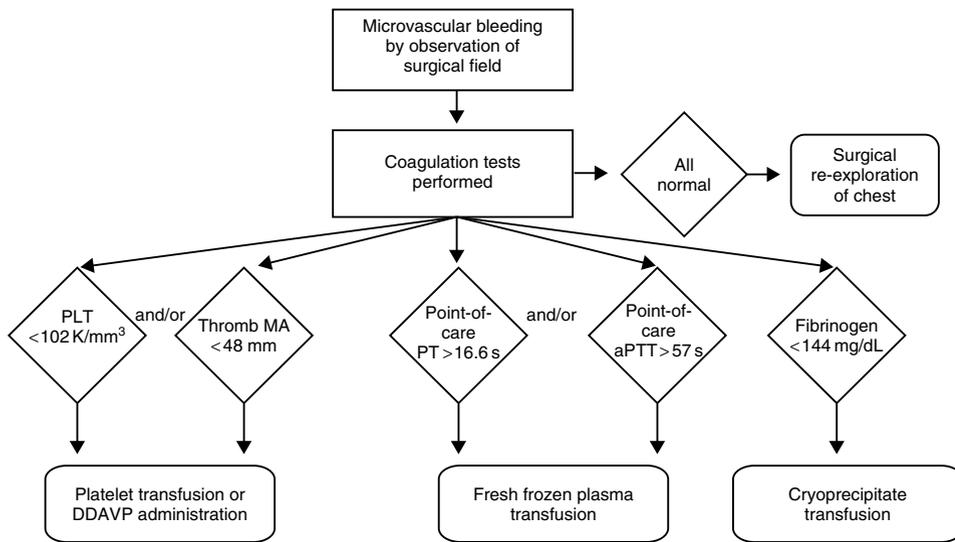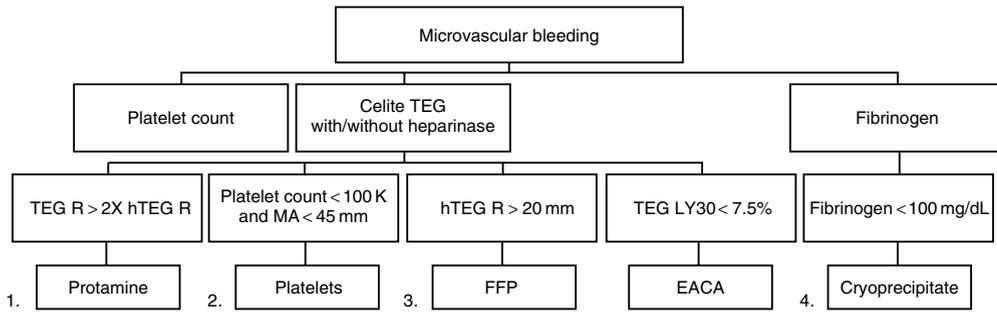
Fig. 10.13 Two adult transfusion algorithms using point-of-care testing to determine nonerythrocyte transfusion requirements. aPTT, activated partial thromboplastin time; EACA, ε-aminocaproic acid; FFP, fresh frozen plasma; hTEG, heparinase thromboelastograph; MA, TEG maximal amplitude; LY30, TEG % lysis at 30 minutes; PT, prothrombin time; R, TEG reaction time; TEG, thromboelastograph. (From Shore-Lesserson L, Manspeizer HE, DePerio M *et al*. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg* 1999;**88**:314 and Nuttall GA, Oliver WC, Santrach PJ *et al*. Efficacy of a simple intraoperative transfusion algorithm for non-erythrocyte component utilization after cardiopulmonary bypass. *Anesthesiology* 2001;**94**:775, with permission.)

Management of unusual problems on CPB

For patients requiring CPB, there are several conditions that present difficult management problems.

Cold-reactive proteins

Cold-reactive proteins are proteins that, when cooled below a specific temperature (their thermal amplitude or critical temperature) precipitate or cause red cell agglutination. The subsequent microvascular occlusion can lead to cerebral and myocardial ischemia and infarction as well as hepatic and renal dysfunction. Subsequent hemolysis also can complicate the picture. Patients with these proteins present difficult management problems for procedures in which systemic hypothermia and cold cardioplegic solutions are normally used. Cold reactive proteins can be classified

as follows:

• *Cold agglutinins (CA).* These are monoclonal or polyclonal immunoglobulin M (IgM) antibodies directed against the I or i antigen of the red cell membrane. These antibodies react most efficiently with red cells at low temperatures. The result is agglutination of red cells, complement fixation with subsequent microvascular occlusion, and ischemia. Antibody binding occurs best at low temperatures, whereas complement fixation occurs best at high temperatures. Hemolysis occurs in the thermal range of 10–30°C because this is the optimal range of overlap between antibody binding and complement fixation.

CA are more common in patients with infectious or lymphoproliferative diseases as well as in human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients. An idiopathic form of CA disease also exists. The idiopathic form is more common in older patients and women, and usually involves monoclonal IgM antibodies to the I antigen of the red cell membrane. The infectious forms such as Myoplasma pneumonia tend to involve polyclonal IgM antibodies while the lymphoproliferative disorders involve monoclonal IgM antibodies. Normal persons have low titers of anti-I antibodies that react at low temperatures <20°C) and are not clinically significant.

Most cases involving cold-reactive proteins and CPB are in patients with CA.

• *Cryoglobulins.* These are serum proteins or protein complexes that undergo reversible precipitation at low temperatures. The result is multiorgan ischemia and dysfunction from microvascular occlusion. Type I cryoglobulins consist of monoclonal IgG (multiple myeloma) or IgM (Waldenstrom's macroglobulinemia). Type II cryoglobulins consists of monoclonal IgM directed against polyclonal IgG and usually are associated with autoimmune, infectious, and lymphoproliferative disorders. Type III cryoglobulins consist of polyclonal IgM directed against polyclonal IgG and are associated with infections and autoimmune diseases.

There is limited experience (three reported cases) in patients with cryoglobulins undergoing procedures requiring CPB.

• *Paroxysmal cold hemoglobinuria.* These IgG antibodies are associated with syphilis, have a critical temperature below 20°C, and are potent hemolysins. There are no case reports of CPB in patients with this disorder.

Recommendations for patients with CA

1 Detection of CA over clinically relevant temperatures can be accomplished at the time of cross-matching by direct Coombs' tests done at 4°C, 25°C, and 37°C. If this is positive, titers at the various temperatures can be performed. This will give an accurate but not precise determination of thermal amplitude and titers preoperatively.

2 Systemic temperatures are kept above the thermal amplitude of the CA. If DHCA is planned, the thermal amplitude of the CA must be known to determine whether temperatures <20°C are feasible.

3 Myocardial preservation can be accomplished as follows:

a Cardioplegia can be avoided entirely and warm ischemic arrest can be used. This method is unacceptable when long cross-clamp times are expected or when preoperative myocardial dysfunction exists.

b Warm crystalloid or blood cardioplegia can be used, but the advantages of hypothermia in reducing myocardial oxygen consumption are lost. In addition, frequent instillations of cardioplegia will be needed to keep the heart arrested.

c Cold crystalloid cardioplegia can be used as in normal circumstances. However, the temperature of the cardioplegia (4–8°C) generally is below the critical temperature and will initiate autoagglutination. This may result in micovascular thrombus formation and infarction, nonhomogenous delivery of cardioplegia, and hemolysis.

d Delivery of warm cardioplegia followed by delivery of cold cardioplegia. The right heart is completely isolated with the use of bicaval cannulation and tourniquets. The right atrium is then opened to allow visualization of the coronary sinus. Warm crystalloid cardioplegia is infused until all of the blood is washed out of the coronaries. Cold crystalloid cardioplegia is then delivered. The presence of noncoronary collaterals may add blood

to the coronary circulation despite aortic cross-clamping. Therefore, efforts must be made to reduce noncoronary collateral flow by keeping perfusion pressures on CPB low as discussed previously.

e For patients who have CA detected preoperatively and in whom the thermal amplitude and titers are high, plasmapheresis may be used to decrease the cold agglutinin titer and increase the margin of safety for use of hypothermia. Plasmapheresis carries the risk of large volume shifts in patients with limited cardiac reserve. Further, it is expensive, carries an infectious risk, and is of uncertain efficacy.

f Efforts should be made to warm all IV fluids.

g Efforts to avoid nonautologous transfusions should be made because donor red cells will not be coated with C3d. C3d is a component of the complement system, which coats some of the patient's red cells after an episode of agglutination and affords some protection from subsequent agglutination and lysis.

h Steroids may help prevent or mitigate the agglutination and lysis process.

Sickle cell disease

Sickle cell disease (SCD) and sickle cell trait (SCT) are heredity hemoglobinopathies resulting from a mutant form of the β-globin gene on chromosome 11. This gene normally codes for the production of the β-globin chains of hemoglobin A (Hb A). The mutant gene codes for production of Hb S. SCD is present in patients who are homozygous for hemoglobin S (Hb SS). SCT is present in patients who are heterozygous for hemoglobin S (Hb AS). Two other hemoglobinopathies exist which include hemoglobin S: Hb SC and Hb S/β-thalassemia. Some patients with these two hemoglobinopathies have disease manifestations as severe as Hb SS patients.

Concern in these patients centers largely on the use of hypothermic CPB. Hypothermia without the benefit of hemodilution can potentially increase blood viscosity, reduce capillary perfusion, promote stasis, and thus increase the risk of sickling. Furthermore, hypoxia and acidosis promote sickling because sickling occurs when the red cell is in the deoxygenated state. Preoperative therapy

focuses on:
- reducing Hb S (the substrate for sickling);
- increasing normal Hb A (the substrate for oxygen-carrying capacity).

Experience suggests that a target of Hb S < 30% and Hct > 30% is reasonable in high-risk (Hb SS, Hb SC and Hb S/thalassemia) patients prior to initiation of hypothermic CPB. Transfusion alone is usually sufficient to reach a target Hct of 30% and exchange transfusions are generally required to reach both targets. Hb AS patients have been treated with exchange transfusions prior to CPB procedures, but recent experience with these patients indicates that hypothermic CPB can be used without prior exchange transfusions if hemodilution is used and hypoxia and acidosis are avoided.

Heparin induced thrombocytopenia (HIT)

Heparin administration normally causes an immediate, transient, reversible reduction in platelet count following due to induction of platelet aggregation. This is commonly referred to as Type I HIT. HIT Type II (unfortunately, also commonly just called HIT) is an immunological process involving the development of anti-heparin platelet factor 4 (PF4) antibodies. Heparin binds with high affinity to PF4 and induces a conformational change in PF4 exposing two or three epitopes capable of binding primarily IgG but also IgA and IgM antibodies. The IgG-heparin-PF4 complex then binds to platelets via their FcγRIIa receptors. Cross-linking of the receptors leads to platelet activation and release of PF4 from α-granules. Platelet bound PF4 on activated platelets complexes with heparin and IgG binds to this complex via its Fab domain leaving its Fc domain free to bind to and activate an adjacent platelet via its FcγRIIa receptor. This amplification process leads to intense platelet activation and aggregation with subsequent production of procoagulant microparticles.

HIT is a clinicopathologic syndrome generally defined as a ≥50% reduction in platelet count and a positive assay for anti-heparin/PF4 antibodies occurring between 5 and 10 days following exposure to UFH. Heparin-induced thrombocytopenia with thrombosis or skin lesions (HITT) is a severe form of HIT with high morbidity and mortality.

Two types of assays (antigenic and functional/biologic) are currently used for detection of anti-heparin PF4 antibodies. ELISA capable of detecting IgG, IgA, and IgM antibodies to PF4 are commercially available. The most commonly utilized functional assay is the ^{14}C-serotonin release assay (SRA). Washed donor platelets previously incubated with ^{14}C-serotonin are mixed with subject plasma suspected to contain to anti-heparin PF4 antibodies. *In vitro* platelet activation is quantitated by measurement of released ^{14}C-serotonin. As such this assay is capable of detecting only titers of anti-heparin PF4 antibodies high enough to induce platelet aggregation. This assay is technically demanding to perform and requires specially designed equipment.

The incidence of anti-heparin PF4 antibody formation in cardiac surgical patients prior to surgery is approximately 13–19%, while the incidence following cardiac surgery is approximately 50% by

ELISA and 20% by SRA. In the absence of continued exposure to UFH there should be clearance of anti-heparin PF4 antibodies within 2–6 weeks. Clinical HIT occurs in approximately 2% of patients following cardiac surgery with about half of those patients experiencing associated thrombosis.

In a patient suspected of having HIT prior to cardiac surgery or in a patient with a previous history of HIT scheduled for cardiac surgery the algorithm presented in Fig. 10.14 is useful.

The best available strategies for anticoagulation for CPB in patients with anti-heparin PF4 antibodies can be summarized as follows:
- *Direct thrombin inhibitors (DTI) without UFH*. The active-site pocket of thrombin catalyzes most of the functions of thrombin while the fibrinogen-binding site (exosite 1) mediates binding of thrombin to fibrinogen. Exosite 2 is the heparin-binding site. Hirudin is the most potent DTI known, isolated from the salivary glands of the medicinal leech. It is
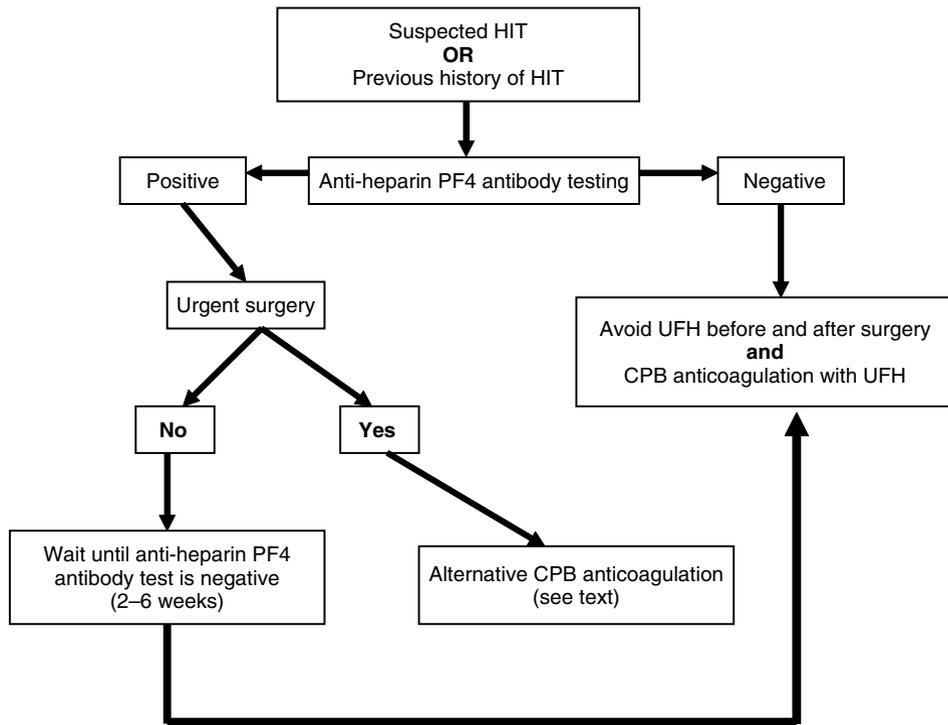
Fig. 10.14 Algorithm outlining care of patients with heparin-induced thrombocytopenia (HIT) or suspected HIT. CPB, cardiopulmonary bypass; UFH, unfractionated heparin; PF4, platelet factor 4.

a bivalent thrombin inhibitor as it binds to both pre- viously described active sites. It binds to both soluble and fibrin bound thrombin. The clinically available direct thrombin inhibitors used in place of UFH for CPB are:

a Lepirudin (recombinant hirudin) is an irreversibly binding bivalent thrombin inhibitor.

b Bivalirudin is a synthetic peptide analog of hirudin and is a bivalent thrombin inhibitor. Unlike lepirudin it reversibly binds to thrombin.

c Argatroban is a monovalent synthetic thrombin inhibitor with reversible activity at the active-site pocket of thrombin. Argatroban does not bind to exosite 1.

There is no antidote available for the reversal of the anticoagulant effect of DTI in the sense that UFH is reversible with protamine. Termination of DTI effect is dependent on metabolism, redistri- bution, and elimination of the drug. In the case of bivalirudin and argatroban disassociation of the drug from thrombin also plays a role.

The ecarin clotting time (ECT) is used to monitor the anticoagulant effect of lepirudin and bivalirudin. The ECT is a modification of the ACT that uses ecarin as an activator. Ecarin activates prothrombin to the intermediate thrombin product meizothrombin. Meizothrombin has limited procoagulant activity as compared to thrombin. However, like throm- bin it binds to lepirudin and bivalirudin with 1:1 stoichiometry. The ECT will thus be prolonged by DTI with the ECT determined by the relative concentrations of meizothrombin and lepirudin or bivalirudin. There is good correlation between ECT and plasma levels of lepirudin and bivalirudin. Unfortunately, the ECT is not commercially avail- able for point of care testing and must be run in a hospital-based laboratory.

• *Platelet inhibition in association with standard UFH use.* Heparin dependant platelet activation in the presence of HIT antibodies can be achieved with a continuous IV infusion of prostaglandin I_2 (prosta- cyclin). Iloprost and Flolan (epoprostenol) are stable forms of prostacyclin that have been used success- fully in conjunction with standard UFH doses for CPB. Success has also been reported with use of con- tinuous IV infusion of prostaglandin E_2 but this has not been as rigorously investigated. Other platelet inhibiting drugs such as dipyridamole and aspirin have been used in conjunction with these agents as well. Recently, success with use of a continuous IV infusion of tirofiban (a short acting GP IIb/IIIa inhibitor) in conjunction with standard UFH has been reported.

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CHAPTER 11

Mechanical Circulatory Support

This chapter focuses on mechanical circulatory support devices currently available for clinical use in the United States. The intra-aortic balloon pump (IABP), centrifugal pumps, axial flow pumps, ventricular assist devices (VAD), and the total artificial heart (TAH) will be covered. These devices are summarized in Tables 11.1–11.3.

Indications for mechanical circulatory support

The indications for mechanical circulatory support are the presence of left ventricular (LV) failure, right ventricular (RV) failure, or both in the setting of maximal intravenous (IV) inotropic support following correction of acid-base and electrolyte abnormalities and hypovolemia. Maximal inotropic support is defined as use of two or more of the following:

- Dobutamine >10 μg/kg/min.
- Dopamine >10 μg/kg/min.
- Epinephrine >0.2 μg/kg/min.
- Milrinone >0.75 μg/kg/min, after a loading dose of 50 μg/kg/min.

Ventricular failure is defined as one or both of the following:

- LV dysfunction:

a cardiac index < 1.8–2.0 L/min/m^2;
b systolic blood pressure < 90 mmHg or mean arterial pressure (MAP) < 70 mmHg;
c left atrial (LA) pressure > 18–25 mmHg;

- RV dysfunction:

a cardiac index < 1.8–2.0 L/min/m^2;
b systolic blood pressure < 90 mmHg or MAP < 70 mmHg;
c right atrial (RA) pressure > 18–20 mmHg.

Device selection

The type of mechanical circulatory device selected depends, in large part, on the setting in which the device is to be used. The goal of mechanical support is to initiate support prior to development of end-organ dysfunction and to prevent end-organ dysfunction from developing. Mechanical circulatory assist devices are currently used in three major capacities.

Bridge to recovery

Temporary circulatory support is used in the subset of patients with cardiogenic shock in whom recovery of significant myocardial function is expected. Patients in this category receive short-term to intermediate (days to weeks) mechanical circulatory support during a critical interval while ventricular function recovers. The assist device is then weaned and explanted. The most common indications for this type of circulatory support are:

- Postcardiotomy cardiogenic shock. This is estimated to occur in 2–6% of all patients undergoing surgery for coronary revascularization or valve repair or replacement. One percent of all these

Table 11.1 Extracorporeal devices.

Device	Mechanism	Support	Indications
IABP	Pneumatic counterpulsation	LVAD	Short term • postcardiotomy

ECMO	Centrifugal or
	  nonocclusive roller head
	Nonpulsatile
		Partial or total CPB	Short term (adults)
			• postcardiotomy
			• post-cardiac arrest
			
			Short to intermediate term
			  (infants/children)
			• postcardiotomy
			• post-cardiac arrest
			• bridge-to-transplant

BioMedicus	Centrifugal Nonpulsatile	LVAD and/or RVAD In parallel	Short term • postcardiotomy
TandemHeart	Centrifugal Nonpulsatile	LVAD In parallel	Short term • postcardiotomy • post-catheter intervention
Abiomed BVS 5000	Pneumatic membrane Pulsatile	LVAD and/or RVAD In parallel	Short term • postcardiotomy
Thoratec	Pneumatic membrane Pulsatile	LVAD and/or RVAD In series or in parallel	Short to intermediate term • postcardiotomy • bridge-to-transplant
Abiomed AB5000	Pneumatic membrane Pulsatile	LVAD and/or RVAD In series or in parallel	Short to intermediate term • postcardiotomy • bridge-to-transplant
Berlin Heart	Pneumatic membrane Pulsatile	LVAD and/or RVAD In series or in parallel	Short to intermediate term • postcardiotomy • bridge-to-transplant • pediatric sizes
Medos VAD	Pneumatic membrane Pulsatile	LVAD and/or RVAD In series or in parallel	Short to intermediate term • postcardiotomy • bridge-to-transplant • pediatric sizes

ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; RVAD, right ventricular assist device; VAD, ventricular assist device.

postcardiotomy patients require mechanical circulatory support. This is probably the largest patient subset requiring bridge to recovery support. The use of centrifugal pumps and VAD as temporary circulatory support in patients with cardiogenic shock after cardiac surgical procedures has been less successful than the bridge to transplantation experience. Although small individual series have survival rates as high as 40%, the Combined Registry for the Clinical Use of Mechanical Ventricular Assist Pumps and Artificial Hearts reports that the overall hospital discharge rate is 25%. This low survival rate is similar for patients supported with both VAD and centrifugal pumps. Factors that have been associated with poor outcome include renal failure, perioperative myocardial infarction, and infection.

Table 11.2 Intracorporeal devices.

Device	Mechanism	Support	Indications
HeartMate IP	Pneumatic pusher plate Pulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy
HeartMate XVE	Electric pusher plate Pulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy
Novacor	Electric pusher plate Pulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy
Jarvik 2000	Electric axial flow Nonpulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy
MicroMed VAD	Electric axial flow Nonpulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy • pediatric version
HeartMate II	Electric axial flow Nonpulsatile	LVAD In series	Intermediate to long term • bridge-to-transplant • destination therapy

LVAD, left ventricular assist device; VAD, ventricular assist device.

Table 11.3 Orthotopic prosthetic ventricles.

Device	Mechanism	Support	Indications
CardioWest	Pneumatic membrane Pulsatile	Total artificial heart	Intermediate to long term • bridge-to-transplant
Abiocor	Electrohydralic membrane Pulsatile	Total artificial heart	Intermediate to long term • bridge-to-transplant • destination therapy

Most patients who do survive are New York Heart Association (NYHA) functional class I or II.
• Post acute-myocardial infarction (MI) cardiogenic shock.
• Myocarditis-induced cardiogenic shock.
• Support during medical or ablative therapy for intractable dysrhythmias.
• Support during or following complicated interventional cardiac catheterization procedures.

Bridge to cardiac transplantation

In the case of a bridge to transplantation, a mechanical assist device is implanted with the intention of providing intermediate to long-term (weeks to months) support until a suitable donor heart is found or until the patient dies from irreversible damage to other organ systems. Devices used for a bridge to transplantation must allow patient mobilization and discharge from an intensive care unit

Table 11.4 Criteria for left ventricular assist device (LVAD) placement as a bridge to cardiac transplantation.

Inclusion criteria
1 Patient is a transplant candidate
2 Hemodynamic data:
    Cardiac index $< 2.0\,L/min/m^2$
    Systolic BP $< 80\,mmHg$
    PAOP $> 20\,mmHg$

Exclusion criteria
1 Technical issues:
    BSA $< 1.5\,m^2$
    Aortic valve insufficiency (if valve not repaired or
     replaced with a bioprosthesis)
    Right-to-left intracardiac shunt (if left unrepaired)
    Severe aortic atherosclerotic disease
    Abdominal aortic aneurysm
    Mechanical cardiac valves
    LV thrombus
2 Fixed PVR with PVR > 8 Wood units
3 Factors deemed to increase perioperative risk:
    Mechanical ventilation
    Urine output $< 30\,mL/h$
    Pyrexia
    Elevated WBC count
    RAP $> 16\,mmHg$
    PT > 16 seconds
    Re-operation

BP, blood pressure; BSA, body surface area; LV, left ventricle; PAOP, pulmonary artery occlusion pressure; PT, prothrombin time; PVR, pulmonary vascular resistance; RAP, right atrial pressure; WBC, white blood cell.

(ICU) setting because the wait for a donor heart may be long. The criteria for use of a left ventricular assist device (LVAD) as a bridge to transplantation are shown in Table 11.4.

At present, the limiting factor in the number of patients who can be offered a heart transplant is the availability of donor hearts. It is estimated that while 5–10% of the total population suffers from end-stage, refractory heart failure that could benefit from a heart transplant, only approximately 2500 donor hearts are available per year. Furthermore, 25–30% of suitable transplant candidates die before a donor heart can be found. In the subset of heart failure patients eligible for mechanical support up to 70% will die without mechanical support while awaiting transplant. As a result, mechanical assist devices and the TAH are being used with greater frequency as a bridge to cardiac transplantation. For transplant candidates at immediate risk of end-organ dysfunction, these devices provide mechanical circulatory support until a suitable donor heart is found.

The outcome after bridge to transplantation is very good. Currently, approximately 70% of patients who receive an assist device as a bridge survive to transplant and 70% of those patients go on to hospital discharge. After hospital discharge, LVAD patients without pre-existing organ dysfunction have 1- and 2-year actuarial survival rates similar to patients receiving orthotopic heart transplantation without mechanical circulatory support.

The HeartMate (IP, XVE, and II), Novacor, MicroMed, and Jarvik 2000 devices are all intracorporeal (implantable) devices used exclusively for bridge to transplantation in patients requiring only LV support. The Thoratec VAD and Abiomed AB5000 also can be used in this capacity. Bridge to transplantation patients who require biventricular assist device (BiVAD) support are candidates for a TAH, the Thoratec VAD, or the Abiomed AB5000. In infants and small children the Berlin Heart or Medos VAD could serve this purpose.

Destination therapy

In this setting permanently implanted LVAD serve as an alternative to chronic medical therapy in patients who are not cardiac transplant candidates. In general, patients selected for destination therapy are older (age >65 years) with end-organ dysfunction from diabetes or other chronic medical problems and with other significant physical and/or psychiatric co-morbidities. The REMATCH trial, which made use of the HeartMate XVE device demonstrated improved survival and quality of life over a 2-year period in patients with an implanted VAD as compared to patients receiving chronic medical therapy. Currently, the HeartMate XVE device is Food and Drug Administration (FDA) approved for this purpose and the Novacor device is undergoing trials for this use in the RELIANT Trial. As shown

in Table 11.2, other devices are likely to be used in this capacity in the future.

Complications

Thromboembolism, perioperative hemorrhage, and infection are the three major complications associated with use of circulatory assist devices and the TAH, particularly when used long term for a bridge to transplantation or destination therapy.

Classification of devices

Several classifications of mechanical circulatory support devices exist, and there is considerable overlap between classifications.

Orthotopic and heterotopic prosthetic ventricles

Heterotopic prosthetic ventricles provide mechanical support in parallel or in series with the intact native ventricles. These devices are commonly called ventricular assist devices (VAD). Some VAD are designed only for LV support, whereas others may be used for left ventricular (LVAD), right ventricular (RVAD), or biventricular support (BiVAD). Table 11.1 summarizes the uses of the clinically available devices.

Orthotopic devices provide mechanical support in place of the excised native ventricles. The native atria are surgically placed in continuity with the prosthetic ventricles. Orthotopic prosthetic ventricles are described more commonly as total artificial hearts (TAH).

Series versus parallel circulatory support

A circulatory support device may be used in parallel or in series with the native ventricular system, depending on how cannulation for the device is achieved. When inflow to the device is achieved via cannulation of the native atrium and outflow is via cannulation of the corresponding great vessel, the device is said to be "in parallel" with the native ventricular system. When inflow to the device is achieved via cannulation of the apex of the native
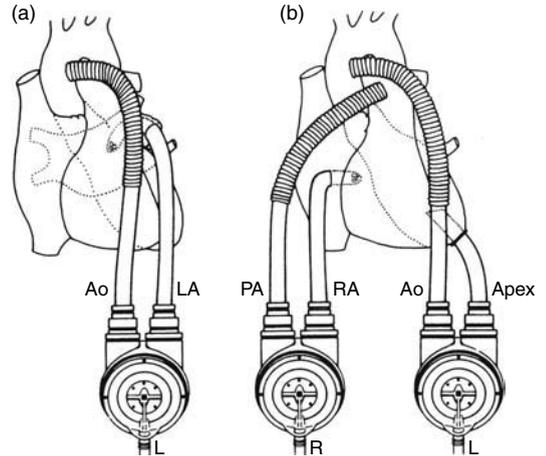
Fig. 11.1 (a) Schematic of a Thoratec ventricular assist device (VAD) in parallel with the left heart. (b) Schematic of a Thoratec VAD in parallel with the right heart and in series with the left heart. Ao, aorta; LA, left atrium; PA, pulmonary artery; RA, right atrium.

ventricle and outflow is via cannulation of the corresponding great vessel, the device is said to be "in series" with the native ventricle. Some devices always are used in series with the native ventricle, some are always used in parallel, and some can be used in either a series or parallel arrangement. Figure 11.1a,b illustrates parallel and series arrangement. Tables 11.1 and 11.2 describe which devices are used in series and in parallel.

In general, the series arrangement provides better filling and a higher device output for two reasons. First, the device does not compete with the native ventricle for atrial blood the way it must in a parallel arrangement. Second, native ventricular systole serves to fill the prosthetic ventricle. The series arrangement also provides the native ventricle with a low-impedance outflow tract into the prosthetic ventricle, which greatly reduces native ventricular diameter and systolic wall stress. The major disadvantage of a series arrangement is that the ventricular apex may become akinetic or dyskinetic after removal of the ventricular cannula. For patients who are to be transplanted, this is not an important issue. However, it is a very important issue for patients who are ultimately to be weaned off mechanical support.

Pulsatile versus nonpulsatile flow

Both orthotopic and heterotopic prosthetic ventricles provide pulsatile flow, whereas centrifugal and axial pumps provide nonpulsatile flow. Two types of pulsatile prosthetic ventricles are currently in use: pneumatic and electromechanical. Pulsatile pneumatic pumps use pressurized air to eject blood from the prosthetic ventricular chamber. Pulsatile electromechanical pumps convert electrical energy to the mechanical energy necessary to eject blood from the prosthetic ventricular chamber.

Extracorporeal versus intracorporeal (implantable) devices

Some devices are extracorporeal, whereas others are intracorporeal. With extracorporeal devices, the pumping device is located outside the body, with both the inflow and outflow conduits entering the patient's thoracic cavity. Implantable devices are implanted in the patient's pericardial cavity or pre-peritoneally. Anatomical constraints generally make it difficult to implant intracorporeal devices into patients with a body surface area (BSA) $< 1.5\,m^2$.

Triggering modes and percentage of systole

Pulsatile pumps have a number of different ways in which ejection can be triggered. In the case of TAH, the ejection rate is set by the operator and is analogous to the heart rate. Because VAD are used in conjunction with the native ventricular system, more options are available to trigger a VAD ejection cycle.

Manual

This mode, also known as the single stroke mode, is used for de-airing of the device after implantation. It allows a single ejection with the touch of a button.

Asynchronous

In the asynchronous mode, the VAD ejects at a rate decided upon by the operator. This produces a fixed rate, variable stroke volume mode of operation. At higher device rates, the time available for diastolic filling will be reduced. This can in part be offset by increasing preload to the device. In this mode there

will be beats in which the device and the ventricle eject at the same time.

Fill-to-empty

In this mode, also known as the volume mode, the device is programmed to trigger ejection only when the VAD is filled with blood in diastole. This produces a fixed stroke volume variable rate mode of operation. In this triggering mode, the VAD ejection rate will vary with preload. When preload to the VAD is high, the VAD ejection rate will be high; likewise, when preload to the VAD is poor, the VAD ejection rate will be low.

Device and ventricular ejection rates will differ and will vary phasically. In the case of series LVAD, aortic valve opening is rarely seen at rest in this mode but may be present during exercise. In a series device, when device filling coincides with LV diastole, filling is said to be synchronous. In this setting, LV volume at the commencement of LV contraction is small and ejection is insufficient to open the aortic valve. In a series device, when device filling coincides with LV systole, filling is said to be counter-synchronous. In this setting, there is no ejection out of the aortic valve as the low-impedance pathway during native ventricular systole is into the device.

Synchronous

In the synchronous mode, an external electrical signal, usually the R wave of the electrocardiogram (ECG) is used to trigger VAD ejection. Using a programmable delay, the operator can use this mode to reduce ventricular afterload by preventing the device from ejecting into the aorta or pulmonary artery at the same time as the native ventricle.

In addition to having various triggering modes, some devices allow the operator to program the percentage of systole. This allows the operator to decide what percentage of each prosthetic ventricular cycle is devoted to ejection. Obviously, as the prosthetic ventricular ejection rate increases, the time between cycles diminishes. The advantage of reducing the percentage of systole is that it allows a greater proportion of each cycle to be devoted to prosthetic ventricular filling. However, for a given ejection rate, reducing the percentage of systole increases

the rapidity of the ejection phase. The more rapid the ejection phase, the more likely are turbulent flow and damage to formed blood elements with resultant hemolysis.

Device description

Intra-aortic balloon pump

The Intra-aortic balloon pump (IABP), first introduced into clinical use in 1968, has become an important method of providing circulatory support in a wide variety of patients.

The IABP consists of a catheter-mounted balloon, a pump, a gas source, and a microprocessor console. The balloon is thin-walled, measures 2×20 cm, and contains 30–40 mL of volume when inflated. The catheter has a hollow central lumen, which allows percutaneous placement over a guide wire, as well as the recording of central aortic pressure. The pump inflates and deflates the balloon at precisely timed intervals, with either carbon dioxide or helium as the inflating or shuttle gas. Carbon dioxide carries less of an embolic risk if the balloon ruptures because it is absorbed quickly. Helium has a lower density, allowing faster inflation and deflation, and currently is the preferred gas. The console displays the ECG, the arterial waveform, and the balloon pressure trace. The console controls exactly when the pump inflates and deflates the balloon.

Proper functioning of the IABP depends on the precise timing of balloon inflation and deflation relative to the cardiac cycle. Balloon inflation (Fig. 11.2) optimally occurs immediately after the closure of the aortic valve as represented by the dicrotic notch on the central arterial pressure tracing. The resultant increase in aortic volume increases diastolic arterial pressure (diastolic augmentation) and improves systemic and coronary artery perfusion pressure. The increase in aortic diastolic pressure depends on a number of variables: the nonaugmented aortic diastolic pressure, the compliance of the aorta, the size of the balloon, and the volume of gas in the balloon (from minimal to full volume). Balloon inflation in the noncompliant aorta of an elderly patient will produce a higher augmented diastolic pressure than the same balloon in a compliant aorta.
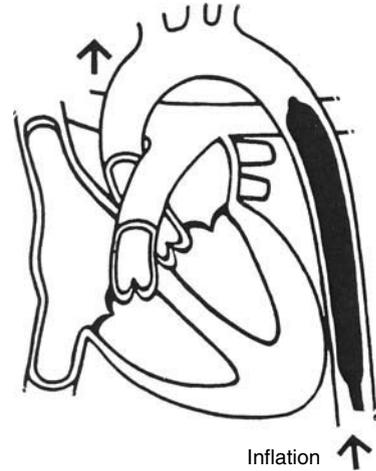
Fig. 11.2 A properly positioned intra-aortic balloon pump (IABP) inflating in the proximal descending aorta.

In the absence of coronary stenoses, augmentation of aortic diastolic blood pressure increases coronary blood flow in both the proximal and distal coronary arteries. In the presence of critical coronary stenoses, the IABP does not improve coronary blood flow distal to the stenoses. It is conceivable that coronary beds distal to a stenosis could have improved coronary perfusion with IABP counterpulsation if collaterals from a nonstenosed coronary artery supply the beds.

Deflation of the balloon (Fig. 11.3) is adjusted to occur immediately before LV ejection, at the onset of the upstroke of the central arterial waveform. Optimal balloon deflation is established when the arterial diastolic pressure is maximally reduced (unloading). The duration of isovolumic contraction of the left ventricle is determined by the pressure gradient between the left ventricle and the proximal aorta. Balloon deflation quickly lowers proximal aortic pressure, thereby reducing afterload by decreasing the impedance to ejection out the left ventricle. This shortens the duration of isovolumic contraction, which in turn reduces myocardial oxygen consumption. Reduction of myocardial oxygen consumption, rather than augmentation of coronary blood flow, is the primary method by which the IABP ameliorates myocardial ischemia.

In addition to reducing myocardial oxygen consumption, properly timed IABP deflation improves
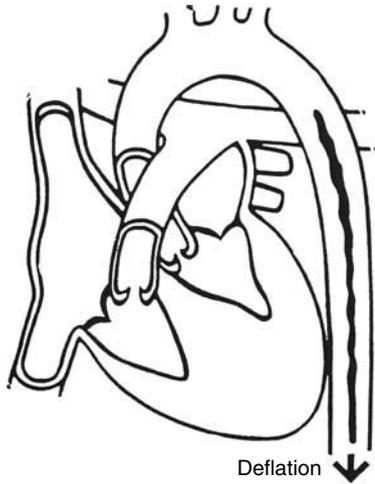
Deflation

Fig. 11.3 A properly positioned intra-aortic balloon pump (IABP) deflating in the proximal descending aorta.

LV systolic function on a beat-to-beat basis by decreasing systolic wall stress. Increases in ejection phase indices of systolic function, such as ejection fraction, are directly proportional to IABP-induced decreases in systolic wall stress.

Indications and contraindications

The indications for IABP use are summarized below:

1 Patients with refractory myocardial ischemia.

2 Patients with cardiogenic shock:

a myocardial infarction;

b myocarditis;

c cardiomyopathy;

d pharmacologic depression.

3 Stabilization of patients before cardiac surgery:

a myocardial infarction;

b postinfarction ventricular septal defect (VSD);

c mitral regurgitation;

d bridge to cardiac transplantation.

4 Support of patients after cardiac surgery:

a reversible LV dysfunction;

b intraoperative myocardial infarction;

c allograft dysfunction after heart transplantation.

5 Support of non cardiac surgical patients:

a support during percutaneous coronary angioplasty;

b to maintain coronary artery patency after thrombolytic therapy or angioplasty in the setting of acute myocardial infarction;

c support during noncardiac surgical procedures.

There are few absolute contraindications to the use of the IABP. Aortic valve incompetence is a contraindication because balloon inflation in diastole will increase the regurgitant fraction. Aortic dissection and aortic aneurysm are contraindications because balloon inflation could promote frank aortic rupture. Severe peripheral vascular disease may make placement of the IABP via the femoral artery impossible.

Insertion

Most IABP catheters are inserted percutaneously using the Seldinger technique via the femoral artery retrograde into the descending aorta. Surgical cut down to expose the femoral artery, followed by cannulation of the artery under direct vision using the modified Seldinger technique, is reserved for situations in which location of the femoral artery percutaneously may be difficult, such as with hypotension, lack of pulsatile flow on cardiopulmonary bypass (CPB), obesity, and peripheral vascular disease. The IABP usually is placed through an arterial sheath, but newer models allow placement of the IABP catheter directly into the femoral artery without a sheath. This is a useful alternative for patients with small femoral arteries or with peripheral vascular disease.

The balloon should be placed so that the proximal tip is distal to the left subclavian artery and the distal end is proximal to the renal arteries. The length of IABP catheter required is estimated by the distance from the femoral artery to the sternomanubrial junction. Final position can be verified with a chest radiograph, fluoroscopy, transesophageal echocardiography (TEE), or direct palpation of the descending aorta by the surgeon.

When severe peripheral vascular disease precludes retrograde insertion via the femoral artery, the balloon catheter can be placed antegrade in the descending thoracic aorta via the right subclavian artery, the axillary artery, or the ascending aorta. Placement via the ascending aorta requires

a sternotomy. The technique is used only for postcardiotomy patients who cannot otherwise be weaned from CPB and necessitates subsequent removal under anesthesia in the operating room.

Complications

The incidence of complications from intra-aortic balloon counterpulsation that are severe enough to require balloon removal or surgical intervention ranges from 17 to 35%. The most common complication is lower limb ischemia. However, there are reports of every major branch of the aorta being occluded by thrombus, embolus, or balloon-induced dissection. Other complications include thrombocytopenia and balloon or console failure.

Management of the IABP

Optimal performance of the IABP depends on proper triggering and timing. The microprocessor is capable of using a number of signal modalities to trigger IABP inflation and deflation.

- *ECG*. This is the signal most commonly used to trigger the IABP. The R wave is used as the central timing event that directs balloon inflation to occur during the T wave (diastole) and balloon deflation immediately before the subsequent QRS complex (onset of systole). Due to the time necessary for R wave detection, and for the time necessary to shuttle helium out of the balloon, triggering IABP deflation from the immediately preceding R wave generally results in less than optimal timing and unloading. As a result, consoles detect the R wave and inflate in diastole after a preset interval that allows completion of mechanical systole. After another preset interval, the balloon deflates in anticipation of the next mechanical systole.

The ECG signal to the IABP console can be the ECG transmitted by a cable from the operating room monitor or the ECG derived from a separate set of patient leads directly to the IABP console. The former is preferable if the skin leads have not been placed before surgical prepping and draping. Radiofrequency current from the electrocautery used in the operating room can interfere with the ECG trigger. The IABP leads have a special built in radiofrequency filter that helps alleviate this problem. Alternatively, using the operating room

monitor in the more heavily filtered nondiagnostic mode will help filter out some of the noise. Other maneuvers that diminish the effect of radiofrequency current include placing all ECG leads in a single frontal plane, which reduces the potential difference between any of the leads, and using the lowest electrocautery current setting possible, in short bursts. In the ECG triggering mode pacer spikes are rejected as a triggering stimulus by the microprocessor.

- *Arterial waveform*. The upstroke of the arterial waveform can be used by the microprocessor in a manner similar to the R wave of the ECG. A pressure trigger threshold (systolic pulse height from baseline) between 7 and 30 mmHg can be set.
- *Internal*. This mode is used during a systole, CPB or ventricular fibrillation. A fixed rate of 80 b/min or a variable rate of 40–120 b/min in increments of five can be set. Some models allow fixed internal rates of 40, 60, 80 or 120 b/min.
- *Pacer spikes*. Atrial, ventricular, and atrioventricular (AV) sequential pacer spikes can complicate balloon triggering. IABP consoles can be programmed to use the atrial and/or ventricular pacer spikes as a trigger or to ignore ("reject") the pacer spikes. With some consoles, when the balloon is in the ECG trigger mode, pacer spike rejection is automatic. If the microprocessor has difficulty ignoring a pacer spike, the use of bipolar pacing or ECG leads that minimize the pacer spikes may be necessary. Pacer spikes are used as triggers only when an ECG trigger is not effective.

Although the ECG is normally used to trigger balloon inflation and deflation, proper counterpulsation timing can only be confirmed by examination of an arterial pressure waveform. When the radial artery is transduced, there is a 60 ms delay in waveform transmission from the central aorta. When the femoral artery is used, there is a 120 ms delay in waveform transmission from the central aorta. Inflation using these arterial pressure-monitoring sites must be adjusted accordingly. Ideally, balloon inflation occurs at the dicrotic notch in the central aorta. When the radial artery pressure is monitored, inflation should be adjusted to occur 60 ms before the radial artery dicrotic notch. When the femoral artery pressure is monitored, balloon
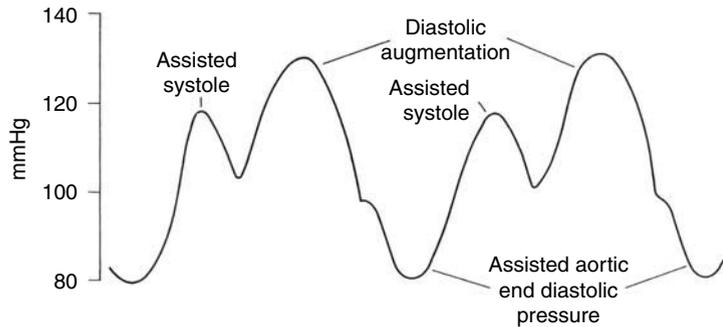
Fig. 11.4 Arterial pressure trace from a patient receiving 1:1 intra-aortic balloon pump (IABP) support with proper timing.
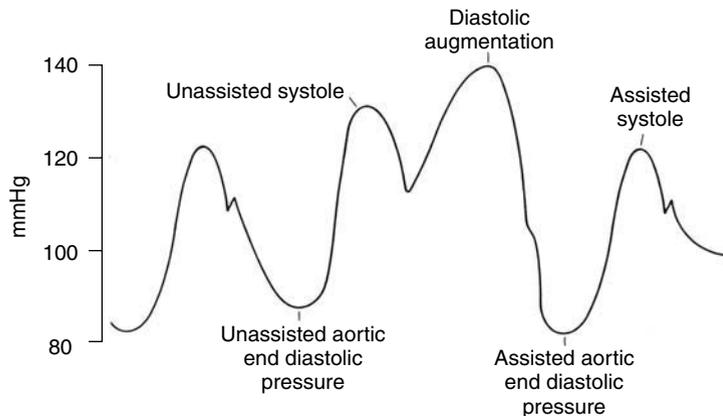
Fig. 11.5 Arterial pressure trace from a patient receiving 1:2 intra-aortic balloon pump (IABP) support with proper timing.

inflation should be adjusted to occur 120 ms before the femoral artery dicrotic notch.

The details of proper timing are illustrated in Figs 11.4–11.7. Proper timing requires that the IABP be triggered every second or third R wave (1:2 or 1:3). This allows observation of assisted and unassisted systole and of assisted and unassisted aortic end-diastolic pressure. Some IABP consoles contain a "verify" option that highlights the period of balloon inflation in real time on the arterial waveform (Fig. 11.8). This feature is a useful aid in obtaining proper timing. Timing may be accomplished in the automatic or manual mode. The automatic mode uses the R wave and an algorithm that triggers balloon inflation after an interval based on heart rate, which allows completion of mechanical systole. Balloon deflation is triggered after another preset interval based on heart rate. Fine-tuning of timing is obtained by use of the inflation and deflation controls on the console (Fig. 11.9). Inflation is

made to occur later in the cardiac cycle by using the rightward facing "Later" arrow or by moving the inflation slide "out" or to the right on older models. Inflation is made to occur earlier in the cardiac cycle by using the leftward facing "Earlier" arrow or by moving the inflation slide "in" or to the left on older models. A similar control slide is used to fine tune deflation. In the manual mode, the inflation and deflation slides are much more responsive and cause greater changes in timing than they do in the automatic mode. In the manual mode, changes in heart rate >10 b/min require retiming. In the automatic mode, changes in heart rate are adjusted for automatically.

Observation of the balloon pressure waveform also yields useful information about IABP function (Figs 11.10–11.12).

Timing will be complicated by the presence of arrhythmias and large variations in heart rate. Recall that the timing of balloon deflation in systole

(a) *Early inflation*
Inflation of the IAB prior to aortic valve closure

Waveform characteristics:
Inflation of IAB prior to dicrotic notch
Diastolic augmentation encroaches onto
systole (may be unable to distinguish)

Physiologic effects:
Potential premature closure of aortic valve
Potential increase in LVEDV and LVEDP or PCWP
Increased left ventricular wall stress or afterload
Aortic regurgitation
Increased MV_{O_2} demand
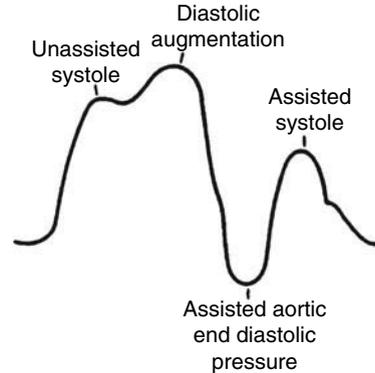
(b) *Late inflation*
Inflation of the IAB markedly after closure
of the aortic valve

Waveform characteristics:
Inflation of the IAB after the dicrotic notch
Absense of sharp V
Sub-optimal diastolic augmentation

Physiologic effects:
Sub-optimal coronary artery perfusion
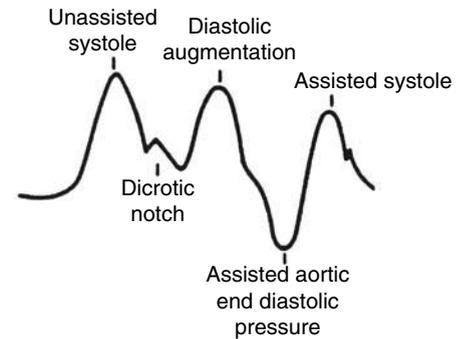
Fig. 11.6 Arterial waveforms resulting from (a) early balloon inflation and (b) from late balloon inflation. The physiologic consequences of these timing errors are summarized. IAB, intra-aortic balloon; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; PCWP, pulmonary capillary wedge pressure.

is determined by a preset interval from the previous QRS. As a result, premature beats or acute increases or decreases in heart rate may result in poor timing. Newer software allows better adjustment of timing to these events. Random rate changes as seen with atrial fibrillation are problematic as timing cannot be easily defined by the microprocessor. As a result, software has been developed that allows timing to be changed from predictive to R-wave triggered deflation. The trade off is less accurate balloon deflation timing in favor of preventing balloon inflation in systole.

At very high heart rates (>130–140 b/min), the IABP may be incapable of inflation and deflation rapid enough to provide proper timing. In this setting, using the balloon pump at a 1:2 ratio usually is necessary. At slow heart rates, premature balloon deflation will occur in pumps that have a preset limit on the duration of inflation.

Anticoagulation

Anticoagulation is necessary both to prevent thrombus formation on the balloon or catheter and in the cannulated peripheral vessel. An unfractionated heparin (UFH) infusion is used to maintain an activated clotting time (ACT) between 150 and 200 seconds or a partial thromboplastin time (PTT) between 60 and 80 seconds (1.5–2.0 times control). In the postoperative setting, initiation of heparin infusion may be delayed for 12–24 hours or until chest tube drainage is minimal. Alternative approaches include aspirin or low-molecular weight dextran in place of or in addition to UFH.

CardioWest TAH

The CardioWest TAH is the direct descendent of the Symbion (Jarvik) J7-70 TAH. Because implantation of the TAH requires excision of the native ventricles, this device is used only as a bridge to cardiac

(a) **Early deflation**

Premature deflation of the IAB
during the diastolic phase

Waveform characteristics:

Deflation of IAB is seen as a sharp
drop following diastolic augmentation
Suboptimal diastolic augmentation
Assisted aortic end diastolic pressure
may be equal to or less than the
unassisted aortic end diastolic pressure
Assisted systolic pressure may rise

Physiologic effects:

Sub-optimal coronary perfusion
Potential for retrograde coronary and
cartoid blood flow
Angina may occur as a result of retrograde
coronary blood flow
Sub-optimal afterload reduction
Increased MVo_2 demand
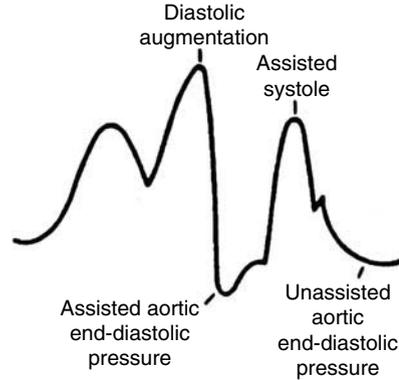
(b) **Late deflation**

Waveform characteristics:

Assisted aortic end-diastolic pressure may
be equal to the unassisted aortic end
diastolic pressure
Rate of rise of assisted systole is prolonged
Diastolic augmentation may appear widened

Physiologic effects:

Afterload reduction is essentially absent
Increased MVo_2 consumption due to the
left ventricle ejecting against a greater
resistance and a prolonged isovolumetric
contraction phase
IAB may impede left ventricular
ejection and increase the afterload
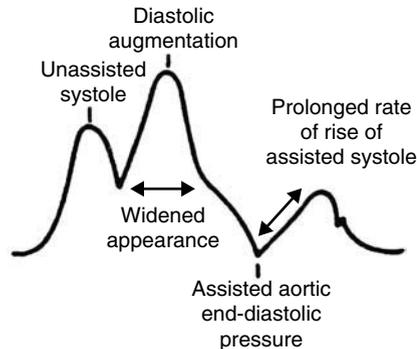
Fig. 11.7 Arterial waveforms resulting from (a) early balloon deflation and (b) from late balloon deflation. The physiologic consequences of these timing errors are summarized. IAB, intra-aortic balloon.

transplantation. Patients who are not suitable candidates for cardiac transplantation are not candidates for the TAH.

The CardioWest has a 70-mL stroke volume and can deliver cardiac outputs of 9.5 L/min. It is a pneumatically driven device and each ventricle has a pneumatic driveline. The drivelines are attached to a drive console on wheels. The drive console is large because it contains four air compressors, a primary and a backup for each ventricle (Fig. 11.13).

The prosthetic ventricles are rigid polyurethane, Dacron mesh shells divided into a blood and a pneumatic chamber by a four-layer polyurethane diaphragm. The diaphragm is flexible but non-compliant and each layer is separated by a small amount of graphite for lubrication. Unidirectional Medtronic-Hall tilting disc valves are located in the blood chamber. The ventricles are identical, except that the spacing between the inflow and outflow valves in the right ventricle is larger to allow for aortic outflow when the ventricles are attached together with a Velcro patch (Fig. 11.14).

The pneumatic chamber communicates with the pneumatic drive system via the pneumatic
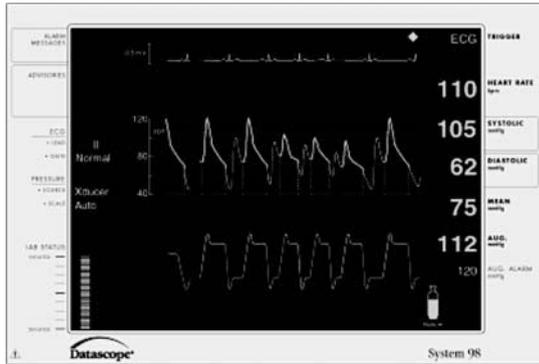
Fig. 11.8 Use of the "verify" feature highlights the period of balloon inflation in real time on the arterial waveform. A balloon pressure waveform is displayed on the third channel.

driveline. As pressurized air is introduced into the pneumatic chamber, the diaphragm moves such that the blood chamber becomes pressurized as well. When the pressure in the blood chamber exceeds the device filling pressure, the inflow valve will close. When pressure in the blood chamber exceeds aortic or pulmonary artery pressure, the outflow valve opens and ejection commences. These processes constitute the isovolumic and ejection phases of systole in the prosthetic ventricle (Fig. 11.15a,b).

At the end of systole, air is vented passively from the pneumatic chamber to the atmosphere and the pressure in the blood chamber falls. This constitutes isovolumic relaxation. When the pressure in the right atrium and left atrium exceeds the pressure in the blood chamber of the corresponding prosthetic ventricle, the inflow valve opens. The diaphragm is free to move in such a manner that virtually

Fig. 11.9 Intra-aortic balloon pump (IABP) control console showing the inflation and deflation "Earlier" and "Later" buttons to fine balloon timing. Earlier models had actual slides. IAB, intra-aortic balloon.

Peak inflation
(positive overshoot)

Plateau (full inflation of IAB)

IAB
inflation

IAB
deflation

Zero baseline

Return to zero baseline

Peak deflation
(negative
overshoot)
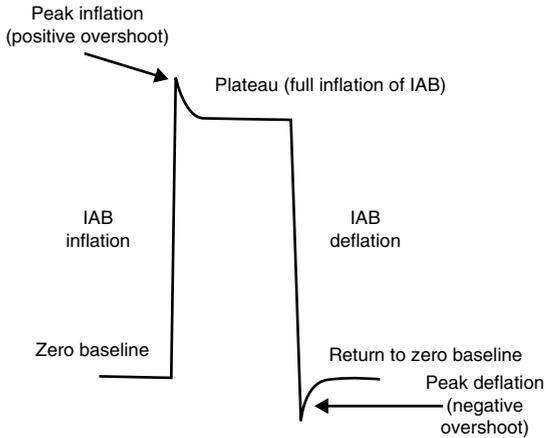
Fig. 11.10 A normal balloon pressure waveform. IAB, intra-aortic balloon.

Catheter kink
Rounded balloon pressure waveform. Loss of plateau resulting from kink or obstruction Of shuttle gas. This may be caused by a kink in catheter tubing, improper IAB catheter position, the sheath not pulled back to allow inflation of IAB, IAB too large for aorta, IAB is not fully unwrapped, or H_2O condensation in external tubing.
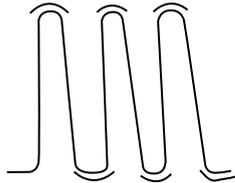
Fig. 11.11 A balloon pressure waveform from a kinked balloon catheter. IAB, IAB, intra-aortic balloon.

Gas loss
Leak in the closed system causing the balloon pressure waveform to fall *below* zero baseline. This may be due to a loose connection, leak in IAB catheter, H_2O condensation in external tubing, or a patient who is tachycardic and febrile which causes increase gas diffusion through the IAB membrane.
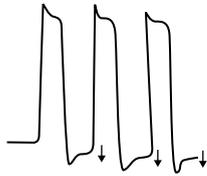
Fig. 11.12 A balloon pressure waveform from a balloon with a gas leak. IAB, intra-aortic balloon.

the entire volume of the prosthetic ventricle can fill with blood as all the air leaves the pneumatic chamber. This constitutes diastole in the prosthetic ventricle (see Fig. 11.15).

Insertion

Placement of the TAH requires CPB with aortic cross-clamping and bicaval cannulation. The device
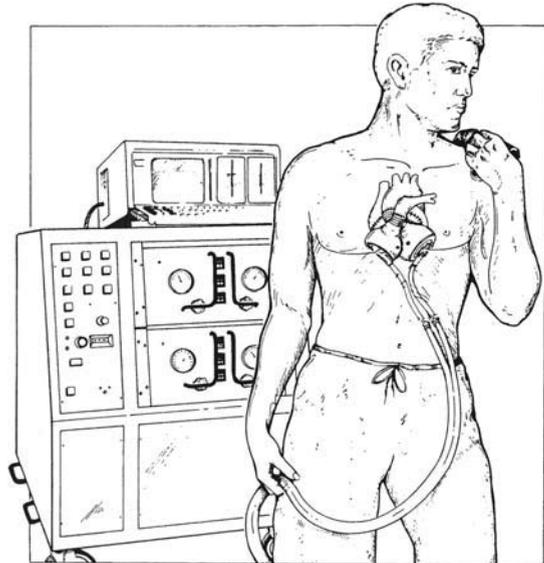
Fig. 11.13 Schematic of the CardioWest total artificial heart (TAH) showing the pneumatic drivelines, drive console, and cardiac output monitor and device unit (COMDU).
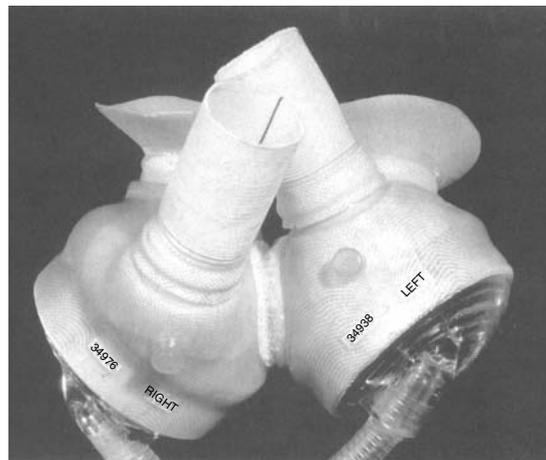
Fig. 11.14 Close-up of the CardioWest total artificial heart (TAH) prosthetic ventricles joined by a Velcro patch. The atrial inflow cuffs are shown in the background. The Dacron outflow grafts are shown in the foreground. The pneumatic drivelines are at the bottom of the picture.
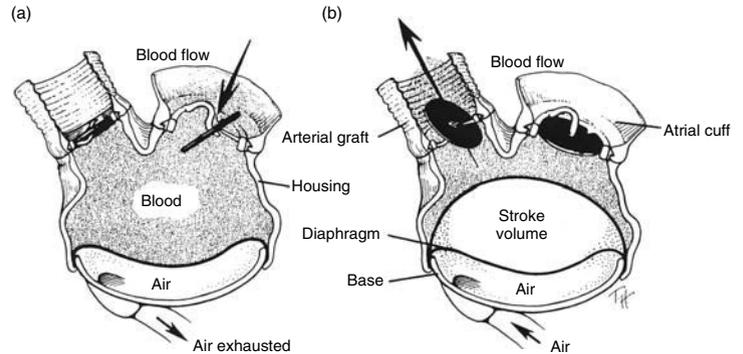
Fig. 11.15 Schematic of the CardioWest total artificial heart (TAH) in (a) end-diastole and (b) end-systole.

is placed in the patient's pericardial cavity with the RV and LV pneumatic drivelines exiting through the skin. The patient's native ventricles are excised, leaving a large cuff of right and left atrium. The inflow cuff of each ventricle is anastomosed to the appropriate atrium. End-to-end anastomoses are created between the outflow graft of the prosthetic ventricle and the appropriate great vessel. The TAH has been placed in patients weighing as little as 50 kg, but the best fit is in patients with weights in the 80-kg range (BSA>1.7 m^2) with large hearts. Closure of the chest after device implantation in patients who are too small can produce pulmonary and systemic venous obstruction. The inferior vena cava (IVC) and the left upper and left lower pulmonary veins are at particular risk of obstruction. Venous obstruction limits device output and is ultimately fatal.

Management of the TAH

The TAH is monitored with the cardiac output monitor and diagnostic unit (COMDU). COMDU allows analysis of air exhaust flow during diastole through transduction of a pneumotach. The flow is displayed as a curve with respect to time (Figs 11.16 & 11.17). Integration of this curve yields the volume of air displaced from the pneumatic chamber during diastole. When averaged over several beats, this is equal to cardiac output. The system allows computation of cardiac output for each ventricle. In addition, transduction of the driveline pressure allows device filling and emptying to be monitored over time, as illustrated in Figs 11.18 and 11.19.

The heart rate and percentage of systole are set by the operator and complete ejection is sought on
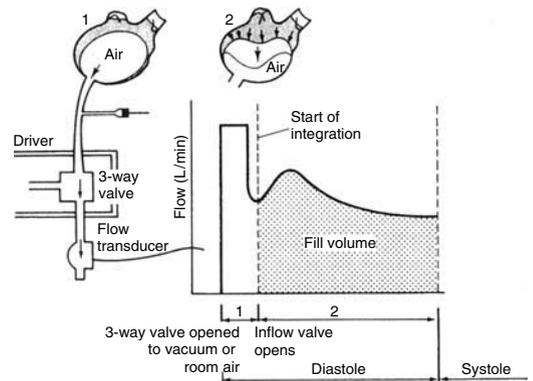
Fig. 11.16 Schematic of the CardioWest total artificial heart (TAH) pneumotach and the resulting fill-rate curve derived from air flow out of the device in diastole.

each cycle. The drive pressures are set just high enough to completely empty the ventricle. The occurrence of a full eject pattern is then seen on the air-pressure waveform. The device is not allowed to fill completely on each beat. This allows automatic adjustment for the difference in volumes pumped by the two ventricles; the LV pumps more than the RV because of the existence of bronchial flow. It also provides for preload reserve. As venous return increases (such as with patient position changes or exercise), stroke volume can increase up to the limit of the 70 mL.

The maximum end-diastolic volume of the prosthetic ventricle may be difficult to achieve when diastole is short (slow ejection rate, high percentage of systole) and filling pressure is low. The pneumatic drive system of the CardioWest TAH allows vacuum to be applied to the pneumatic chamber
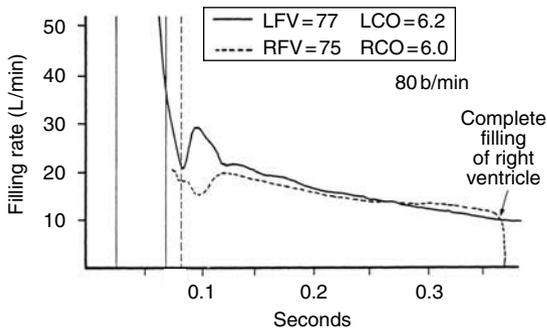
Fig. 11.17 Actual fill rate curve from a CardioWest total artificial heart (TAH) patient. There is complete filling of the right ventricle. Left fill volume (LFV) and right fill volume (RFV) are obtained by integrating the area under the left and right fill rate curves. The product of LFV and device rate (80 b/min) yields the left cardiac output (LCO). The product of RFV and device rate (80 b/min) yields the right cardiac output (RCO).
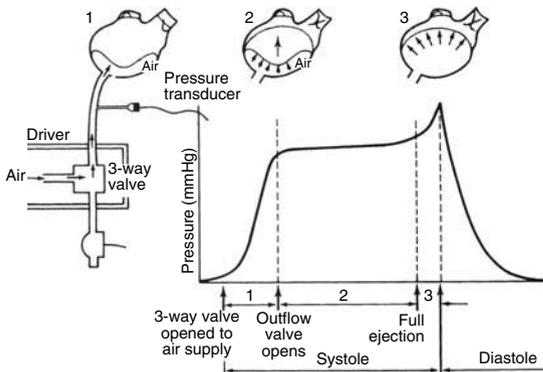
Fig. 11.18 Schematic of the CardioWest total artificial heart (TAH) pressure transducer and the resulting pressure waveform in systole and diastole.

during isovolumic relaxation and diastole to hasten the fall in blood chamber pressure and enhance diastolic filling. To reduce the likelihood of entraining air around anastomotic sites and introducing the risk of air embolism, vacuum generally is not applied until the patient's chest is closed. Normally, −25 to −50 mmHg of vacuum is applied.

Anticoagulation

Anticoagulation generally is started after protamine reversal of intraoperative UFH and chest
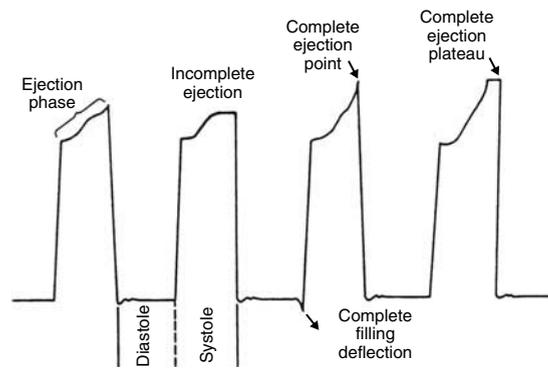
Fig. 11.19 Actual pressure waveform from a CardioWest total artificial heart (TAH) patient. The second waveform from the left indicates incomplete emptying of the prosthetic ventricle. This can be rectified either by afterload reduction or by increasing driveline pressure. The third waveform from the left indicates driveline pressure just high enough to ensure complete emptying of the prosthetic ventricle. The fourth waveform from the left also indicates complete emptying of the prosthetic ventricle. An excessive plateau is indicative of a driveline pressure that is higher than necessary. Complete filling of the prosthetic ventricle is indicated by the negative deflection in the pressure waveform during diastole. This is produced by the compliant diaphragm rebounding over the air exhaust port in the base of the prosthetic ventricle. In the instance illustrated here, complete filling of the prosthetic ventricle occurs at end-diastole following the second waveform.

tube drainage less than 100 mL/h for 3 consecutive hours. Low-molecular-weight dextran (dextran 40) infused at 25 mL/h and oral or nasogastric dipyridamole (75–100 mg 3–4 times/day) are started. When chest tube drainage is minimal and serous, the dextran is stopped and a continuous UFH infusion is initiated; the goal is to keep the PTT 1.5–2.0 times control. At 1–2 weeks postoperatively, the UFH is discontinued and coumadin is started; the goal is an international normalized ratio (INR) of 1.5–2.0. Some centers add aspirin (325–975 mg/day) as well.

Thoratec VAD system

The Thoratec VAD or Pierce–Donachy VAD (Figs 11.19 & 11.20) is an extracorporeal, pulsatile VAD that can be used in parallel with the RV and in parallel or in series with the LV. The device has
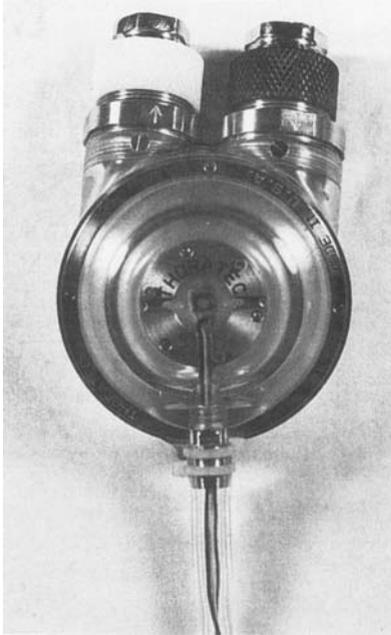
Fig. 11.20 Thoratec ventricular assist device (VAD). The inflow to the device is on the right and the outflow is on the left. The pneumatic drive and incorporated electric cable are at the bottom of the device.

an effective stroke volume of 65 mL and can deliver a cardiac output of 6.5 L/min. It is a pneumatically driven device and has a pneumatic driveline. The driveline is attached to a drive console on wheels. The drive console is large because it contains four air compressors, two for each driver, a primary and a backup. A Hall sensor built into the rigid case monitors movement of the pump diaphragm. A small magnet mounted on the diaphragm triggers the Hall sensor when the two come in contact. This information is transmitted to the console via an electrical cable and allows the control console to know when the blood chamber is full. In addition, transduction of the driveline pressure allows device filling and emptying to be monitored over time as described for the CardioWest TAH.

The prosthetic ventricle is a rigid polysulfone case divided into a blood and a pneumatic chamber by a flexible, noncompliant polyurethane diaphragm. Unidirectional Bjork–Shiley monostrut Derlin inflow and outflow valves are located in the blood chamber. The pneumatic chamber communicates with the pneumatic drive system via the pneumatic driveline. The same principles for systole and diastole as described for the CardioWest TAH apply.

Insertion

The device rests on the anterior abdominal wall. The device is extracorporeal thereby limiting patient mobility. The inflow and outflow conduits are tunneled into the thoracic cavity. For use as an RVAD, the inflow cannula is inserted in the right atrium and the Dacron outflow conduit is anastomosed end-to-side to the pulmonary artery. For use as a parallel LVAD, the inflow cannula is inserted in the left atrium and the Dacron outflow conduit is anastomosed end-to-side to the aorta. For use as a series LVAD, the inflow conduit is inserted in the LV apex and the Dacron outflow conduit is anastomosed end-to-side to the aorta.

Insertion requires a median sternotomy. In the postcardiotomy setting, CPB already is in use because failure to wean from CPB is the indication for placement of the device. Postcardiotomy support is generally accomplished with atrial cannulation rather than cannulation of the LV apex. This facilitates subsequent weaning of the device. For patients with a bridge to transplantation, CPB is necessary for LV apical cannulation.

Management of the Thoratec VAD

Four triggering modes are available: manual, asynchronous, fill-to-empty, and synchronous. In the asynchronous mode, the operator chooses the pumping rate and percentage of systole. In the fill-to-empty mode, the Hall sensor detects a full blood chamber and triggers ejection. The device typically is used in the fill-to-empty mode. In this mode, device output is calculated by the console as the product of stroke volume (65 mL) and device rate. Device output, as determined by the console, is accurate only when complete filling occurs.

The drive pressures are set approximately 100 mmHg higher than systolic pressure (230–250 mmHg for the LVAD and 140–160 mmHg for the RVAD). The percentage of systole is set to

equal one-half the device rate (percentage of systole at 60 b/min = 30%; percentage of systole at 80 b/min = 40%). These measures produce complete emptying with an ejection time of 300 ms. The occurrence of a full eject pattern is then seen on the air pressure waveform (see Fig. 11.19). Complete device filling also can be seen on the pressure waveform (see Fig. 11.19).

The maximum end-diastolic volume of the prosthetic ventricle may be difficult to achieve when diastole is short (slow ejection rate, high percentage of systole) and filling pressure is low. Vacuum can be applied to the pneumatic chamber during diastole as described for the CardioWest TAH.

Anticoagulation

Anticoagulation is as described for the CardioWest TAH.

Abiomed AB5000, Medos VAD, and Berlin Heart

These devices are very similar to the Thoratec VAD. They are extracorporeal, pulsatile VAD that can be used in parallel with the RV and in parallel or in series with the LV. The prosthetic ventricle is a rigid case divided into a blood and a pneumatic chamber by a flexible, noncompliant diaphragm. Unidirectional inflow and outflow valves are located in the blood chamber. The pneumatic chamber communicates with the pneumatic drive system via the pneumatic driveline. Vacuum can be applied to the pneumatic chamber during diastole. The indications for use and anticoagulation management of these devices are the same as the Thoratec VAD. The following important differences exist between these devices and the Thoratec VAD:

• Neither the Medos VAD nor Berlin Heart has a Hall sensor and therefore cannot operate autonomously in a fill-to-empty mode (fixed stroke volume, variable rate). They operate asynchronously in a fixed rate (set by the operator) variable stroke volume mode. They all allow control of percent systole, device rate, and right and left drive pressures. The Medos VAD and Berlin Heart are applicable to the pediatric population as they have pumps of variable blood chamber volume.

The Medos system has four sizes:

a Infant. RVAD 9 mL, LVAD 10 mL;
b Pediatric. RVAD 22.5 mL, LVAD 25 mL;
c Adult. RVAD 54 mL, LVAD 60 mL;
d Adult. RVAD 72 mL, LVAD 80 mL.

The Berlin Heart has six sizes; 10, 25, 30, 50, 60, and 80 mL for either RVAD or LVAD use.

• The Abiomed AB5000 has a 120 mL blood chamber with a 95 mL stroke volume and a 25 mL residual end-systolic volume. This device has a sensor that triggers ejection when full filling (cessation of diastolic gas flow) is detected. Because ejection pressure is fixed (420 mmHg for LVAD, 300 mmHg for RVAD) the ejection time for complete emptying increases as afterload increases. The device operates autonomously in a fill-to-empty mode (fixed stroke volume, variable rate). Increases in afterload and decreases in preload will decrease pump output as a result of decreased pump rate with a fixed stroke volume.

HeartMate IP and XVE left ventricular assist system

The HeartMate VAD (Figs 11.21–11.23a,b) is an implantable, pulsatile LVAD used in series with the native heart. The device has a stroke volume of 83 mL and is capable of providing 11 L/min of cardiac output. It is available in pneumatically (IP) and electromechanically (XVE) driven versions. The pneumatic version has an external driveline. The driveline is connected to the pneumatic drive system and system controller, which are on wheels. The pneumatic drive system and system controller are small because there are no air compressors. An electric motor is used to drive a diaphragm air pump. The electromechanically driven, vented electric version has a percutaneous electric and air vent line that attaches to a portable system controller and battery pack that can be worn by the patient. The sealed electric (SE) version under development is totally implantable and has power transduction occurring through transcutaneous induction coils with no percutaneous lines.

The outer shell of the device is titanium; the inner blood-contacting surface of the shell is lined with sintered titanium microspheres. A rigid pusher plate covered by a flexible, biocompatible, polyurethane
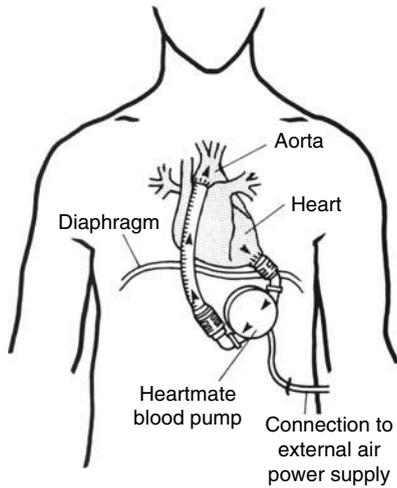
Fig. 11.21 Schematic of an implanted pneumatic HeartMate IP left ventricular assist system (LVAS). Cannulation of the left ventricle (LV) apex and the end-to-side anastomosis to the aorta are depicted. The percutaneous driveline is depicted exiting the abdominal wall.

Fig. 11.23 Schematic cross-section of the pneumatic HeartMate IP LVAS. Both diastole (a) and systole (b) are depicted.

Fig. 11.22 Photograph of the HeartMate IP left ventricular assist system (LVAS). Device inflow is on the left and outflow to the Dacron graft is on the left. The pneumatic driveline is being held.

diaphragm divides the prosthetic ventricle in two. On one side of the pusher plate is the blood chamber; on the other side is the pneumatic or electromechanical pumping mechanism. 25 mm porcine unidirectional inflow and outflow valves are placed in the blood chamber. The textured surfaces are intended to promote formation of a pseudointimal lining after contact with blood.

In the pneumatic version, a preset volume of air is delivered to the blood pump during each beat. Each stroke of the console air pump corresponds to one beat of the blood pump delivered via a piston that drives the pusher plate into the blood chamber. In the electromechanical version, the rotary motion of a low-speed torque motor is converted to the linear action of the pusher plate via helical cams. Energy is transferred to a copper coil, creating an intra-LVAD electromagnetic field to actuate rotor assembly rotation. One revolution of the motor is required for complete excursion of the pusher plate. In both instances, the excursion of the pusher plate reduces the volume of and pressurizes the blood chamber.

When the pressure in the blood chamber exceeds native LV pressure, the inflow valve closes. When the pressure in the blood chamber exceeds aortic pressure, the outflow valve opens and pumping commences. This represents the isovolumic and ejection phases of device systole.

When the pneumatic piston or the motor is switched off, air is vented to the atmosphere from

the pumping chamber and the pusher plate is free to move. When the pressure in the native left ventricle (the chamber filling the prosthetic ventricle) exceeds the pressure in the blood chamber, the inflow valve opens and diastolic filling commences. A Hall sensor in the pneumatic pump detects a full blood chamber and triggers ejection. This allows beat-to-beat stroke volume and device output data to be derived and displayed. In addition, a six-beat moving average of LVAD output also is displayed.

Insertion

The device can be implanted intraperitoneally or in a preperitoneal pocket in the left upper quandrant. The inflow and outflow conduits are tunneled into the thoracic cavity. The inflow conduit is inserted into the LV cavity via the LV apex and the Dacron outflow conduit is anastomosed end-to-side to the ascending aorta. Insertion requires a median sternotomy and use of CPB. A single cable containing the necessary electrical and pneumatic conduits to power, control and vent air from the device is tunneled through the abdominal wall.

Management of the HeartMate devices

The pneumatic device can function in the asynchronous, fill-to-empty, or synchronous modes. The device usually is operated in the fill-to-empty mode with pump ejection triggered by the transducer when the pump is full. LVAD ejection duration can be set by the operator from 200 to 450 ms to achieve complete emptying of the device without compromising device filling. Because minimal LVAD filling time is 50% of the selected LVAD ejection duration LVAD rate varies inversely with ejection duration. The LVAD rate varies from 89 b/min at an ejection duration of 450 ms to 140 b/min at an ejection duration of 200 ms. The control console monitors device output as the product of device stroke volume and rate on a beat-to-beat basis.

The vented electric version does not use a Hall sensor to measure diaphragm displacement. Ejection duration is constant and LVAD rate varies by automatic changes in LVAD filling time as determined by the pump controller. This is feasible because the device is relatively afterload-insensitive. As preload increases,

the pump controller detects a shorter interval between diaphragm and rotor interaction and subsequently shortens LVAD filling time.

Anticoagulation

Formation of the pseudointimal membrane obviates the need for full anticoagulation with heparin or coumadin. Aspirin (81 mg/day) and dipyridamole (75 mg three times/day) have been used as the sole long-term anticoagulants. Coumadin may be added for patients with pre-existing thrombus in the native heart.

Novacor LVAD

The Novacor LVAD (Figs 11.24–11.26a–c) is an implantable pulsatile LVAD used in series with the native heart. The device has a stroke volume of 70 mL and is capable of providing 10 L/min of cardiac output. It is the prototypical pulsatile electromechanical pump, configured to convert electrical energy to the mechanical energy necessary to eject blood from the prosthetic ventricular chamber. The newest version of the Novacor has a percutaneous electric conduit and air vent line, which attaches
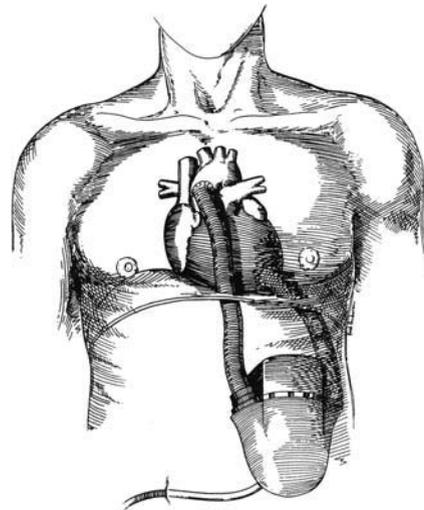
Fig. 11.24   Schematic of an implanted electromechanically driven Novacor left ventricular assist system (LVAS) device. Cannulation of the left ventricle (LV) apex and the end-to-side anastomosis to the aorta are depicted. The percutaneous driveline is depicted exiting the abdominal wall.
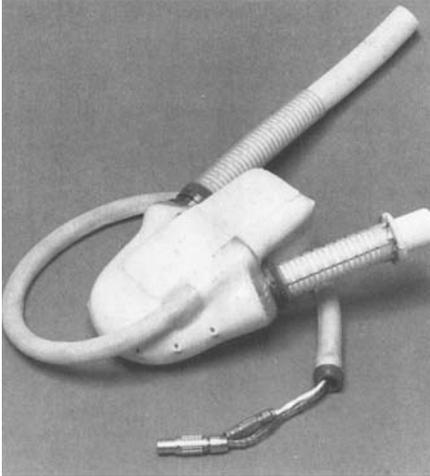
Fig. 11.25 Photograph of the Novacor left ventricular assist system (LVAS) device. Device inflow with the left ventricle (LV) apex cannula in place is on the right and device outflow to the Dacron graft is on the left. The driveline with enclosed electrical cables is seen looped under the pump.

to a portable microprocessor/system controller and battery pack that can be worn by the patient.

This prosthetic ventricle consists of a biocompatible sac bonded to symmetrically opposed pusher plates housed in a lightweight shell. 21 mm Carpentier–Edwards porcine unidirectional inflow and outflow valves are placed in the blood chamber. A solenoid energy converter is used to transfer electrical energy to mechanical energy via preloaded beam springs, which then drive the pusher plates. When the solenoid is open, energy is stored in the beam springs, the pusher plates and blood sac are free to expand, and diastolic filling of the prosthetic ventricle via the left ventricle takes place. When the solenoid is closed, the energy stored in the beam springs is released. The resulting compression of the blood sac between the pusher plates creates the pressure necessary for the isovolumic and ejection phases of systole. Displacement transducers within the solenoid energy converter monitor pusher-plate position. This allows beat-to-beat fill volume, residual volume, and stroke volume to be determined. This information, in combination with device rate, allows device output data to be derived and displayed.

Insertion
Device insertion is as described for the HeartMate IP and XVE left ventricular assist system (LVAS).

Management of the Novacor
The system was originally designed to operate in the fill rate trigger mode. In the fill rate trigger mode, the rate at which the pump fills is used to trigger ejection. At the start of device filling, the pump fill rate is high. Toward the end of device filling, the pump fill rate falls. By adjusting the *end of fill threshold* setting, the percentage by which the fill rate must fall to trigger device ejection can be set. In actual clinical practice, filling of the Novacor occurs during LV diastole in some beats and during LV systole in other beats while in the fill rate trigger mode. This occurs as the result of changes in preload and heart rate with changes in patient activity level. Despite this, the aortic valve rarely opens. Patients who have been discharged from the hospital with the Novacor device have the *end of fill threshold* set to 100%. This allows the device to function as if in a fill-to-empty mode. This allows reliable pump function with no operator intervention. The control console displays beat-to-beat LVAD output as the product of LVAD stroke volume and rate. Beat-to-beat visualization of the fill-rate curve also is available.

Anticoagulation
Anticoagulation is as described for the TAH.

Abiomed BVS 5000
The Abiomed BVS 5000 (Fig. 11.27) is an extracorporeal pulsatile VAD used in parallel with the native ventricles. The device has an effective stroke volume of 80 mL and a cardiac output of 5 L/min. It is a pneumatically driven system and has a pneumatic driveline attached to a computerized control console on wheels.

The device consists of atrial and ventricular chambers arranged vertically in a rigid polycarbonate housing (Fig. 11.28). The atrial and ventricular chambers are polyurethane bladders. The ventricular chamber contains polyurethane unidirectional tri-leaflet inflow and outflow valves.

The atrial bladder fills continuously by gravity from the patient's native atrium. The ventricular
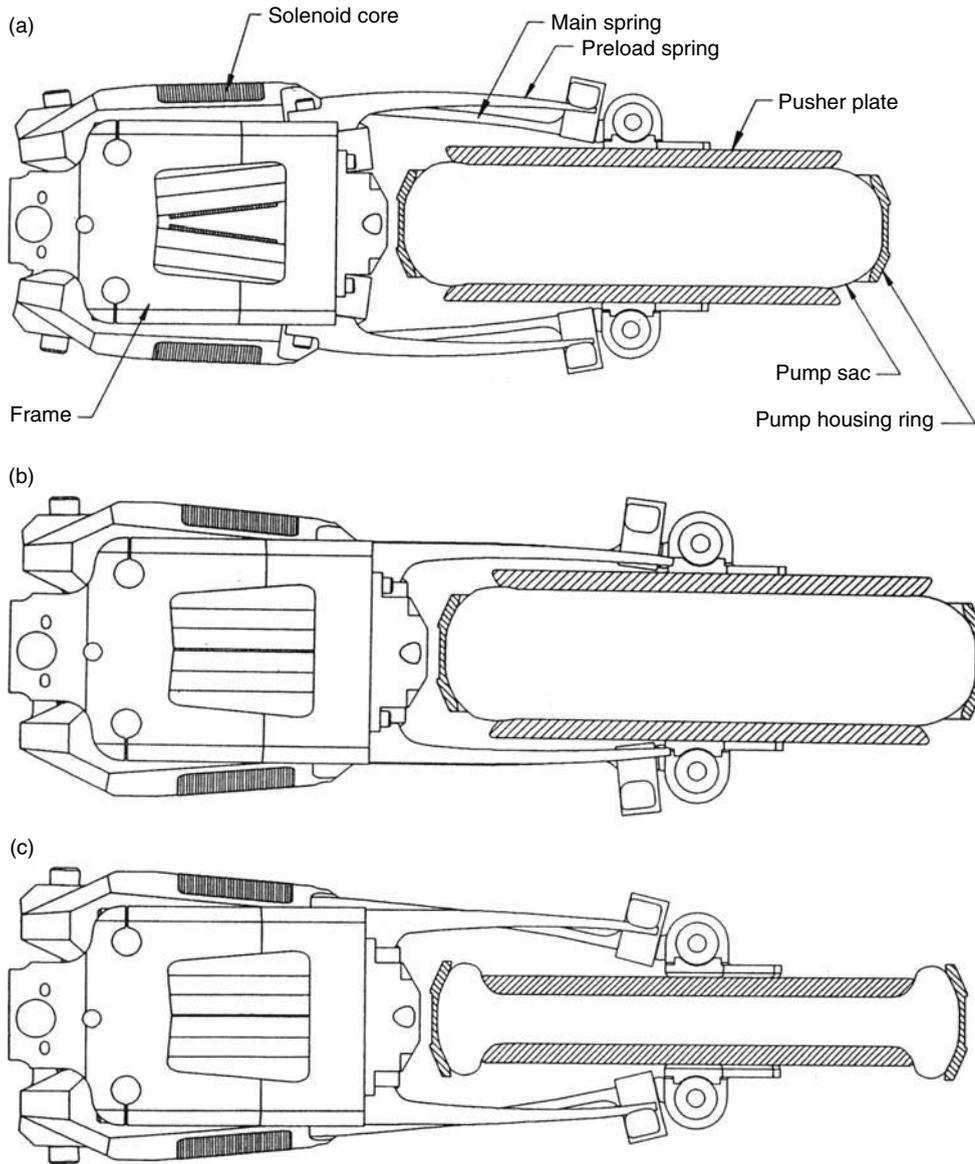
Fig. 11.26   Schematic cross-section of the Novacor left ventricular assist system (LVAS). (a) The pump is filled, the solenoid is opened. The preload spring limits expansion of the pump sac to 70 mL. (b) The solenoid is closed and magnetically latched. This constitutes isovolumic contraction. (c) End of ejection with complete pump emptying.

bladder is pressurized by introduction of pressurized air into rigid air chamber around the bladder. When the pressure in the air chamber is atmospheric, atrial bladder pressure exceeds ventricular bladder pressure, the inflow valve opens, and the ventricular bladder fills with blood. This constitutes diastole in the device. When the ventricular bladder is full, the air chamber is pressurized. When ventricular bladder pressure exceeds atrial bladder pressure, the inflow valve closes. When pressure in the ventricular bladder exceeds aortic or pulmonary artery pressure, the outflow valve opens
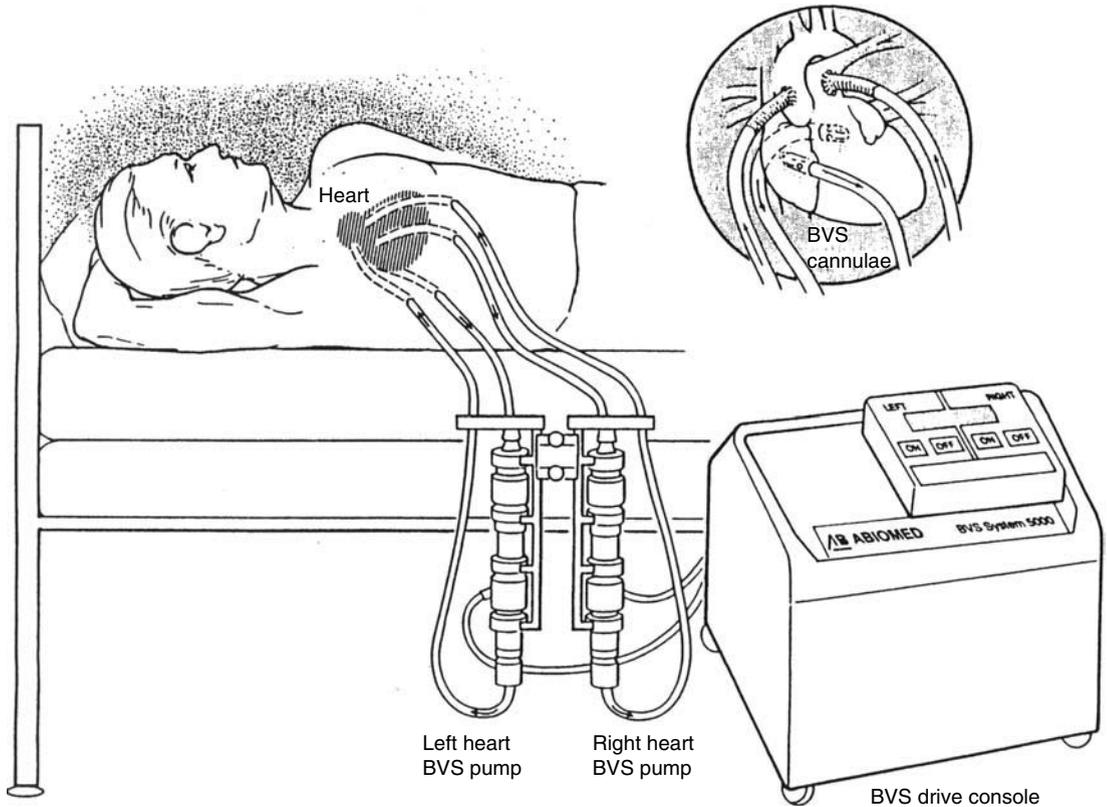
Fig. 11.27 Schematic of an implanted pneumatically driven Abiomed BVS5000 used as a biventricular assist device (BiVAD). Cannulation of the left atrium (LA) and the end-to-side anastomosis to the aorta are depicted, as are cannulation of the right atrium (RA) and the end-to-side anastomosis to the main pulmonary artery. The percutaneous drivelines are depicted exiting the abdominal wall. The device is seen to be located below the level of the patient's heart.

and ejection commences. These processes constitute the isovolumic and ejection phases of systole in the prosthetic ventricle (Fig. 11.29a,b).

Insertion
The device is mounted on IV poles below the level of the patient's heart. Polyvinyl chloride (PVC) tubing brought through the chest wall connects the inflow and outflow cannulas to the device. For use as an RVAD, the inflow cannula is inserted in the right atrium and the Dacron outflow conduit is anastomosed end-to-side to the pulmonary artery. For use as an LVAD, the inflow cannula is inserted in the left atrium and the Dacron outflow conduit is anastomosed end-to-side to the aorta. Insertion requires a median sternotomy. Although CPB is

not absolutely necessary for insertion of the device, it is commonly used. In the postcardiotomy setting, CPB already is in use because failure to wean from CPB is the indication for placement of the device. When intermediate- to long-term support is needed the inflow and outflow cannula of the BVS5000 can be used with the Abiomed AB5000 system so that a device "device swap" can take place.

Management of the Abiomed BVS 5000
The pneumatic control console monitors pump function by analysis of air return from the pneumatic driveline. Pump rate and diastolic/systolic intervals are determined automatically and the pump functions in the fill-to-empty mode. Device

Fig. 11.28 Photograph of the Abiomed BVS5000 device. Device inflow is at the top, outflow is at the bottom. The pneumatic driveline is seen entering the bottom third of the device on the left.

Fig. 11.29 Schematic cross-section of the Abiomed BVS5000 device. (a) End-systole and (b) end-diastole are depicted.

output is monitored and displaced by the control console. A unique feature of this device is that the system is operator-independent. Therefore, engineering and perfusion staff is not necessary during operation of the device.

When the device is used as a BiVAD, differential recovery of the RV and LV function requires careful management due to the limitation of 5 L/min on device output. As RV function recovers, total pulmonary output will be a combination of RVAD output and native RV output. If at the same time there is no LV recovery, systemic output will be determined by LVAD output. If the combined pulmonary output exceeds the maximal output of the LVAD (5 L/min), then LV, LA, and pulmonary venous congestion will occur. The solution is to reduce RVAD output so that pulmonary and systemic outputs are matched. A similar scenario can be described for LV recovery in the absence of RV recovery.

Anticoagulation

Anticoagulation is maintained with an UFH infusion to keep the ACT at 150–200 seconds.

Centrifugal pumps

Centrifugal pumps are extracorporeal, nonpulsatile pumps used in parallel with the native ventricles (Fig. 11.30). The BioMedicus pump can be used as both a RVAD and LVAD. This device is capable of providing outputs of 2.0–6.0 L/min. The Tandem-Heart is intended for LVAD use. It is small with a 7 mL prime volume and can provide flows of 3.5–4.0 L/min.

Centrifugal pumps use a constrained vortex to impart kinetic energy to fluid in a rotating head. The rotating head consists of a series of concentrically arranged cones or fins contained within a rigid plastic shell (see Fig. 10.3). Rotary motion is imparted to the cones or fins by a drive console. Coupling of the drive console to the pump head is accomplished with magnets in the base of the pump head. Rotation of the cones or fins creates a vortex that is constrained by the rigid plastic housing. This creates lower pressure at the center of the pump than at the periphery. The pressure gradient draws blood into
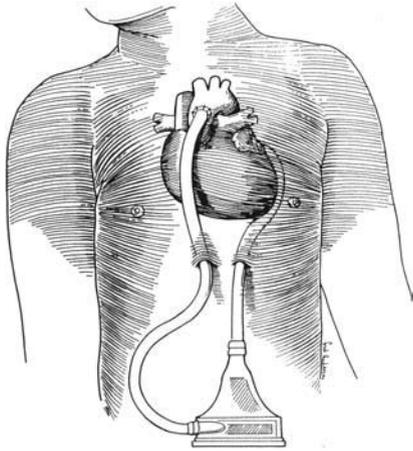
Fig. 11.30 Schematic of a centrifugal pump used for left ventricular support. Cannulation of the left atrium and the aorta are depicted. The centrifugal pump drive console is not shown.

the center of the pump and imparts pressure to the blood as it leaves the pump at the periphery.

This arrangement produces a pump that is very afterload and preload dependent. As a result, pump output at a given revolutions/min can vary greatly. At a given revolutions/min increasing outlet pressure or decreasing preload will reduce pump output. Outlet pressure is a combination of the pressure drop across the outlet cannula and the resistance of the recipient vascular bed. For example, at an outlet pressure of 200 mmHg, a Bio-Medicus pump can generate 4 L/min of flow at 200 revolutions/min. Increasing outlet pressure to 400 mmHg requires 3000 revolutions/min to maintain 4 L/min of flow.

At the extremes, clamping the inflow or outflow line will result in no pump output despite the fact that the pump head continues to rotate. Because pump output decreases as afterload increases, line pressure in a centrifugal pump can never reach the point at which connections will come apart or the pumping mechanism will fail. This is a major advantage of centrifugal pumps over occlusive roller pumps. Because pump output does not vary directly with revolutions/min, monitoring centrifugal pump output requires use of a Doppler or electromagnetic flow probe on the outflow line.

Another advantage of centrifugal pumps over occlusive roller pumps is the reduced potential to pump air into the circulation. Inadvertently introduced air tends to remain in the low-pressure center of the pump and is not introduced into the circulation.

Insertion

The BioMedicus device is mounted on the drive console. Polyvinyl chloride (PVC) tubing brought through the chest wall or sternotomy connects the inflow and outflow cannulas to the device. Standard CPB arterial and venous cannulas are used. For use as an RVAD, the inflow cannula is inserted in the right atrium and the outflow cannula is inserted into the main pulmonary artery. For use as an LVAD, the inflow cannula is inserted in the left atrium and the outflow cannula is inserted into the ascending aorta. Insertion is accomplished via a median sternotomy. Due to the high incidence of postoperative bleeding, impairment of venous drainage into the device and pulmonary dysfunction in the postcardiotomy setting the sternal edges often are left unopposed and an occlusive dressing is placed over the sternotomy. The chest is then closed after the device has been removed in the operating room.

Although CPB is not absolutely necessary for insertion of the device, it is commonly used. In the postcardiotomy setting, CPB is already in use as failure to wean from CPB is the indication for placement of the device.

The TandemHeart device and the small drive console can lie on the patient's leg. The inflow and outflow to the device are placed percutaneously. The femoral vein is cannulated and the inflow cannula is directed across the atrial septum into the LA under direct vision in the operating room (OR) or with use of fluoroscopy or TEE in the catheterization laboratory. The femoral artery is used for device outflow. The device provides parallel LVAD support.

Management of the centrifugal pump

The centrifugal pump requires the presence of a trained individual. Flow is adjusted to meet metabolic demands. If flow does not increase with increases in pump revolutions/min, reduced preload or elevated afterload should be treated. Elevated MAP should be treated by reducing systemic

vascular resistance (SVR) with a vasodilator. Elevated pulmonary artery pressure (PAP) may require treatment with a pulmonary vasodilator. A pulmonary artery catheter will allow low assessment of both RVAD preload (central venous pressure (CVP)) and LVAD preload (pulmonary artery occlusion pressure (PAOP)).

Centrifugal pumps are prone to thrombus formation in the pump head due to heat produced in the bearing housing during rotation. As a result, some manufacturers recommend changing the pump head every 24–48 hours. In addition, pump flows lower than 2 L/min are associated with pump head and cannula thrombus formation.

Anticoagulation

A UFH infusion is used to maintain an ACT between 100 and 200 seconds or a PTT between 60 and 80 seconds (1.5–2.0 times control). The pump head must be monitored for thrombus formation and must be changed if there is evidence of thrombus.

Axial pumps

Axial pumps are intracorporeal pumps used in series with the left ventricle. These compact pumps employ an impeller mechanism that is the only moving part. At the proximal end of the pump stationary airfoil-shaped vanes may be used to straighten blood flow prior to entry into an impeller. The impeller then imparts radial velocity (kinetic energy) to the blood as it draws blood into the pump. At the distal end of the pump there is a set of stationary diffuser (stator) vanes serving to impart axial velocity by straightening flow. This converts kinetic energy to static pressure (potential energy) as blood leaves the pump.

These pumps are small; about the size of a C or D cell battery. They have small priming volumes but operate at very high rotational speeds (8000–10 000 revolutions/min) allowing them to generate 6–8 L/min of nonpulsatile flow (Figs 11.31 & 11.32). There are three axial pumps available for clinical use:

Jarvik 2000

The two-blade impeller is a neodymium-iron-boron magnet mounted on two ceramic bearings mounted
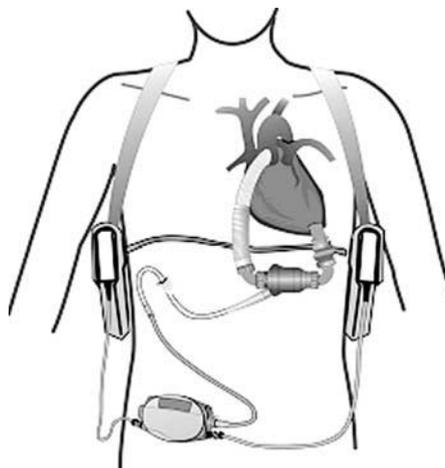
Fig. 11.31 Schematic of an implanted electromechanically driven HeartMate II axial flow left ventricular assist system (LVAS). Cannulation of the left ventricle (LV) apex and the end-to-side anastomosis to the aorta are depicted. The percutaneous driveline is depicted exiting the abdominal wall.
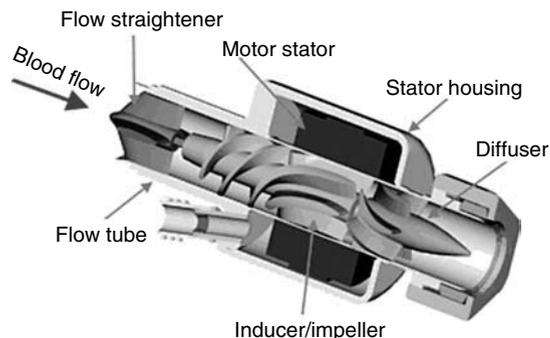
Fig. 11.32 Schematic cross-section of the MicroMed DeBakey ventricular assist device (VAD) axial pump. Blood enters through the flow straightener drawn in by the combination inducer (helical blades) and impeller. Radial flow is converted to axial flow by the stationary blades of the diffuser prior to blood exiting the pump. The electric motor is depicted as well. The percutaneous driveline is depicted at bottom left.

in a titanium housing. Outflow stator blades direct flow into a 16 mm outflow graft. A brushless DC current motor within the titanium housing creates the electromagnetic force to rotate the impeller. The motor is driven via a percutaneous power cable connected to a system controller and 12-volt battery

pack system that can be worn by the patient on a belt. The controller allows manual adjustment of the impeller revolutions/min. Infant and child versions of the Jarvik 2000 are currently under development.

MicroMed (DeBakey) VAD

This pump has a 25 mL prime volume including the titanium inflow cannula. Stationary airfoil-shaped vanes are used to straighten blood flow prior to entry into the inducer/impeller (a combination of helically and axially oriented blades). The inducer/impeller has six blades with eight magnets sealed in each blade. Outflow diffuser (stator) blades direct flow into the outflow graft. A brushless DC current motor within the titanium housing creates the electromagnetic force necessary to rotate the impeller. The motor is driven via a percutaneous power cable connected to a system controller and 12-volt battery pack system that can be worn by the patient. An ultrasonic flow probe on the outflow cannula allows continuous measurement and display of pump output on the laptop driven Clinical Data Acquisition Unit. Changes in pump revolutions/min are made using this unit as well. The cable for the flow probe is bundled in with the percutaneous power cable. A pediatric version of the MicroMed VAD; the DeBakey VAD® Child now has FDA humanitarian device exemption (HDE) status. This device is intended for patients with a BSA between $0.7\,m^2$ and $1.5\,m^2$ and thus suitable for children between approximately 5–16 years of age.

HeartMate II

Three stationary airfoil-shaped vanes are used to straighten blood flow prior to entry into a three-vane impeller that is suspended in the sintered titanium pump housing on two composite ball and cup bearings. Outflow diffuser (stator) blades direct flow into the outflow graft. A magnet is incorporated into the impeller rotor and a DC current brushless electric motor is used to generate the electromagnetic current necessary to rotate the impeller. The motor is driven via a percutaneous power cable connected to a system controller and 12-volt battery pack system that can be worn by the patient.

Insertion

These devices are implanted in a preperitoneal pocket in the left upper quadrant. The inflow and outflow conduits are tunneled into the thoracic cavity. Insertion requires a median sternotomy (MicroMed and HeartMate II) or left thoracotomy (Jarvik 2000) and use of CPB. The inflow conduit of the MicroMed and HeartMate II devices is inserted into the LV cavity via the LV apex and the Dacron outflow conduit is anastomosed end-to-side to the ascending aorta. The Jarvik 2000 device is implanted directly into the LV without an inflow conduit and the Dacron outflow conduit is anastomosed end-to-side to the proximal descending aorta. The power cable of all three devices is tunneled through the abdominal wall.

Management of axial pumps

These devices are remarkably simple to operate with pump output determined by revolutions/min and ΔP (aortic pressure–LV pressure). Increasing pump revolutions/min will increase pump flow until the negative inflow pressure is low enough to cause suction and collapse of the LV around the inflow portion of the pump. In addition, for a given revolutions/min pump flow is inversely proportional to ΔP. In other words, the lower the ΔP the higher the pump flow at a given revolutions/min. As a result, these pumps are highly afterload and preload sensitive. ΔP is most effectively reduced by lowering aortic pressure (afterload reduction) or by increasing LV pressure (preload augmentation, LV contraction). In fact, in the presence of increased LV contractility semi-pulsatile flow may occur both as the result of aortic valve opening and as the result of cyclic increases in pump output with the ΔP reduction that accompanies LV contraction. Most centers program axial pumps at a revolutions/min that allows the native aortic valve to open at least several times per minute as a method of preventing stasis and potential thrombus formation on the aortic valve.

Anticoagulation

Anticoagulation is as described for the TAH.

Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation (ECMO) circuits (Fig. 11.33) are a modification of the CPB circuit described in detail in Chapter 10. Specifically, ECMO circuits differ from the typical CPB circuit in the following aspects:

• A silicone membrane oxygenator is used in place of a microporous membrane oxygenator. Silicone membranes remain functional for days as compared to hours for microporous membranes.

• No cardiotomy suction is used in an ECMO circuit.

• A closed venous reservoir (bladder) system is used in conjunction with a servomechanism. The servomechanism functions to control pump flow relative to bladder pressure.

• ECMO circuits can be used for venovenous (VV) or venoarterial (VA) support. VA support is similar to CPB and is used for mechanical circulatory support. VV support is used for patients with severe pulmonary dysfunction in the setting of preserved myocardial function. Venous blood is drained from a proximal location in the central venous circulation
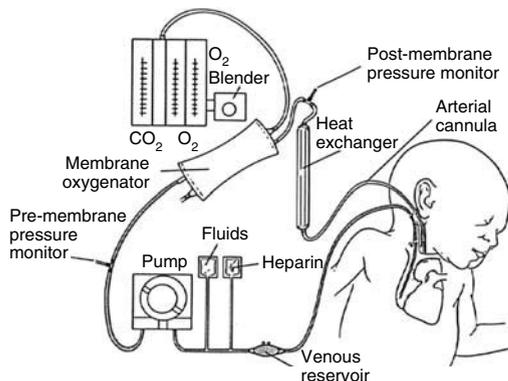
Fig. 11.33 Schematic of a venoarterial (VA) extracorporeal membrane oxygenator (ECMO) circuit. Peripheral cannulation via the right internal carotid artery and right internal jugular vein is depicted. A nonocclusive roller pump is depicted; some circuits use a centrifugal pump in this same location. Unlike cardiopulmonary bypass (CPB), rapid cooling and rewarming is not necessary and as a result the heat exchange unit can be located distal to the silicone gas exchange membrane. The servomechanism linking the closed venous reservoir and the pump is not shown. Drugs and fluids in limited quantities can be added to the circuit in the locations depicted.

(superior vena cava (SVC) or high right atrium). After gas and heat exchange take place in the ECMO circuit this blood is returned to a more distal site in the central venous circulation (mid right atrium) to be pumped by the patient's heart.

VA ECMO is particularly useful in the pediatric population and is commonly used for post-cardiotomy support and as a bridge to transplant. ECMO can be initiated with peripheral vascular cannulation, provides biventricular support, and can provide adequate systemic oxygen delivery in the presence of pulmonary hypertension and intra-cardiac right to left shunting. In addition, many pediatric patients are too small for placement of currently available VAD. Rapid initiation of ECMO (rapid response ECMO) is used in both the adult and pediatric population to facilitate resuscitation following acute hemodynamic decompensation or cardiac arrest. In adults and older children, an initial period of resuscitation with ECMO may provide sufficient cardiopulmonary stabilization and reversal of end-organ injury to permit VAD insertion.

Insertion

ECMO can be initiated with either peripheral or central cannulation. VA ECMO in pediatric patients is commonly initiated by surgical exposure of the right internal carotid artery and right internal jugular vein. In adults and older children peripheral cannulation of the femoral artery and vein can be utilized. In the postcardiotomy setting cannulation is generally via the right atrium and aorta.

Management of ECMO

VA ECMO is managed much like CPB. When venous drainage is adequate the heart will be completely empty, no ejection will occur, and ventilation will be unnecessary. More commonly ECMO is conducted in a manner similar to partial CPB. There will be incomplete capture of all venous drainage, some systemic ventricular ejection will occur, and some minute ventilation will be necessary. Since there is a small (30 mL) closed venous reservoir the amount of blood pumped to the patient can only exceed the amount of blood returning to the venous reservoir for a matter of seconds. When this occurs the venous bladder begins to collapse and the

servomechanism slows the pump rate appropriately to equalize drainage and pump output. Generally, pumps flows of 100–150 mL/kg/min are needed in pediatric patients in the absence of significant ventricular ejection.

Anticoagulation

An UFH infusion is used to maintain an ACT of 180–250 seconds.

Anesthetic considerations

The cardiac anesthesiologist is likely to encounter patients with a circulatory assist device or a TAH in the following circumstances:
- Heart transplantation candidates who require placement of a VAD or a TAH as a bridge to transplantation to prevent deterioration in their medical condition.
- Heart transplantation candidates with a VAD or TAH in place who present for cardiac transplantation.
- Postcardiotomy shock patients who require a circulatory assist device or a TAH to allow separation from CPB.
- Postcardiotomy shock patients who have had their circulatory assist device weaned and who require operative explanation of the device.
- Patients with end-stage cardiomyopathies who undergo permanent implantation of a VAD.

Device insertion

Induction and maintenance of anesthesia for insertion of a VAD or TAH in a patient with an end-stage cardiomyopathy should be managed as described for patients undergoing heart transplantation. Implantation of VAD and the TAH requires a median sternotomy or thoractomy and CPB. In addition, placement of the TAH requires bicaval venous cannulation and aortic cross-clamping. Anastomosis of the outflow graft to the side of the ascending or descending aorta can often be performed off CPB with application of a partially occluding or side-biting aortic clamp. Application of this clamp may increase impedance to LV ejection and cause LV afterload mismatch with subsequent LV distention. If this technique is chosen, careful monitoring of LV function with TEE is essential. Placement of

the inflow conduit into the apex of the LV is generally performed on CPB although off-CPB techniques have been described. Some surgeons place the inflow conduit during induced ventricular fibrillation, whereas others apply an aortic cross-clamp and administer cardioplegia. Centrifugal pumps are used almost exclusively for postcardiotomy support. As a result, they are placed while on CPB as well.

Many of the patients presenting for placement of a mechanical assist are anti-coagulated with coumadin because of their dilated cardiomyopathy. These patients usually require replacement of coagulation factors, particularly when there is dilution of factors on CPB as they already have reduced factor levels. When the PT is markedly elevated, adding fresh frozen plasma to the pump prime in place of a crystalloid solution is warranted. An additional risk for blood loss is the fact that up to 50% of bridge-to-transplant patients have had previous cardiac surgeries.

Limiting transfusion of homologous blood products helps reduce the risk of postoperative pulmonary dysfunction, which can seriously impair RV function. In addition, avoidance of homologous blood products limits patient exposure to antibodies, which may make subsequent typing for heart transplantation difficult. Leukocyte filters should be used when administering homologous blood products. Cytomegalovirus (CMV) negative blood should be used in CMV-negative patients.

Use of aprotinin has been shown to reduce blood loss and transfusion requirements for packed cells and components in patients receiving a LVAD. Aprotinin is discussed in detail in Chapter 10. The incidence of both mild and severe allergic reactions on re-exposure in adults and children is similar and is approximately 2.8%. Nine percent of the re-exposure reactions are fatal. The likelihood of a reaction on re-exposure is increased if the re-exposure occurs within 6 months of the initial exposure with 95% of all reported re-exposure events occurring within 6 months of initial exposure. When aprotinin is used at the time of device insertion and again at transplantation, re-exposure within this interval is not uncommon.

The existence of a patent foramen ovale (PFO) or any site for intracardiac shunting must be excluded

before placement of any mechanical assist device that is capable of reducing LA pressure below RA pressure. Decompression of the LV and reduction in LA pressure below RA pressure will produce right-to-left intracardiac shunting and hypoxemia. This is particularly likely in the setting in which RA pressure is elevated, such as when there is concomitant RV dysfunction or elevated pulmonary artery (PAP pressure. In addition, it introduces the possibility of producing systemic air emboli from bubbles introduced into the RA by IV lines. All of the devices described in this chapter except the IABP, are capable of producing such shunting. Either surgical examination or TEE can be used to determine whether a PFO exists. Two-dimensional echocardiographic views of the intra-atrial septum in conjunction with color flow imaging may be sufficient to detect a PFO. However, because most patients receiving mechanical assist devices have elevated LA pressures, the presence of a PFO by TEE should not be ruled out without the use of provocative measures to reduce left atrial pressure (LAP) below right atrial pressure (RAP). Release of a Valsalva maneuver (actually release of sustained positive inspiratory pressure) will transiently reduce LAP below RAP. When this is used in conjunction with agitated saline contrast, TEE imaging of the RA, LA, and intra-atrial septum detection of a PFO is reliable.

TEE should be used to assess the ascending aorta and thoracic aorta for the presence of atheromatous disease and calcifications that will influence the site of aortic outflow cannula placement. Epiaortic scanning may be useful in guiding placement of the device outflow conduit on the ascending aorta. TEE should be used to assess for the presence of intracardiac thrombi.

Comprehensive assessment of all four valves by TEE is necessary prior to VAD placement:

- *Aortic valve*. Placement of an LVAD is contraindicated in the presence of a mechanical aortic valve or significant aortic insufficiency. Thrombus formation on the mechanical aortic valve can result from the absent or minimal aortic valve opening that occurs when the LVAD is functioning normally. Aortic valve insufficiency will not permit effective (decompression of LA and LV) or efficient (high cardiac output) LVAD functioning because a large

portion of LVAD ejection will be regurgitated into the native LV. The problem worsens as LVAD output increases. In these circumstances, the aortic valve can either be replaced with a bioprosthesis or more uncommonly removed and pericardial patch closure of the aortic annulus performed. Aortic stenosis is not a contraindication to LVAD placement.

- *Pulmonary valve*. RVAD placement is contraindicated in the setting of pulmonary valve insufficiency as it will not permit effective (decompression of RA and RV) or efficient (high cardiac output) RVAD functioning because a large portion of RVAD ejection will be regurgitated into the native RV.

- *Mitral valve*. The presence of significant mitral stenosis is a contraindication to placement of an LVAD in series with the LV. Significant mitral stenosis will impede inflow into the LV and subsequently into the inflow cannula of the LVAD and will not allow decompression of the LA. Mitral valve repair or bioprosthetic replacement will be necessary. With parallel LVAD placement (LA and aortic cannulation) mitral stenosis is not a contraindication.

- *Tricuspid valve*. Assessment of the tricuspid valve prior to LVAD placement. The etiology of any pre-existing tricuspid regurgitation should be carefully delineated, as regurgitation is likely to be worsened by LVAD placement as described below.

Following device placement, meticulous deairing of the native cardiac chambers and the assist device is necessary to prevent systemic air emboli. The patient usually is kept in steep Trendelenberg position until deairing is completed. TEE is useful in detecting intracardiac air and in guiding the de-airing process.

Management of patients with devices in place

Post-device implantation management is tailored to the patient, the specific device, and the setting. The following issues must be considered.

Function of the nonassisted ventricle

Proper functioning of an LVAD requires an RV that functions well enough to match the combined output of the LV and the LVAD. An RV that is capable of delivering only 3 L/min to the

pulmonary circulation and LA will severely compromise optimal functioning of an LVAD that can deliver 6 L/min. Because many patients requiring LVAD implantation have concomitant RV dysfunction, there may be a need for inotropic/vasodilator or mechanical support (RVAD) of the RV after LVAD implantation.

Approximately 10% of patients implanted with an LVAD require placement of an RVAD for RV failure. Preoperative clinical factors that are useful in predicting the need for mechanical support of the RV after LVAD implantation are younger patients, low BSA patients, female patients, patients with a nonischemic cardiomyopathy (more likely to involve both ventricles than ischemic origin), and patients receiving mechanical ventilatory support. In addition, patients with low preoperative PAP (systolic, mean, diastolic), significant tricuspid regurgitation (TR), and low right ventricular stroke work index (RVSWI) are at risk. Low PAP in these patients is not an indication of low pulmonary vascular resistance (PVR) but rather of severely depressed RV function and low RV output.

The indications for RVAD support following LVAD placement are as follows:

- Maximal inotropic support in the setting of nitric oxide (NO) and/or prostaglandin.
- Low mean and diastolic PAP, elevated CVP, and diminished RVSWI.
- Decreased LVAD flow (<2.4 L/min).
- Dilated, hypokinetic RV by echocardiographic examination.
- Decreased urine output and/or a high fraction of inspired oxygen (Fio_2) requirement.

The effects of LVAD implantation on RV function are complex and are summarized:

- *Contractility*. Complete pressure unloading of the LV with an LVAD shifts the intraventricular septum to the left and reduces the LV contribution to RV contraction. Systolic ventricular interdependence is such that LV contraction may account for most RV-developed pressure and volume outflow. In addition, there may be loss of RV contraction in the areas adjacent to the leftward-shifted intraventricular septum. As a result, LVAD insertion generally results in impairment of RV systolic function.

- *Afterload*. Insertion of an LVAD generally produces a reduction in RV afterload. Insertion of an LVAD results in reduction of LA pressures by reducing LV distention. Reduction in LA pressures results in reduced pulmonary venous congestion and a reduction in PVR and PA pressures despite the increase in cardiac output and pulmonary blood flow that accompanies implantation. Reduction of RV afterload improves RV function through enhanced shortening of the RV free wall. Not all patients have immediate normalization of PVR and PA pressures. Patients with longstanding pulmonary venous congestion may have an additional component of pulmonary hypertension that may take days or weeks to resolve. In addition, although PA pressures decrease routinely after LVAD implantation, the transpulmonary gradient (mean pulmonary arterial pressure–left atrial pressure) routinely increases slightly post implantation but falls by 24 hours postoperatively. This is most likely due to the residual pulmonary edema, and the effects of CPB and blood product administration on the pulmonary vascular bed.

- *Preload*. LVAD insertion increases cardiac output that in turn produces an increase in RV preload. In addition, LVAD insertion improves RV compliance and RV end-diastolic volume (EDV) increases while RV end-diastolic pressure (EDP) decreases.

- *Tricuspid valve function*. LVAD implantation generally acutely decreases mitral regurgitation while worsening tricuspid regurgitation both acutely and chronically. Poor apposition of the tricuspid valve leaflets after LV decompression with a LVAD occurs as the result of a leftward shift of the intraventricular septum and the increased RV volume load. There is generally dilation of the tricuspid annulus and leftward deviation of the septal components of the tricuspid subvalvular (chordae and papillary muscles) apparatus.

- *Coronary perfusion*. LVAD insertion may improve RV function by increasing aortic blood pressure and improving RV coronary blood flow.

On balance, LVAD insertion results in global impairment of RV systolic function, which is offset by increased RV preload and reduced RV afterload such that RV output is maintained or increased. As mentioned, 10% of patients receiving an LVAD will

require placement of an RVAD for RV failure that persists despite aggressive pharmacologic therapy to improve RV function. These patients usually have a component of pulmonary vascular resistance that is not immediately reduced by decompression of the LV, and underlying RV contractile dysfunction particularly of the intraventricular septum. Septal dysfunction causes the intraventricular septum to move away from the RV free wall during systole. The RV free wall cannot compensate for this movement, even in the setting of reduced afterload and RV stroke volume falls.

Treatment of RV dysfunction and TR with pulmonary vasodilators and inotropes will be necessary for patients who manifest severe RV dysfunction after LVAD implantation. Severe RV dysfunction will produce a low LVAD output in conjunction with a high CVP and TR with RV distention and hypokinesis seen with TEE. TEE is valuable in guiding therapy to reduce TR and improve RV function. In some circumstances a tricuspid annuloplasty may be warranted at the time of LVAD implantation.

Preload to the device

Proper functioning of all assist devices excluding the IABP are dependent on delivery of adequate volume to the device. TEE is useful in determining the etiology of poor preload to a device. The following causes should be considered:

- Hypovolemia.
- Poor positioning/obstruction of the inflow cannula. This is particularly important in RVAD and LVAD operating in parallel with the native heart as cannulas are placed in the RA or LA. TEE is used to ensure unobstructed inflow to the device. Care must be taken to ensure that atrial cannula do not cross the AV valve or impinge on the intra-atrial septum. For devices in series with the native heart, the ventricular cannula must not impinge on the ventricular free wall, septum, or papillary muscles. No substantial pressure gradient should exist across the inflow conduit. In addition, significant mitral stenosis will impede inflow into the LV and subsequently into the inflow cannula of the LVAD and will not allow decompression of the LA.
- IVC, SVC, or pulmonary venous obstruction in TAH patients. In TAH patients, TEE is used to ensure

that there is no obstruction of the SVC, IVC, or pulmonary veins.
- Impaired RV function with delivery of inadequate volumes of blood across the pulmonary circulation to a LVAD.

Afterload presented to the device

The performance of both pulsatile and nonpulsatile assist devices is influenced by afterload. As addressed previously, centrifugal and axial pumps have reduced performance as vascular resistance increases. At very high afterload, pulsatile pumps will develop increasing residual volumes as they fail to empty completely. This is analogous to an increasing end-systolic volume in the native ventricle with the end result being a reduced stroke volume. By increasing driveline pressure, pneumatic pumps can be made to empty completely at higher afterload. The result will be elevated MAP or PAP and the potential for more hemolysis. At systolic pressures in excess of 160 mmHg, the Novacor device exhibits increased residual volume and begins to overheat. As SVR increases in patients with the pneumatic HeartMate the ejection time necessary to completely empty the device increases. This, in turn, reduces maximal pump rate/min because minimal LVAD filling time is a fixed proportion of the selected LVAD ejection duration. With the Abiomed BVS 5000 and AB 5000 devices increased afterload will increase the duration of ejection and for a given diastolic filling period will reduce the pump rate/min. In all of these circumstances, afterload reduction is warranted.

Another source of device malfunction related to afterload is obstruction to outflow. TEE is used to ensure that there is no significant pressure gradient distal to the outflow cannulas or conduits in the great vessels.

Arrhythmias

Atrial and ventricular arrhythmias are not uncommon in the subset of patients requiring circulatory assist devices. They often resolve as the patient's hemodynamic status improves. The presence of atrial and ventricular arrhythmias in patients with an LVAD is often not of significant hemodynamic consequence provided the PVR is not elevated.

In these patients there may be adequate passive delivery of blood across the pulmonary vascular bed to the LVAD even during ventricular tachycardia (VT) and ventricular fibrillation (VF) in a manner similar to Fontan patients (total cavopulmonary connection without pulsatile RV function). In patients with elevated PVR the inability to control these arrhythmias will require placement of an RVAD.

Catecholamine resistant vasodilatory shock (CRVS)

A subset of patients will exhibit CRVS following placement of a mechanical circulatory support device. This manifests as low SVR and high unstressed venous volume (high venous capacitance) that is resistant to high doses of potent catecholamine vasoconstrictors such as norepinephrine. Hypotension is common as SVR is low and preload to the assist device is low as well. In circumstances where preload to an LVAD or TAH is maintained, hypotension may persist despite and output in excess of 6–7 L/min. CRVS is due to a combination of factors including endogenous NO release, arginine vasopressin (AVP) deficiency, intracellular acidosis (opens K_{ATP} channels), and contact phase activation-induced systemic inflammatory response. These patients generally have a favorable response to AVP infusion (0.01–0.05 units/min) in combination with lower doses of norepinephrine. AVP infusion repletes AVP deficiency, restores α_1-receptor responsiveness to norepinephrine by closing K_{ATP} channels, and potentiates the vasoconstrictor effects of norepinephrine by suppressing cyclic guanosine monophosphate (cGMP) release induced by NO. In addition, AVP administration increases release of corticotropin (ACTH). Patients receiving an LVAD are often treated with amiodarone, angiotensin-converting enzyme (ACE) inhibitors, and milrinone in the perioperative period that will exacerbate hypotension.

Cardiac output determination

The determination of cardiac output in patients with mechanical circulatory assist devices is summarized.

- *TAH.* Cardiac output is displayed by the COMDU of the CardioWest TAH. A thermodilution pulmonary artery catheter is not necessary and, in fact, must be removed before device implantation.
- *LVAD.* Device output is equal to systemic cardiac output as long as the aortic valve remains closed. TEE will readily determine if this is true. This situation is likely for devices in series with the LV and less likely for devices in parallel with the LV. If there is ejection from the native LV in conjunction with device output, then thermodilution cardiac output can be used as an accurate measure of the combined native ventricular and device output. Patients with LVAD require pulmonary catheters to aid in management of concomitant RV dysfunction.
- *RVAD.* Device output is equal to pulmonic output as long as the pulmonic valve remains closed. TEE will readily determine if this is true. Because RVAD are generally placed in series with the RV, the total pulmonic output is more likely to be a combination of native RV output and RVAD output. In this setting, thermodilution cardiac outputs will not be accurate because the transit times of blood and saline through the native RV and the RVAD will be different. This will interfere with the thermodilution technique.

Effects of ventilation

Positive-pressure ventilation may adversely affect RV function by mechanically compressing the pulmonary vasculature if peak airway pressures are high. This can reduce native RV output and delivery of blood to an LV assist device.

The TAH ventricle functions as an extra-thoracic chamber surrounded by atmospheric pressure in diastole and connected to an atrium and great vessels that are surrounded by intrathoracic pressure. Because there is no compliant intraventricular septum, there is no ventricular interdependence. Increases in intrathoracic pressure will reduce filling of the native atria from the systemic and pulmonary veins but will enhance filling of the prosthetic ventricles. Despite this, respiratory variation of systemic blood pressure will occur in the setting of hypovolemia or dilation of venous capacitance vessels.

Effects of induction and maintenance agents

Induction and maintenance of anesthesia in the patient with an assist device or TAH should take into account the hemodynamic effects of the chosen anesthetic agents. The effect of induction agents on myocardial contractility must be taken into account. Although the effects of agents on myocardial contractility are not important in TAH patients, the effects of agents on the peripheral vasculature do influence hemodynamics.

Device weaning

Devices are weaned by gradually withdrawing support while assessing ventricular function and hemodynamics. This usually requires the presence of a PA catheter and arterial line. The IABP is weaned by decreasing the pump rate from 1:1 to 1:2 to 1:3. Centrifugal and axial pumps are weaned by decreasing the pump flow rate. The risk of thrombus formation is enhanced when the pump flow rate is at or less than 2 L/min. Therefore, adequate anticoagulation should be maintained and the pump should be withdrawn promptly after weaning down to this level. Weaning of pulsatile devices involves adjustment of the device to operate at a decreased fixed rate. TEE has proved to be very valuable in guiding weaning of circulatory assist devices because it allows on-line assessment of RV and LV function during the weaning process.

Monitoring considerations

Arterial line placement may be difficult and pulse oximetry monitoring inconsistent in patients with nonpulsatile flow from axial and centrifugal pumps. Allowing the native ventricle to eject by temporarily reducing pump rate may be necessary for arterial line placement. Insertion of central venous catheters in patients with pulsatile RVAD imposes an increased risk of entraining air into the central circulation particularly when vacuum is applied to cannulas situated in the RA. Vacuum should be temporarily discontinued when this procedure is undertaken. In addition, care must be taken when a central venous line is accessed for volume or drug infusion while vacuum is applied.

Suggested reading

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CHAPTER 12

Myocardial Preservation during Cardiopulmonary Bypass

Myocardial preservation techniques are a fundamental component of contemporary cardiac surgery. The ability to suspend metabolic demand and preserve myocardial viability during the operative procedure allows the surgeon opportunity and time to complete complex repairs. Early efforts in cardiac surgery were hindered by postoperative myocardial failure after technically successful operative procedures due to extensive damage sustained during the operative procedure. Myocardial necrosis was common in patients dying after cardiac surgery and this necrosis occurred during cardiopulmonary bypass (CPB). Researchers soon found myocardial preservation techniques to reduce myocardial injury after CPB.

Initially, surgeons attempted to operate on both normothermic and hypothermic empty, beating, or fibrillating hearts. These conditions provided poor operative exposure and resulted in myocardial necrosis. Eventually, aortic cross-clamping evolved as the method of choice to exclude the heart from the circulation thereby enhancing surgical exposure by providing a bloodless field. A bloodless field however, came at the cost of myocardial perfusion. The heart must survive this interval of ischemia (cross-clamp interval) without injury (Fig. 12.1). Myocardial preservation techniques soon evolved and now provide optimal protection of the heart during aortic cross-clamping and in the reperfusion period following clamp release. This chapter reviews myocardial preservation

during aortic cross-clamping and in the immediate reperfusion interval.

Consequences of aortic cross-clamping

Myocardial ischemia occurs as the result of severely compromised or absent myocardial perfusion. In contrast, hypoxia refers to a reduction in substrate delivery with maintained perfusion. Because aortic cross-clamping isolates the coronary circulation from perfusion, global myocardial ischemia results unless they are adjunct protective measures. To understand the nature of these protective measures, it is necessary to examine the consequences of global myocardial ischemia.

Cessation of oxidative phosphorylation

This is the first metabolic derangement to occur. There is disruption of the electron transport chain and the Kreb's cycle is inhibited. This occurs within minutes of cross-clamping and results in termination of high-energy phosphate production in the form of adenosine triphosphate (ATP) and creatine phosphate (CP).

Depletion of ATP and CP stores

ATP supplies energy directly to the myocardium; whereas CP acts as an intermediate energy source to resupply ATP. During ischemia, there is immediate depletion of CP stores. Within 15 minutes, ATP stores are reduced by one-half and CP stores are essentially depleted.

Cross-clamp
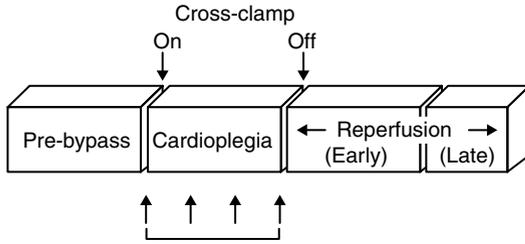
Fig. 12.1 A schematic diagram representing the chronology of a cardiac surgical procedure in which extracorporeal circulation and intermittent cardioplegia are used. Injury from ischemia can occur (a) before cardiopulmonary bypass is initiated, as a result of coronary artery disease or other disease processes, hypotension, or ventricular fibrillation; (b) during intermittent cardioplegia between infusions of solution, or when cardioplegia is poorly distributed because of coronary lesions present before revascularization or obstructions in the grafts; (c) during the reperfusion period, which can be divided into early and late components. In reality, the potential for reperfusion injury exists at each of these intervals when (a) resolution of pre-bypass hypotension or dysrhythmias restores blood flow; (b) cardioplegia solution is infused at high delivery pressures ("perfusion" injury) or has an inappropriate composition; and (c) coronary blood flow with unmodified systemic blood is restored after removal of the cross-clamp, especially if a terminal "reperfusion" dose of cardioplegia is not given. Systemic hypotension and physical or embolic obstructions to coronary blood flow can also induce injury during this period. (From Vinten-Johansen J, Ronson RS, Thourani VH, Wchsler AS. Surgical myocardial protection. In: Gravlee GP, Davis RF, Kurusz M, Utley JR (eds). *Cardiopulmonary Bypass: Principles and Practice,* 2nd edn. Philadelphia: Lippincott Williams & Wilkins, 2000:214–64, with permission.)

Anaerobic metabolism

Glucose is the only substrate available for anaerobic metabolism in the myocardium. To provide substrate for glycolysis, glycogenolysis must occur. Large glycogen stores may provide ample substrate for anaerobic production of ATP, but unless there is adequate washout of the hydrogen ions and lactate produced from anaerobic glycolysis, further glycolysis is inhibited by sufficiently high concentrations of these metabolites. Generally, anaerobic production of ATP ends a few minutes after it starts in the globally ischemic myocardium.

Inhibition of free fatty acid oxidation

Normally, free fatty acids are the major energy source for the myocardium in the post-absorptive state. Ischemia interferes with free fatty acid oxidation, fatty acid uptake, and transfer into the myocardium.

Depletion of the adenine nucleotide pool

After 30–40 minutes of global ischemia, the progressive degradation of ATP to adenosine 5-diphosphate (ADP), ADP to adenosine monophosphate (AMP), and AMP to inosine and hypoxanthine depletes the myocardium of its adenine sources. Therefore, reperfusion of energy sources to replenish ATP levels will be fruitless at this time unless the adenine precursors to form ATP are provided as well.

Impairment of calcium homeostasis

The consequences of impaired calcium homeostasis are summarized in Fig. 12.2. Homeostasis of intracellular calcium is dependent on two ATP-dependent processes: sequestration of calcium into the sarcoplasmic reticulum and extrusion of calcium across the sarcolemma. At 30 minutes of global ischemia, the myocardium's ability to regulate intracellular calcium is impaired by depletion of ATP stores. Loss of calcium homeostasis results in sustained myocardial contracture because sequestration of calcium is necessary to break the actin–myosin cross-bridges that allow diastolic relaxation to occur. In addition, high intracellular calcium levels cause further depletion of ATP stores through activation of myosin adenosine triphosphatase (ATPase).

Disruption of cellular architecture

By 30 minutes of global ischemia, there is swelling of the mitochondria and sacroplasmic reticulum due to increased osmolarity generated by the metabolites of anaerobic metabolism. After 30 minutes, there is progressive accumulation of the products of membrane degradation. Ischemia-induced reduction of free radical scavengers results in continued lipid peroxidation and membrane destruction via oxygen-free radicals. After 60 minutes, there is destruction of the cell membrane such that cell death occurs.

Reduced coronary flow

↓

Reduced availability of oxygen

↓

Reduced synthesis of ATP

↓

Failure of Ca^{2+} homeostasis

↓

Raised cytosolic Ca^{2+}

Mitochondrial Ca^{2+} overload

Activation of Ca^{2+} ATPases

Activation of Ca^{2+} lipases

↓

Impaired mitochondrial function

↓

Failure of ATP production

Increased usage of ATP

↓

Reduced ATP

Loss of structure and function
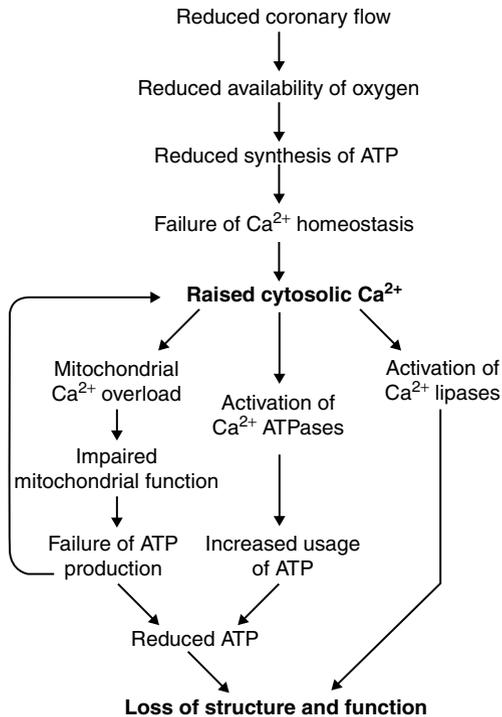
Fig. 12.2 Consequences of impaired calcium homeostasis secondary to reduced coronary blood flow. ATP, adenosine triphosphate; ATPases, adenosine triphosphatases. (From Nayler WG. The role of calcium in the ischemic myocardium. *Am J Pathol* 1981;**102**:262–70, with permission.)

Cardioplegia

Cardioplegia the solution used to arrest and protect the heart during aortic cross-clamping. Since the introduction of cardioplegia in 1955, the composition and mode of administration has evolved greatly. Cardioplegia solutions arrest the heart in diastole resulting in a profound reduction in metabolic demand. In addition, cardioplegia plays a restorative role replenishing energy stores in ischemic hearts. There is great variability in the administration, timing, composition, and temperature of the various cardioplegia regimens. Despite these variations, the basic components of cardioplegia systems are similar (Fig. 12.3), and the goals of cardioplegia administration remain unchanged.

Aortic cross-clamping drastically reduces oxygen and substrate supplies to the myocardium.

Cardioplegia solutions, administered immediately upon cross-clamp application, promptly reduce myocardial oxygen consumption. In addition, cardioplegia provides substrates to meet these reduced energy demands so that pre-ischemic energy stores are not depleted. Cardioplegia solutions induce electromechanical arrest of the heart in diastole. Arrest in diastole can be induced by depolarized arrest (elevated potassium), polarized arrest (adenosine, potassium channel openers, procaine, lidocaine), or arrest by influencing calcium mechanisms (elevated magnesium, calcium antagonists).

Because electromechanical work constitutes 95% of total myocardial oxygen consumption, the arrested heart will have very low energy requirements. In the arrested state, only basal energy requirements (those required to keep cellular metabolic processes intact) must be met. Figure 12.4 illustrates the very low oxygen consumption associated with induced arrest. Aerobic and anaerobic metabolism can provide enough energy to meet basal energy requirements as long as there is periodic replenishment of substrates and washout of metabolites.

There is considerable variability in the composition of cardioplegia solutions used in different institutions. Despite this wide variety of composition, there are certain properties all solutions must share. Cardioplegia must:
- induce prompt arrest of the heart in diastole to reduce myocardial oxygen consumption.
- incorporate hypothermia to further reduce myocardial oxygen consumption.
- provide sufficient substrates to meet the metabolic demands of the arrested heart.
- provide buffering to counteract the acidosis that accompanies ischemia.
- provide increased osmolarity to prevent the cellular edema that accompanies ischemia.
- provide membrane stabilization with additives or avoidance of hypocalcemia.
- have no adverse effects of its own.
- have a composition suitable for delivery to all areas of the myocardium.

Table 12.1 lists a typical cardioplegia solution used in contemporary practice. To fulfill these requirements, a typical cardioplegia solution
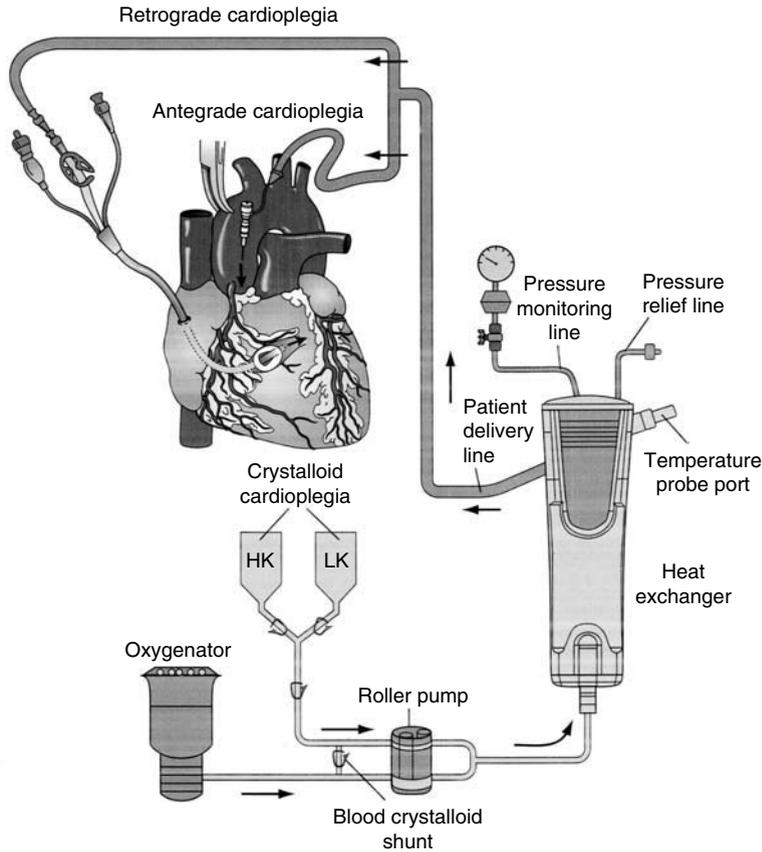
Fig. 12.3   Components of a cardioplegia delivery system. A modern cardioplegia delivery system is demonstrated. Oxygenated blood may be diverted from the oxygenator of the cardiopulmonary bypass (CPB) circuit and mixed with a high potassium (HK)-containing crystalloid cardioplegia solution for induction of electromechanical arrest or with a low potassium (LK)-containing cardioplegia solution. The ratio of blood to crystalloid may be varied and the solution is pumped via a roller pump to a heat exchanger for warming or cooling before administration. The line pressure and temperature of the cardioplegia solution is monitored. Perfusion of the myocardium may be antegrade through the coronary arteries or retrograde through a catheter in the coronary sinus. The retrograde catheter is usually placed before CPB through the right atrial wall and not the coronary sinus. Evidence of successful cannulation of the coronary sinus includes dark blood (secondary to the high oxygen extraction of the heart) returning from the catheter, visualization of the catheter in the coronary sinus by transesophageal echocardiography (TEE), and intravascular pressure monitoring. During retrograde perfusion, a pressure of 30–50 mmHg is desirable. (From Schell RM, Applegate RL, Reves JG. Cardiopulmonary bypass. In: Miller RD (ed). *Atlas of Anesthesia*. Philadelphia: Current Medicine (Churchill Livingstone), 1999:9.1–30, with permission.)

contains the components described in the following sections.

Potassium

Increasing extracellular potassium concentration to induce depolarized arrest is the primary method used to induce electromechanical arrest in most cardioplegia solutions.

Extracellular hyperkalemia results in depolarization of the cell membrane, inactivation of the voltage-dependent fast sodium channel, and sustained diastole. This effect is reversed after
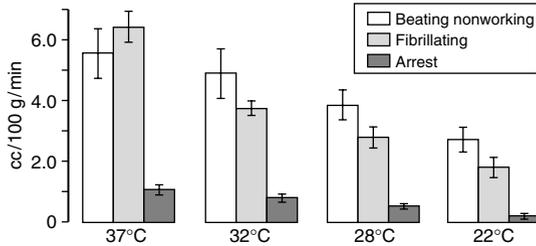
Fig. 12.4 Left ventricular oxygen consumption during three functional states (beating empty, fibrillating, and arrested) and at four temperatures. Hypothermia reduces myocardial oxygen consumption for any of the functional states. Below 37°C, the beating empty heart consumes the most oxygen, followed in decreasing order by the fibrillating and the arrested heart. (From Buckberg GD. Studies of the effects of hypothermia on regional myocardial blood flow and metabolism during cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1977;**73**:87–94, with permission.)

Table 12.1 Components of a typical cardioplegia solution.

Induction cardioplegia solution		
THAM solution	2.11 g	71.60 mL
Glutamate*	32.43 g	44.27 mL
Aspartate[†]	27.72 g	44.27 mL
CPD		17.76 mL
KCl	26.6 mEq	13.25 mL
Lidocaine	49.77 mg	2.53 mL
D_5W		88.125 mL
	Total volume	282.500 mL
Subsequent cardioplegia solution		
THAM solution	1.59 g	53.3 mL
Glutamate	24.39 g	33.3 mL
Aspartate	20.80 g	33.3 mL
CPD		13.3 mL
KCl	0.00 mEq	0.00 mL
Lidocaine	49.77 mg	2.53 mL
D_5W		66.8 mL
	Total volume	202.5 mL

CPD, citrate phosphate dextrose; KCl, potassium chloride; THAM, Tris-hydroxylmethyl aminomethane.
* Glutamate concentration is 7.32% in H_2O.
[†] Aspartate concentration is 6.25% in H_2O.

15–20 minutes by the normal metabolism and ionic currents present in the myocyte. The potassium concentration necessary to induce prompt arrest varies from solution to solution. For example, myocardial hypothermia reduces the extracellular potassium concentration required to induce arrest. Crystalloid cardioplegia solutions require lower extracellular potassium concentrations to induce arrest than do blood cardioplegia solutions.

Nonetheless, cardioplegia solutions generally have a potassium concentration ranging from 15–30 mEq/L. This concentration produces prompt electromechanical arrest. Concentrations of potassium higher than 40 mEq/L are detrimental because they increase calcium influx by increasing calcium conductance. Recall that increased intracellular calcium will increase wall tension and myocardial oxygen consumption. In addition, increasing calcium conductance while ischemia-induced loss of calcium homeostasis is occurring will exacerbate ischemic damage.

Hypothermia

Hypothermia is an important component of cardioplegia solutions because it reduces myocardial oxygen consumption even in the arrested heart, reduces the degree of extracellular hyperkalemia needed to cause electromechanical arrest and is additive with potassium-induced arrest in preventing ischemic damage. Cardioplegia is typically administered in one of three temperatures: cold 5–10°C, tepid 27–30°C , and warm 33–38°C. Generally, a combination of temperatures is used with initial cold or tepid administration later followed by a "hot shot" of warm cardioplegia just before removal of the aortic cross-clamp. Despite delivery of these cold solutions into the coronary arteries, it often is difficult to cool the myocardium to <15°C. Incomplete cooling may be due to the presence of coronary stenoses preventing homogenous delivery of the cold cardioplegia solution, noncoronary collaterals perfusing the heart with warm blood or systemic venous return warming the heart.

Calcium

Loss of calcium homeostasis is associated with cell dysfunction and death after ischemia. For this

reason, one might assume that the addition of calcium to cardioplegia solutions is detrimental. In fact, a small amount of calcium (>50 mM) is necessary to prevent the calcium paradox and to allow functional recovery after aortic cross-clamp removal. Calcium paradox is the massive cellular destruction that occurs when the myocardium is perfused with a calcium-containing solution after a period of calcium-free perfusion. Calcium paradox is due to washout of calcium from the sarcolemma with subsequent inability of the sarcolemma to limit calcium influx when presented with a calcium load. Calcium paradox is more likely to occur if the cardioplegia solution is alkalotic.

Despite this risk, most crystalloid cardioplegia solutions do not have calcium added to them; they contain <1 mM/L of calcium. Blood cardioplegia requires no additional calcium. Calcium paradox is prevented by delivery of an adequate concentration of calcium via the systemic perfusate from noncoronary collaterals and by the presence of hypothermia. Blood cardioplegia solutions deliver varying concentrations of calcium to the myocardium. The exact concentration depends on how extensively the blood solution is diluted before it is used as a medium for cardioplegia. In fact, most cardioplegia solutions contain the anticoagulant citrate-phosphate-dextrose (CPD) to chelate calcium thereby making calcium unavailable in the coagulation system. The CPD solution acts to chelate calcium, buffer the blood, and provide dextrose as a substrate for glycolysis.

Sodium

The optimal sodium concentration is unknown, but most cardioplegia solutions avoid extreme hypo- or hypernatremia relative to intracellular sodium concentration. Perfusion of the heart with a hyponatremic solution may predispose accumulation of intracellular calcium with subsequent increases in wall tension and myocardial oxygen consumption. Perfusion of the heart with a hypernatremic solution results in accumulation of intracellular sodium. This may result in cellular edema. It also may result in an accumulation of intracellular calcium as the sodium–calcium exchange pump moves sodium out and calcium into the cell. For these reasons, most

cardioplegia solutions have sodium concentrations in the range of 100–120 mEq/L.

Magnesium

High-dose magnesium can induce cardiac arrest in the absence of other agents. Magnesium in lower doses acts to stabilize cell membranes, block phosphorylation of myosin (preserving high energy substrates), and acts as a slow channel calcium blocker.

Buffering

Anaerobic metabolism accompanying ischemia results in cellular acidosis. Acidosis results in negative inotropy, reduced glycolysis, and depression of myocardial contractile proteins. The accumulation of acid results in inhibition of further anaerobic metabolism. Buffering allows anaerobic metabolism to continue and reduces ATP depletion in the ischemic myocardium. As myocardial temperature decreases, the appropriate uncorrected pH becomes more alkalotic. Therefore, the buffers chosen must be effective at the alkalotic pH found in the hypothermic myocardium. Tromethamine (THAM), bicarbonate, phosphate, and histidine are all used as buffers in cardioplegia solutions.

Histidine is a common buffer and is superior to the others because the pKa shifts into the alkaline range as temperature decreases; therefore it is an effective buffer over a wide variety of temperatures and pH levels. In addition, there is greater buffering capacity than crystalloid cardioplegia solutions buffered with standard concentrations of either bicarbonate or THAM. Blood cardioplegia provides better myocardial buffering than crystalloid cardioplegia buffered with bicarbonate due to the presence of the histidine buffering system in blood. Histidine added to crystalloid cardioplegia can provide a buffering capacity similar to that of blood cardioplegia.

Osmolarity

Because myocardial edema accompanies ischemia, cardioplegia solutions are formulated to minimize further accumulation of intracellular fluid. Cardioplegia solutions with osmolarities >400 mOsm/L exacerbate myocardial edema, probably by inducing increases in intracellular sodium. On the other hand, solutions with a low osmolarity will result

in accumulation of intracellular water and further edema. The ideal osmolarity remains undetermined, but probably is approximately 370 mOsm/L. Mannitol and albumin are the additives commonly used to manipulate osmolarity in cardioplegia solutions.

Substrates

Energy production during anaerobic metabolism requires provision of a substrate. Glucose and insulin as components of a cardioplegia solution allow uptake of glucose into the myocardium for use during anaerobic metabolism. Anaerobic metabolism results in the production of lactic acid and nicotinamide adenine dinucleotide (NADH). Accumulation of these metabolites leads to the eventual shutdown of further anaerobic metabolism. Substrate provision is useful only if there is periodic washout of the metabolites that inhibit anaerobic metabolism. In fact, in the absence of periodic washout of metabolites, substrate enhancement has been demonstrated to be deleterious to myocardial recovery after aortic cross-clamping. In clinical practice, this washout occurs through noncoronary collateral flow or through intermittent infusion of cardioplegia.

The use of glucose and insulin before aortic cross-clamping may result in improved post-cross-clamp myocardial function. Infusion of insulin and glucose before aortic cross-clamping results in a shift from oxidative lipolysis to glycolysis. There is an increase in glycogen stores. This pre-ischemic accumulation of glycogen stores and the early shift to anaerobic metabolism may have a protective effect during ischemia.

Glucose and insulin concentrations in cardioplegia solutions vary greatly from institution to institution. In fact, some institutions do not add either entity to their solutions. Some glucose is present in blood cardioplegia and, therefore, little or no glucose must be added when blood is used as a cardioplegia vehicle.

Crystalloid versus blood cardioplegia solutions

Cardioplegia solutions are delivered in either a crystalloid or a blood medium. There are important differences between the two formulations. Crystalloid solutions generally are prepared by the hospital pharmacy in containers that are delivered to the perfusionist. Blood solutions are prepared by drawing off oxygenated blood from the CPB circuit into a separate reservoir and mixing it with a prepepared crystalloid base solution. The ratio of blood to crystalloid base varies from institution to institution (4:1 to 1:4). Potassium and other additives are then added to the blood in the sufficient amounts to obtain the desired concentration. Both solutions can be temperature regulated and administered cool, tepid, or warm. Cold blood cardioplegia is diluted to a hematocrit of 10–15% to reduce microcirculatory sludging.

Blood cardioplegia is formulated using oxygenated blood from the CPB circuit. The amount of oxygen delivered to the myocardium by a blood cardioplegia solution is only a fraction of the solution's total oxygen content. The fraction of total oxygen content available for delivery is dependent on the solution's temperature and the hematocrit. The lower the temperature and the higher the hematocrit, the less oxygen will be available for delivery to the myocardium. The hypothermia-induced leftward shift of the oxyhemoglobin dissociation curve increases hemoglobin's affinity for oxygen and decreases oxygen availability to the myocardium. The delivery of oxygen carried in the dissolved state is unaffected by changes in hemoglobin's affinity for oxygen. For this reason, solutions with high hematocrit, in which the quantity of oxygen carried dissolved in plasma is reduced, will have a reduced oxygen-delivery capacity at low temperatures.

Crystalloid cardioplegia is not routinely oxygenated. Oxygenation of crystalloid solutions is accomplished easily by bubbling gas into the solution before delivery. Aeration of a bicarbonate containing crystalloid cardioplegia solution with 100% oxygen drives off carbon dioxide and results in severe alkalosis. For this reason, aeration with a 95–98% oxygen and 2–5% carbon dioxide mixture is recommended. An increase in the total oxygen content of a crystalloid solution occurs with decreasing temperature due to the enhanced solubility of oxygen in crystalloid at low temperatures. Crystalloid cardioplegia solutions are capable of delivering

Table 12.2 Advantages of blood cardioplegia.

Improved capillary perfusion due to the presence of red cells

More homogenous delivery of blood cardioplegia in the presence and absence of coronary stenoses

Improved buffering due to the presence of the histidine buffering system present in red cells

Reduced myocardial edema due to the oncotic tension of blood

Reduced risk of calcium paradox and improved functional recovery after ischemia due to the physiologic calcium concentration provided by blood

Presence of red cell enzyme catalase to scavenge free radicals produced by ischemia

their entire oxygen content to the myocardium because all oxygen is carried in the dissolved state. Therefore, as the temperature of a crystalloid cardioplegia solution decreases, the quantity of oxygen it delivers to the myocardium increases.

Blood cardioplegia solutions offer several potential advantages over crystalloid solutions (Table 12.2). Whether these differences between blood and crystalloid cardioplegia solutions offer any clear clinical advantage remains less clear. There is an extensive literature in both animals and humans on this topic. Meta-analysis of randomized clinical trials for all types of cardiac surgery demonstrates that blood cardioplegia is associated with fewer episodes of post-bypass low cardiac output syndromes, but there is no difference in myocardial infarction and death. In surgery for coronary artery bypass grafting, there is little to no evidence to support the superiority of cold blood versus cold crystalloid cardioplegia. Oxygenated blood cardioplegia solutions provide better preservation of myocardial high-energy phosphate stores, myocardial architecture, and function than nonoxygenated crystalloid cardioplegia solutions in animals. Likewise, animal work demonstrates that oxygenated crystalloid cardioplegia provides better myocardial preservation than nonoxygenated crystalloid cardioplegia. When differences in calcium concentration are controlled, oxygenated blood cardioplegia and oxygenated crystalloid cardioplegia provide comparable degrees of left ventricular functional recovery and ATP preservation.

Comparison of blood and crystalloid cardioplegia solutions remains challenging. Review of the literature demonstrates a lack of controlled, randomized trials, marked differences in the compositions, delivery, and temperatures of the various solutions, and wide variation in patient populations and end-points. Despite these obstacles, there is general agreement in the surgical community that for patients with preserved left-ventricular function undergoing coronary artery bypass surgery, intermittent delivery of oxygenated blood cardioplegia solution is at least equal or superior to intermittent delivery of nonoxygenated crystalloid cardioplegia solution. In patients with compromised preoperative left-ventricular function, oxygenated blood cardioplegia provides superior preservation of postoperative left-ventricular function.

Adjuvant agents

There is almost an infinite number of adjuvant agents added to cardioplegia solutions in clinical practice. In addition to the essential components described above, there are a number of adjuvant agents that can be added to cardioplegia. Many of the agents have been well tested in *in vitro* and animal experiments, yet lack rigorous clinical scrutiny. These adjuvant agents are added to cardioplegia for different reasons, but usually are employed to preserve myocardial function and diminish reperfusion injury. Some of these agents include calcium channel blockers, allopurinol, free radical scavengers, and adenine nucleotides.

Loss of calcium homeostasis is a major factor in causing ischemia-induced myocardial damage. The addition of calcium channel blockers in cardioplegia solutions may prevent calcium influx and subsequent high-energy phosphate hydrolysis during cardioplegic arrest by preventing calcium influx during reperfusion. Animal studies have demonstrated improved preservation of myocardial function with the addition of calcium channel blockers to crystalloid and blood cardioplegia solutions. The evaluation of calcium channel blockers in cardioplegia is more difficult. There are reports of benefit; however, study differences in the composition of cardioplegia solutions, in the dosages of calcium channel blockers added to

the cardioplegia solutions, in the operative procedures, and in the extent of preoperative ventricular dysfunction make it difficult to draw any firm conclusions about the efficacy of calcium channel blockers added to cardioplegia solutions. The issue of whether their routine use is justified is unresolved, but the data suggest that their addition will be of greatest value in patients at highest risk for calcium-induced ischemic damage. The benefits of calcium channel blockers in cardioplegia are balanced against associated negative inotropy and atrioventricular (AV) nodal dysfunction.

Allopurinol is a competitive inhibitor of xanthine oxidase; whereas, its chief metabolite, alloxanthine, is a noncompetitive inhibitor. Xanthine oxidase is an important enzyme in the generation of the free radicals implicated in causing myocardial damage upon reperfusion of the ischemic myocardium. Allopurinol added to cold blood and crystalloid cardioplegia improves myocardial protection in the severely ischemic animal ventricle.

An alternative to inhibition of free radical production is supplementation with agents capable of scavenging free radicals. Animal studies have demonstrated improved myocardial protection in the ischemic myocardium after use of crystalloid cardioplegic supplemented with the free radical scavengers superoxide dismutase (SOD), catalase, deferoxamine, and mannitol.

Myocardial ischemia promotes production of adenosine. Adenosine added to cardioplegia mitigates postischemic ventricular function in animals. Acadesine, a purine nucleoside analog, raises adenosine levels in ischemic myocardium. Acadesine selectively augments adenosine production in ischemic myocardium without increasing production in nonischemic myocardium. Although the mechanism of action is unclear, the action of acadesine seems to be mediated through adenosine A_1- and A_2-receptors and may act through activation of the ATP-sensitive potassium channel. Acadesine added to cold cardioplegia improves postischemic ventricular function in animal models.

Cardioplegia and reperfusion injury

Reperfusion injury is defined as the functional, metabolic, and structural alterations caused by reperfusion after a period of temporary ischemia. Cardioplegia solutions can protect the heart during the ischemic insult and reduce reperfusion injury. Reperfusion injury is characterized by intracellular calcium accumulation, cellular swelling, microcirculatory dysfunction, and reduced ventricular compliance. Reperfusion solutions are infused into the myocardium after completion of the surgical procedure and before removal of the aortic cross-clamp. They are formulated to prevent or minimize the reperfusion injury that accompanies reperfusion of the heart with systemic blood.

Restorative cardioplegia to reduce reperfusion injury improves ventricular function after aortic cross-clamping. As with cardioplegia, there are *in vitro* and animal data to support its use. Controlled clinical trials are more difficult to conduct. Differences in the composition, temperature, delivery of the solutions used, and in the operative procedures performed, make it difficult to draw any firm conclusions regarding the efficacy of reperfusion solutions in humans.

Despite this, there is support for use of reperfusion solutions in patients with preexisting, poor ventricular function and in those who require long cross-clamp times.

Resuscitation of ischemic myocardium can be accomplished through warm induction of cardioplegic arrest. The goal is to resuscitate ischemic areas while optimizing preservation of the nonischemic areas. Warm induction of cardioplegic arrest after aortic cross-clamping combined with rapid ventricular decompression on CPB improves repletion of myocardial energy stores and improves myocardial recovery after an acute ischemic event in patients with ventricular hypertrophy. Table 12.3 lists the ideal qualities present in restorative cardioplegia to reduce reperfusion injury.

Many of the same concerns for cardioplegia solutions are present for reperfusion solutions. For reperfusion solutions, sufficient potassium to maintain arrest in diastole is required. This is accomplished clinically using 8–10 mEq/L in a blood medium. For warm induction solutions, 25 mEq/L of potassium in a blood medium is required. Hypothermia delays the repair of damaged enzyme systems because the repair process

Table 12.3 Restorative cardioplegia to reduce reperfusion injury.

Maintain arrest of the heart in diastole to reduce myocardial oxygen consumption

Induce normothermia to optimize the rate of metabolic recovery

Initiate aerobic metabolism with an oxygenated solution

Provide buffering to counteract acidosis and optimize enzymatic and metabolic recovery

Provide increased osmolarity to minimize reperfusion edema

Provide sufficient substrate to allow aerobic energy production

Temporarily reduce calcium ion availability

Provide substrate to scavenge free radicals

is temperature-dependent. Clinically, use of a normothermic (37°C) reperfusion solution improves functional recovery.

Glutamate and aspartate are amino acids that serve to replenish Kreb's cycle intermediates that are depleted during ischemia and which enhance aerobic metabolism and reparative processes. Reperfusion and warm induction with a monosodium L-glutamate (MSG) and monosodium L-aspartate (MSA) containing solution results in the return of oxidative metabolism, enhanced oxygen uptake, improved ATP repletion, and better preservation of systolic function after ischemic insult. The addition of L-arginine to cardioplegia results in reduced biomarkers of injury in patients. The mechanism of action may be due to increased nitric oxide production.

As previously discussed in detail, maintenance of temperature-appropriate pH is essential to ongoing cellular metabolic processes. Because acidosis accompanies ischemia, any reperfusion solution must counteract acidosis and normalize pH. TRAM is often employed as a buffer in blood reperfusion solutions. Additional buffering capacity is available in the form of histidine when a blood reperfusate is used. The glutamic acid-sodium hydroxide buffer system has been used with clinical success in crystalloid reperfusate.

Similar to cardioplegia solutions used to prevent ischemia, reperfusion solutions must prevent progression of the edema that accompanies ischemia. Maintenance of an osmolarity of 360 mOsm/L and avoidance of perfusion pressures >60 mmHg are effective in this regard. Because loss of calcium homeostasis is the major determinant of reperfusion injury, careful control of calcium concentration in the reperfusate is essential. The optimal concentration of calcium in reperfusate is unknown, but concentrations in the range of 0.15–0.25 mmol/L are common. Clinically, the desired calcium concentration in a blood reperfusate is obtained by using CPD to chelate excess calcium before its administration.

Free radical damage occurs with reperfusion of ischemic myocardium with an oxygen-containing solution. Modification of the reperfusate with the free radical scavengers superoxide dismutase, catalase, and mannitol is common.

There are other reperfusion strategies that may offer clinical benefit. Graded reoxygenation and reperfusion is associated with diminished injury in experimental models. Neutrophil depletion reduces both the clinical and biochemical indices of myocardial reperfusion injury after elective coronary revascularization with CPB. Sevoflurane reduces neutrophil activity when included in the cardioplegia solution. *N*-acetylcysteine, which can increase glutathione levels, reduces the rise in troponin-I when added to cold blood cardioplegia. Esmolol is effective when added to cold continuous retrograde blood cardioplegia. Fructose-1,6-diphospate, an endogenous high-energy gylcolytic pathway intermediary, enhances ATP production and reduces the biochemical markers of injury when added to cardioplegia. Finally, ischemic preconditioning has been found to be beneficial in myocardial protection during surgery on the beating heart, but offers no additional protection when employed in conjunction with CPB and aortic cross-clamping.

Cardioplegia delivery

Cardioplegia is delivered under pressure to the heart via either a pressurized bag or roller pump system. The roller pump system offers several advantages including easy incorporation of a continuous cooling system to maintain cardioplegia hypothermia, easy incorporation of the mixing

apparatus necessary for blood cardioplegia systems, and second-to-second control of cardioplegia infusion pressure and flow rates. The delivery system should have a filter to prevent particular contaminants from reaching the coronary circulation and inducing coronary vasospasm.

It is necessary to have a means of monitoring infusion pressure because excessive infusion pressures can result in myocardial edema and ventricular dysfunction. Infusion pressure is monitored in the cardioplegia line itself or directly at the site of administration. Safe delivery pressure will be dictated by the site of administration.

During the period of aortic cross-clamping, cardioplegia should be infused at least every 20 minutes. This strategy allows washout of metabolites and replacement of the cardioplegia solution components that are either depleted or washed out by noncoronary collateral flow. If electrocardiograph (ECG) or visual evidence of myocardial contraction is present, infusion of cardioplegia is necessary immediately, regardless of the time elapsed since the previous infusion. There is some evidence to support continuous administration of cold blood cardioplegia during aortic cross-clamping. One advantage to this approach includes steady-state hypothermia. A significant disadvantage is the impediment to the surgeon's operative field visibility during distal coronary artery anastomoses.

The optimal cardioplegia infusion volume is unknown. In general, 10–20 mL/kg/min of cardioplegia are delivered during the initial infusion with the larger volumes being reserved for hypertrophied ventricles. Subsequent infusion usually is 10–15 mL/kg. With this method, the infusion site and the safe maximal delivery pressure will limit the rate of infusion. Some centers are more concerned with the duration of cardioplegia delivery than the volume infused and prefer to deliver cardioplegia by controlling infusion pressure and delivering cardioplegia over a specified time interval (i.e. 1.5–3.0 minutes for initial arrest, and 1.0–1.5 minutes for subsequent infusions).

After the initial arrest, the composition of subsequent infusions is modified. After diastolic arrest with hyperkalemic, hypothermic cardioplegia, diastolic arrest can be maintained with a hypothermic solution containing a lower potassium concentration. Patients receiving cold crystalloid high-potassium (20 or 27 mEq/L) cardioplegia in both the initial and subsequent infusions had a higher incidence of postoperative high-grade ventricular ectopy and AV nodal dissociation dysrhythmias than patients receiving an initial infusion of cold crystalloid high-potassium cardioplegia followed by subsequent infusions of cold crystalloid low-potassium (5 or 7 mEq/L) cardioplegia. No differences in postoperative ventricular function could be detected between the two groups in either of these studies.

Optimal delivery of cardioplegia must be tailored to the operative procedure and operative technique. Several methods are available for cardioplegia delivery. Delivery may be via the arterial system (antegrade) or via the venous system (retrograde).

Infusion into the aortic root

This method is accomplished by placement of a cannula into the aorta root between the aortic cross-clamp and the aortic valve and coronary ostia. Placement of a cannula with two lumens, one for cardioplegia delivery and the other for venting or pressure monitoring, is popular and allows measurement of aortic root pressure during cardioplegia delivery (Fig. 12.5). For this method to be effective, the aortic valve must be competent. Otherwise, the cardioplegia solution will flow into the left ventricle with resultant ventricular distension and inadequate delivery of cardioplegia down the coronary arteries.

Infusion into the grafts

In revascularization procedures, cardioplegia can be infused down the free end of each saphenous vein after completion of the distal anastomosis. This is usually performed by the surgeon with a syringe connected to the free end of the coronary graft. The cardioplegia is highly effective but is limited to the distribution of the chosen coronary artery. On occasion, small air emboli may be injected down the coronary graft. Typically, this is an incidental finding on transesophageal echocardiographic (TEE)
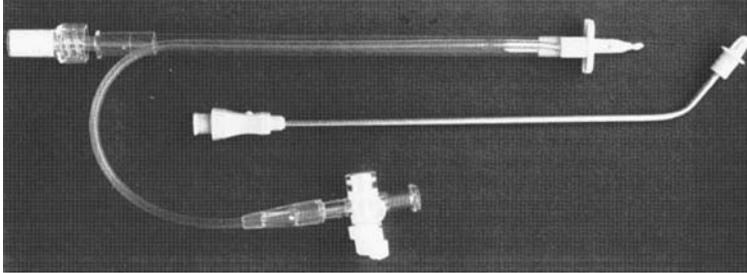
Fig. 12.5 Top: Double-lumen catheter used for delivery of cardioplegia into the aortic root. Lumen connected to a stopcock can be used for venting via aortic root or for measurement of aortic root pressure. Catheter is placed in aortic root with use of purse-string suture and needle-tipped stylet shown in place here. After catheter has been placed in the aorta, the stylet is removed and the central lumen is used for cardioplegia infusion. Bottom: Hand-held cannula used to directly cannulate coronary ostia for delivery of cardioplegia solution. (From DiNardo JA. Myocardial preservation. In: DiNardo JA (ed). *Anesthesia for Cardiac Surgery*, 2nd edn. Stamford, CT: Appleton & Lange, 1998:349–64, with permission.)

examination and is without clinical significance (Fig. 12.6).

Infusion directly into the coronary ostia

This method is used for procedures in which the aortic valve is incompetent and cardioplegia cannot be delivered into the aortic root or for procedures in which the aortic root must be opened (aortic valve replacement). For this method to work effectively, the surgeon must identify the coronary ostia and cannulate them with specially designed catheters through which cardioplegia is infused (see Fig. 12.5). The catheters come in a variety of sizes to allow proper placement without damage to the ostia. Delivery of cardioplegia with this method can be complicated in several ways. The tip of the catheter may extend past the bifurcation of the left main coronary artery such that the catheter may only perfuse either the left anterior descending or the circumflex artery. This is particularly true in patients with bicuspid aortic valves because the left main coronary artery is shorter than normal. In 50% of patients, the conus artery to the right ventricle (RV) arises separately from the aortic sinus and will not be perfused by cannulation of the right coronary ostium. Finally, damage to the ostia with late stenosis can occur with direct cannulation.

For all three of these antegrade delivery sites, the infusion pressure should not exceed 150 mmHg.
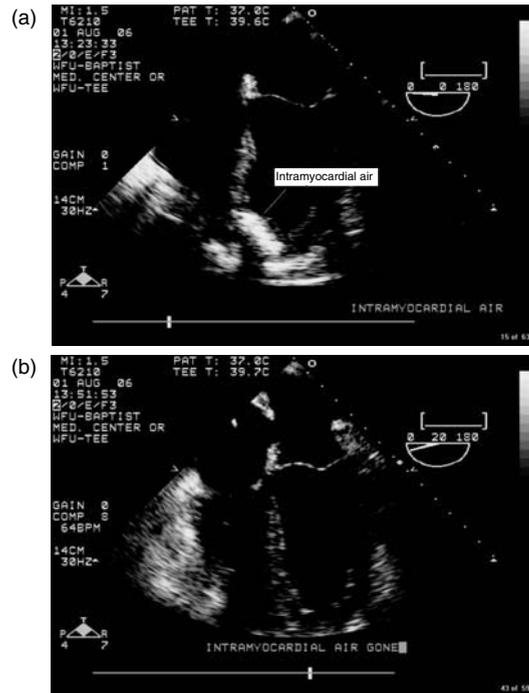
Fig. 12.6 Intramyocardial air is observed in the apical septal wall before separation from cardiopulmonary bypass (a). This air may have come from inadvertent injection of air down a coronary graft during administration of cardioplegia. The area was initially dyskinetic, however, after a short washout interval, the air was absorbed and the wall motion abnormality resolved (b).

Retrograde coronary sinus perfusion

Retrograde coronary sinus perfusion (RCSP) infusions cardioplegia into the coronary sinus retrograde into the great and small cardiac veins. The large venous network is free of atherosclerotic disease allowing adequate retrograde perfusion of the entire myocardium via this route.

This method requires placement of a purse-string suture in the right atrium (RA) and creation of a small atriotomy. A specially designed coronary sinus catheter is placed in the coronary sinus by the surgeon via the atriotomy. TEE is useful to confirm proper positioning of the coronary sinus catheter (Fig. 12.7). A balloon at the tip of the catheter helps secure the catheter and ensures that cardioplegia flow does not spill back into the right atrium. Delivery of cardioplegia commences after application of the aortic cross-clamp. Most of the retrograde perfusion drains via the thebesian veins, but either the aortic root or the left ventricle

is usually vented during cardioplegia infusion to allow egress of the solution. The coronary sinus catheter has an additional central lumen allowing pressure monitoring during cardioplegia infusion. If infusion pressures are too high, there may be injury to the coronary venous system. Normal retrograde perfusion occurs at a pressure of 30–50 mmHg.

Retrograde cardioplegia is popular for a number of reasons. The retrograde route of cardioplegia administration is particularly useful in aortic valve replacement thereby avoiding in direct cannulation of the coronary ostia. Retrograde perfusion is superior to aortic root perfusion when aortic incompetence exists. RCSP results in more homogeneous distribution of cardioplegia than antegrade delivery in animals and humans with coronary stenoses. This may be secondary to the large venous network free of atherosclerotic disease. Troponin I release is reduced immediately after surgery with retrograde cardioplegia compared to antegrade cardioplegia (Fig. 12.8). Retrograde perfusion is useful in reoperative procedures in patients with patent internal mammary artery (IMA) grafts. Retrograde perfusion during IMA occlusion will provide cardioplegia delivery to the myocardium distal to the patent graft.
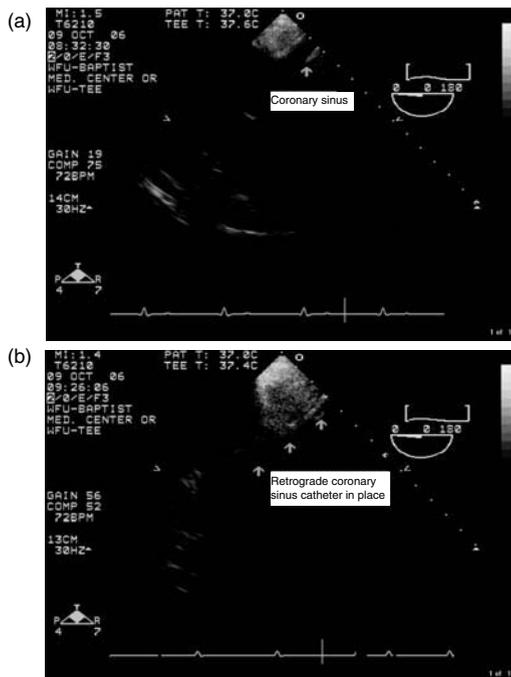
Fig. 12.7 The coronary sinus is easily visualized with transesophageal echocardiography (TEE) (a). The retrograde coronary sinus catheter is seen in the coronary sinus (b).
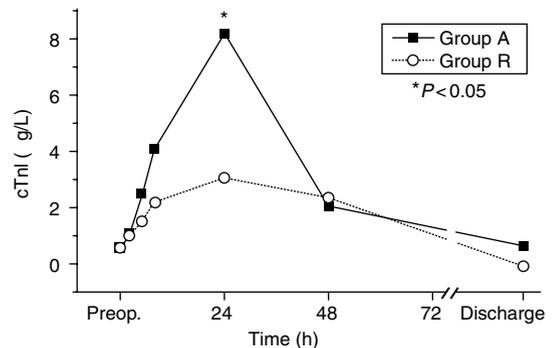
Fig. 12.8 The time course of troponin I (cTnI) concentration for antegrade and retrograde cardioplegia groups in a trial of 58 randomized patients undergoing elective coronary artery bypass grafting. *$P < 0.05$ between groups. (From Franke U, Wahlers T, Cohnert TU *et al*. Retrograde versus antegrade crystalloid cardioplegia in coronary surgery: value of troponin-I measurement. *Ann Thorac Surg* 2001;**71**:249–53.)

RCSP provides poor protection of the RV and posterior septum probably as a result of venovenous shunting through arteriosinusoidal and thebesian vessels directly into the RV. As a result, only 30–70% of delivered retrograde cardioplegia reaches myocardial tissue. Interestingly, antegrade cardioplegia is also associated with diminished right ventricular protection compared to the left ventricle. The reasons for this are unclear; however, it may be related to uneven distribution of cardioplegia solution with antegrade delivery or a baseline metabolic difference between the right and left ventricle. To maximize myocardial protection, many institutions utilize both antegrade and retrograde cardioplegia in a single patient.

Myocardial protection agents in addition to cardioplegia

Myocardial preservation is influenced by factors other than the efficient delivery of cold cardioplegic solution. The most important of these factors are discussed in the sections that follow.

Topical hypothermia

Myocardial oxygen demands drop by 90% in normothermic arrest to 1 mL oxygen (O_2)/100 g/min. At 22°C, oxygen requirements drop to 0.3 mL/ 100 g/min in the arrested heart. Further reduction of oxygen consumption occurs with temperatures <22°C; however, the incremental gain is minimal. Despite this, many clinicians target 4–6°C for optimal myocardial preservation. As discussed previously, it is difficult to achieve this degree of hypothermia in clinical practice. It is possible, with the use of cold cardioplegia solution and topical saline slush or ice chips, to achieve and maintain temperatures lower than 15°C. Unfortunately, the use of saline slush and ice chips has been associated with problems. Myocardial damage due to freezing has been demonstrated in hearts exposed to slush or ice for more than 30 minutes. Phrenic nerve paresis due to freezing has been reported in 60–80% of cases in which slush or ice is used. For these reasons, many centers use either intermittent or continuous infusions of saline at 4°C into the pericardial well to obtain topical cooling.

Control of noncoronary and bronchial collateral blood flow

Excessive bronchial collateral blood flow results in warming of the heart by distending it with blood at the temperature of the systemic perfusate. Excessive noncoronary collateral flow results not only in distension and warming of the heart but in the washout of cardioplegia solutions as well. Systemic hypothermia on CPB is effective in reducing warming, but careful control of systemic flow and pressure on CPB is necessary to reduce the magnitude of collateralized flow.

Decompression of the heart

Distension of the heart has two deleterious consequences: it results in poor distribution of cardioplegia solution to the subendocardium due to the high intracavitary pressures, and it results in warming of the heart due to distension of the heart with blood at body temperature. For these reasons, venting of the heart is usually employed.

Preventing warming of the posterior surface of the heart

Because the posterior surface of the heart lies on top of the mediastinum, which is at systemic temperature, it is at high risk of warming during aortic cross-clamping. To prevent this, many surgeons place a pad soaked in iced saline behind the heart in the pericardium to shield it from the mediastinal structures. This may help prevent mitral valve dysfunction secondary to posterior papillary muscle ischemia. The TEE probe emits energy and heat whenever imaging is in progress. For this reason, imaging should be suspended during this portion of the surgical procedure.

Special considerations in neonates, infants, and children

Despite advances in the surgical correction of congenital cardiac lesions, postoperative low cardiac output leading to long-term ventricular dysfunction or death continues to be a concern. This has focused attention on the effectiveness of current myocardial protection techniques in the repair of congenital heart disease. Most work to date on myocardial preservation has involved adult

humans or adult animal preparations. Unfortunately, the existence of major structural, metabolic, and functional differences between infant and adult hearts makes extrapolation of these studies to neonates and infants difficult. These differences are summarized in the following sections.

Calcium homeostasis

Neonatal hearts have a poorly developed sarcoplasmic reticulum and T-tubule system. In addition, the sarcoplasmic reticulum has reduced calcium storage capacity and a reduced activity of sarcoplasmic calcium ATPase, the enzyme responsible for calcium re-uptake. These differences result in a greater reliance on extracellular calcium to provide excitation-contraction coupling and are a factor in the diminished tension development capabilities of the neonatal myocardium.

Substrate metabolism

In the adult heart 90% of ATP production is derived from fatty acid oxidation. The main ATP substrate in neonatal hearts is glucose. As compared to adults, the noninsulin-dependent glucose transporter (GLU1) is much more highly expressed than the insulin-dependent glucose transporter (GLU4).

ATPase activity

Fetal light-chain myosin has a diminished ability to hydrolyze ATP, which contributes to the diminished tension-development capability of neonatal hearts. This light-chain myosin remains in patients with congenital heart disease.

Capacity for anaerobic metabolism

The neonatal heart has an enhanced capacity for anaerobic metabolism compared with the adult heart secondary to its large glycogen stores. For this reason, the neonatal heart tolerates longer periods of hypoxia.

Tolerance for ischemia

The neonatal heart possesses greater tolerance for ischemia (severely reduced or absent perfusion) than adult hearts due to enhanced glycogen stores, better maintenance of ischemic calcium exchange, higher levels of ATP substrates, and increased amino acid use. In the absence of perfusion, the enhanced capacity for anaerobic metabolism of the immature myocardium leads to a rapid accumulation of the products of anaerobic metabolism such as lactate. Therefore, prolonged ischemia results in severe acidosis and tissue damage and in the rapid inhibition of further production of high-energy phosphates in the neonatal myocardium. Cyanosis further increases the vulnerability of the neonatal heart to ischemia. The myocardium of cyanotic children is more vulnerable to cardiac ischemia/reperfusion injury than the myocardium of noncyanotic children presumably due to depletion of endogenous antioxidant reserve.

Tension development

In comparison to the adult heart, the neonatal heart contains a reduced number of poorly organized contractile units. In the immature myocardium, a larger proportion of the myocyte is devoted to the protein synthetic processes needed for cell growth. In addition to the factors already addressed, this accounts for the reduced tension development capabilities of the neonatal heart. This reduced tension development capability makes the neonate very susceptible to any depression of systolic function after cardiac surgery.

Work done both in animals and in humans suggests that improved myocardial preservation can be obtained in neonates, infants, and children by tailoring myocardial preservation efforts to the specific needs of the immature myocardium:

- Delivery of cardioplegia to neonates, infants, and small children requires some modifications; 20–30 mL/kg of cardioplegia may be necessary to induce arrest. The pressure of antegrade delivery must be modified such that, in the neonate, infusion pressure is no more than 40–50 mmHg to avoid myocardial edema.
- Topical cooling is much more effective in the neonate than in the adult due to the smaller cardiac mass and greater surface area: wall thickness ratio in neonates.
- Improved post-ischemic functional recovery occurs with use of hypothermic blood potassium cardioplegia with a normal serum calcium concentration.

- Infants younger than 3 months of age and infants with preoperative heart failure have an increased susceptibility to ultrastructural myocardial injury despite the use of cold crystalloid cardioplegia and topical hypothermia.
- Children with ventricular hypertrophy have increased vulnerability to ischemia/reperfusion injury. This is due, at least in part, to reduced microvascular (capillary) density and impaired glucose uptake.
- There may be difficulty in obtaining adequate myocardial protection in the presence of voluminous bronchial and noncoronary collateral blood flow. Noncoronary collateral flow will wash out cardioplegia, and that bronchial return will result in warming of the heart. This collateral blood flow can be eliminated through the use of circulatory arrest. In fact, improved recovery of right ventricular function, reduced need for post-CPB inotropic support, and less evidence of myocardial necrosis, as indicated by myocardial band enzymes of creatinine phosphokinase-myocardial band (CPK-MB) levels, have been demonstrated in patients undergoing tetralogy of Fallot repair with systemic deep hypothermic arrest in addition to cardioplegic protection.

Suggested reading

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Special Considerations during Cardiac Surgery

This chapter will address topics that require special consideration during the conduct of cardiac surgery.

Deep hypothermic circulatory arrest

Deep hypothermic circulatory arrest (DHCA) is a technique employed to improve exposure of intracardiac defects and to facilitate aortic arch reconstruction in infants and children. In adults, DHCA is used primarily during aortic arch reconstructions. DHCA allows cessation of cardiopulmonary bypass (CPB), venous and arterial cannula removal, and exsanguination of the patient into the venous reservoir of the CPB circuit. There has been substantial refinement of the technique of DHCA since its successful inception in the 1970s. Currently DHCA is used selectively and for short intervals.

Determination of the safe period of DHCA is problematic because it varies depending on the defined primary acceptable outcome as well as on independent variables such as patient population (infant versus adult), co-morbidities (cerebrovascular, renal, genetic), and DHCA technique (pH management, hematocrit management). In neonates and infants, DHCA intervals generally do not exceed 60 minutes as DHCA intervals longer than 40 minutes are associated with a nonlinear increasing likelihood of adverse neurodevelopmental outcomes including seizures. In adults, DHCA intervals of less than 30–40 minutes are common.

Hypothermia

Hypothermia is arguably the most important component of DHCA. Hypothermia-induced reduction in cerebral metabolic rate for oxygen ($CMRO_2$) slows the rate of depletion of high-energy phosphates and the development of intracellular acidosis. This delays or prevents the neuronal energy failure that leads to terminal membrane depolarization and subsequent neuronal injury or death during an ischemic episode. The Q_{10} defines the ratio of organ oxygen consumption at a defined temperature to the oxygen consumption at a temperature 10°C lower. The cerebral Q_{10} is approximately 3.65 in children and 2.3 in adults. The cerebral metabolic rate is approximately 10–15% of its normothermic baseline at 15°C. If it is assumed that 3–5 minutes of cerebral ischemia can be tolerated at 37°C and the Q_{10} is 3.0, 9–15 minutes of ischemia can be tolerated at 27°C and 27–45 minutes can be tolerated at 17°C.

In addition to reducing $CMRO_2$, hypothermia also serves to ameliorate some of the sequalae of neuronal ischemia when instituted prior to the ischemia insult. Specifically, hypothermia markedly reduces release of the excitatory neurotransmitters glutamate, aspartate, and glycine that accompany cerebral ischemia and subsequent reperfusion. In energy deprived cells, glutamate is neurotoxic in part due to the role it plays in inducing massive calcium influx via N-methyl-D-aspartate (NMDA) receptors. Hypothermia also blunts the inhibitory

effect of hypoxia on nitroxidergic (postganglionic parasympathetic nerve where nitric oxide (NO) is the neurotransmitter) induced cerebral vasodilatation. In addition, hypothermia may attenuate neutrophil migration into ischemic tissue.

pH stat versus α-stat management

pH-stat and α-stat are described in detail in Chapter 10. Experimentally pH-stat management during DHCA offers several advantages over α-stat management:

Suppression of CMRO$_2$

There is better suppression of CMRO$_2$ with pH-stat as compared to α-stat management. pH-stat management reduces CMRO$_2$ by 40% over that seen with α-stat management at 17°C.

Brain cooling

During the cooling phase of deep hypothermia, pH-stat management provides faster and more homogenous brain cooling than does α-stat management. This is a direct consequence of the decreased cerebral vascular resistance and increased cerebral blood flow (CBF) that accompanies pH-stat management.

Oxyhemoglobin dissociation curve

Hypothermia induces a leftward shift of the oxyhemoglobin dissociation curve such that during α-stat management at 17°C the P$_{50}$ of fetal hemoglobin is 5.0 as compared to 20.0 at 37°C. The increased affinity of hemoglobin for oxygen reduces the ability of hemoglobin to off-load oxygen to tissue. As a result, a substantial portion (56–96%) of the oxygen delivered to brain during CPB at 17°C is obtained from dissolved oxygen making a high CBF to CMRO$_2$ ratio necessary. pH-stat management is advantageous in this setting because it results in increased CBF compared to α-stat management and because the relative acidosis which accompanies pH-stat management induces a rightward shift of the oxyhemoglobin dissociation curve such that the P$_{50}$ of fetal hemoglobin increases to 6.9 at 17°C improving off-loading of oxgyen from hemoglobin to the brain.

Aortopulmonary collaterals

The presence of numerous and often large collateral vessels from the arch vessels and thoracic aorta to the pulmonary arterial system is common in neonates, infants, and children with atretic pulmonary arterial systems. The number and size of these vessels increase in proportion to the duration of cyanosis. On CPB, with α-stat management the resulting alkalosis reduces pulmonary vascular resistance and increases cerebral vascular resistance such that these vessels divert blood from the cerebral circulation to the pulmonary circulation. As a result, pH-stat management results in better cerebral protection than α-stat management when circulatory arrest is induced in the presence of aortopulmonary collaterals (APCs).

Cerebral oxygenation

pH-stat management increases pre-DHCA cortical oxygen saturation (Sco$_2$) and increases the half-life of arrest Sco$_2$ as compared to α-stat management. pH-stat management also provides better preservation of intracellular pH and better preservation of cerebral energy stores (high-energy phosphates) and tissue oxygenation (nicotinamide adenine dinucleotide (NADH), cytochrome aa$_3$). A strategy of pH-stat management during cooling and arrest coupled with pH-stat management during rewarming results in better recovery of cerebral energy stores and intracellular pH than a strategy of pH-stat management during cooling and arrest coupled with α-management during rewarming. These effects are largely mediated through reduction of CMRO$_2$ during arrest and increased cerebral oxygen delivery during the cooling phase prior to arrest and during the reperfusion and rewarming phase after arrest.

Hematocrit

It has long been assumed that hemodilution is an essential component of DHCA because hemodilution offsets the viscosity and rheologic changes that can compromise microcirculatory flow during low temperature CPB. Recent laboratory studies demonstrate that a hematocrit of 30% does not impair cerebral microcirculation during or after DHCA. Furthermore, a hematocrit of 10%

severely compromises cerebral oxygen delivery during cooling prior to DHCA. In addition, a higher hematocrit (30% compared to 20% or 10%) during cooling and at the onset of DHCA extends the interval of DHCA that can be tolerated without neurologic injury.

Arterial oxygen partial pressure (Pao$_2$) management during CPB for DHCA

Normoxic reperfusion is superior to hyperoxic reperfusion in mitigating free radical-induced neuronal injury following neuronal ischemia. Hyperoxic CPB and DHCA results in more free radical damage than normoxic CPB and DHCA. However, this damage is offset by the more severe hypoxic neuronal damage that accompanies normoxic CPB and DHCA. This is likely due to the fact that the majority of the brain's oxygen requirements during DHCA are met by dissolved oxygen. Hyperoxic CPB clearly increases the amount of dissolved oxygen available to the brain.

Conduct of DHCA

Cooling for DHCA involves both surface and core cooling. Surface cooling in neonates and infants surface is very effective and is initiated once surgical preparation begins. In adults, surface cooling is generally less effective given their smaller surface area to weight ratio. Surface cooling is accomplished using unwarmed intravenous fluids, unhumidified gases, reducing the room temperature to 10–12°C, setting the heating/cooling blanket to 4–5°C, and packing the patient's head in ice. These techniques allow the patient to be cooled to 30–32°C before beginning CPB and core cooling. Surface cooling requires close observation of the progression of the operative procedure as premature cooling can predispose to dysrhythmias (bradycardia, ventricular irritability) and hypotension.

The most effective method of cooling for DHCA is core cooling on CPB. A vasodilator such as sodium nitroprusside or phentolamine (0.2 mg/kg) may be administered into the CPB circuit as core cooling commences to promote vasodilation and more homogenous cooling. A vasodilator may also be used before core rewarming. Methylprednisolone (30 mg/kg in infants and neonates, 1 g in adults),

magnesium sulfate, lidocaine, and mannitol are often added to the CPB prime. The minimum hematocrit during cooling, arrest, and rewarming is unknown, however many believe it should be >25%. Based on clinical trial data, many centers aim for a hematocrit of 30% during these intervals in neomates and infanta. Anesthetic agents (synthetic opioid and benzodiazepine) and a muscle relaxant are administered prior to DHCA to minimize oxygen consumption during cooling and arrest.

Ideally, DHCA should commence when the electroencephalogram (EEG) is isoelectric and CMRO$_2$ is minimal. In adults, it is necessary to obtain a nasopharyngeal temperature of 12–18°C or to have cooled the patient on CPB for more than 50 minutes to obtain this goal. In neonates and infants this is generally accomplished with 15–20 minutes of cooling and a tympanic membrane temperature <15°C. At this point the rectal temperature is invariably <18°C. Longer intervals of core cooling should be used for children with extensive systemic to pulmonary artery collaterals.

pH-stat management is generally used in pediatric patients while α-stat management is more commonly used in adults. pH-stat management is used once patient tympanic membrane temperature is below 30°C during both cooling and rewarming. Four different mixtures of oxygen/carbon dioxide for use as the sweep gas in the membrane oxygenator are available: 97% oxygen/3% carbon dioxide, 96% oxygen/4% carbon dioxide, 95% oxygen/5% carbon dioxide, and 94% oxygen/6% carbon dioxide. The use of carbon dioxide in the membrane oxygenator sweep gas is summarized in Table 13.1.

In smaller infants and in patients with extensive APCs the next higher mixture of oxygen/carbon dioxide than normally indicated is utilized. When

Table 13.1 The use of carbon dioxide (CO_2) in the membrane oxygenator sweep gas.

Patient temperature (°C)	% O$_2$/CO$_2$
30–28	97/3
28–22	96/4
22–15	95/5

CPB commences the perfusate is at 30°C having been previously recirculated with the chosen oxygen/carbon dioxide mixture.

Target brain temperature at the end of rewarming on CPB is 35–36°C. Slow core rewarming will allow this target temperature to be reached without inducing cerebral hyperthermia as it is detrimental to neurological outcome following DHCA. At no point in the rewarming process should rectal, esophageal, or tympanic membrane temperatures exceed target brain temperature if cerebral hyperthermia is to be avoided. Slow core rewarming also ameliorates temperature afterdrop following termination of CPB by promoting more homogenous somatic rewarming.

Alternatives to DHCA

In an effort to prevent the potentially deleterious effects of DHCA on cerebral perfusion and oxygenation, efforts have been directed toward technical innovations to avoid the use of DHCA. Currently both antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP) are used clinically. Whether these techniques can reliably extend the period of safe DHCA remains to be determined.

Antegrade cerebral perfusion

Arterial CPB circuit flow can be delivered selectively to the cerebral circulation antegrade via the circle of Willis following cannulation of the innominate artery or right carotid artery. With this technique, the arch vessels are snared and the descending aorta is cross-clamped to provide a bloodless operative field (Fig. 13.1). In neonates and infants, ACP is commonly called regional low flow perfusion (RLFP). The technique is similar to that used in adults except that a graft may be placed on the innominate artery to provide access for the cannula. This graft can then be used as a modified Blalock–Taussig shunt (innominate artery to right pulmonary artery).

The optimal flow rates, delivery pressure, temperature, and acid-base balance (pH-stat or α-stat) of the selective cerebral perfusate have yet to be determined. Cerebral overperfusion is a potential risk with this technique. In adults, flow rates of 200–250 mL/min at a temperature
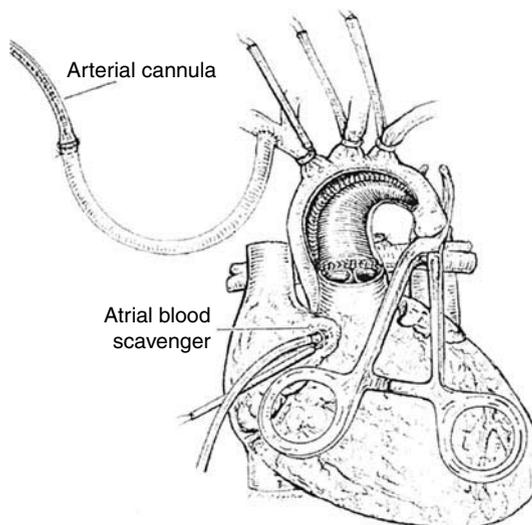
Fig. 13.1 Schematic of the operative field during the ascending aorta and aortic arch reconstruction portion of hypoplastic left heart syndrome repair utilizing antegrade cerebral perfusion (regional low flow perfusion). Cerebral blood flow is supplied by an arterial cannula from the cardiopulmonary bypass (CPB) circuit placed in the distal portion of a graft anastomosed to the innominate artery. The proximal portions of the innominate artery, left carotid artery, and left subclavian artery are snared and the descending aorta is cross-clamped to provide a bloodless operative field. The graft will later be used to create a modified Blalock–Taussig shunt (innominate artery to right pulmonary artery). (From Pigula FA. Arch reconstruction without circulatory arrest: Scientific basis for continued use and application to patients with arch anomalies. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2002;**5**:105, with permission.)

of 8–12°C with α-stat management are generally utilized. In neonates and infants, flow rates of 40–80 mL/kg/min at a temperature of 15–22°C with pH-stat management are generally utilized.

Retrograde cerebral perfusion

Arterial CPB circuit flow can be delivered selectively to the cerebral circulation retrograde via the cerebral venous system. The superior vena cava (SVC) is cannulated with proximal snaring of the SVC below the azygous vein and above the right atrium. Arterial output from the CPB circuit is directed to this cannula to provide retrograde cerebral perfusion via

the SVC and azygous venous system. The descending aorta is cross-clamped but the arch vessels must be left open to atmosphere to provide low-pressure arterial drainage. RCP provides some cerebral perfusion, helps to maintain cerebral hypothermia, and washes debris out of the arterial system. In order to prevent run-off of blood from the cerebral venous circulation into the lower body venous circulation during RCP it is necessary to maintain lower body venous pressure. This is accomplished with partial rather than complete exsanguination of the patient via the venous cannula following DHCA and prior to RCP.

The optimal flow rates, delivery pressure, temperature, and acid-base balance (pH-stat or α-stat) of the selective cerebral perfusate have yet to be determined. Cerebral edema is a potential risk with this technique. In adults, flow rates of 200–300 mL/min at a temperature of 8–12°C with α-stat management at a pressure of 25 mmHg are generally utilized.

Adjuncts to DHCA

In an effort to mitigate the neuronal damage that accompanies the use of DHCA a number of adjunct therapies have been investigated.

Thiopental

Barbiturates offer no protection from global anoxia, which is the primary insult induced by DHCA. Barbiturates administered in association with DHCA (approximately 1.0 g in adults) do offer enhanced cerebral metabolic suppression in the setting of incomplete brain cooling and amelioration of injury induced by cerebral air emboli during rewarming (focal ischemic event). Barbiturates administered during cooling for DHCA are potentially deleterious because they reduce cerebral blood (the primary mechanism of brain cooling) and prevent cooling-induced accumulation of high-energy phosphate stores and increased intracellular pH. Due to a lack of good clinical data, no clear consensus exists as to the utility of barbiturates in ameliorating neuronal injury associated with DHCA.

Steroids

The role of steroids in mitigating neuronal damage following DHCA is unclear. Studies to date have not demonstrated clear benefit. However, it has been suggested that administration several hours prior to initiation of DHCA is of more beneficial than administration in the CPB pump prime.

Investigational agents

Several agents including inhalational anesthetics (particularly desflurane), inhibitors of oxygen free radical generation such as allopurinol and leuko-depleted blood are currently being investigated as agents to mitigate neurologic injury associated with DHCA.

Hematocrit on CPB and transfusion of blood products

The issues surrounding transfusion of red cell and blood component therapy in adult cardiac surgical patients is complex and has received a great deal of attention in the last several years. Both low hematocrit on CPB and perioperative transfusion to treat low hematocrit have been implicated in the full range of adverse outcomes following cardiac surgery. Analysis of this relationship is hampered by the fact that most of the data are drawn from observational studies rather than from controlled randomized trials and by the relative heterogeneity of the study groups compared. Neither the minimal allowable hematocrit on CPB nor the relative risk/benefit of perioperative transfusion to treat low hematocrit are clearly defined.

The risks associated with a reduced hematocrit on CPB can be summarized as follows:

- *Renal dysfunction.* CPB hemodilution to a threshold hematocrit ranging from <21% to <26% is associated with increased likelihood of postoperative renal dysfunction including acute renal failure and the requirement for renal replacement therapy (dialysis). This decrease in renal function is also associated with increased operative mortality and hospital stay. An oxygen delivery <272 mL/min/m^2 in conjunction with CPB hemodilution is associated with postoperative acute renal failure.
- *Neurologic dysfunction.* Nadir hematocrit on CPB is an independent predictor of perioperative stroke with each 1% decrease in hematocrit below 29%

associated with a 10% increase in the odds of suffering a perioperative stroke.

● *Poor overall outcome.* Lowest hematocrit on CPB is associated with increased mortality, intra-aortic balloon pump placement, intensive care unit (ICU) and hospital stay, return to CPB and worse 0–6 year survival.

The risks associated with perioperative transfusion of packed red blood cells (PRBC) and other blood products are summarized as follows:

● *Infectious complications.* Perioperative transfusion of PRBC in patients undergoing cardiac surgery is associated with an increased risk of septicemia and bacteremia, superficial and deep wound infections, and nosocomial pneumonia. Transfusion of other blood products such as platelets, fresh frozen plasma, and cryoprecipitate may also increase the risk of infectious complications.

● *Poor overall outcome.* Perioperative transfusion of PRBC in patients undergoing cardiac surgery is associated with an increased risk of postoperative morbidity from all causes (cardiac, renal, neurologic, respiratory, and infectious). Each unit of PRBC transfused incrementally increases the risk of an adverse outcome. In addition, perioperative transfusion of PRBC is associated with reductions in short-term survival, long-term survival (5–10 years), and quality of life. There is conflicting evidence as to whether platelet transfusions are associated with adverse clinical outcomes.

It is unclear whether use of leukoreduced or leukodepleted blood products mitigates the risk of perioperative blood transfusion. Likewise, there is conflicting evidence as to whether the age of banked transfused PRBC contributes to the risk of transfusion. The most prudent course is to avoid a low hematocrit on CPB and to limit perioperative transfusion of blood products whenever possible. This requires a multi-modal approach using some or all of the techniques outlined in Table 13.2.

Neurologic outcome following cardiac surgery

Neurologic complications following adult cardiac surgery include stroke, encephalopathy, and cognitive dysfunction. Stroke occurs in approximately

Table 13.2 Interventions to limit blood product transfusion in cardiac surgery.

Prevent and treat preoperative anemia
● Limit preoperative blood drawing for testing
● Appropriate interval between preoperative autologous blood donation and elective surgery
● Recombinant human erythropoietin (EPO) and supplemental iron administration more than 1 week prior to surgery

Pharmacological interventions to limit perioperative blood loss
● Antifibrinolytic agents:
a Aprotinin
b Lysine analogues (tranexamic acid, ε-aminocaproic acid)

● Desmopressin (DDAVP, 1-deamino-8-D-arginine vasopressin)
● Recombinant factor VIIa (rFVIIa)

Intraoperative salvage of blood
● Use of cell saver during re-operative procedures
● Salvage and transfusion of CPB circuit volume following termination of CPB

Hemoconcentration on CPB
● Continuous ultrafiltration (CUF)
● Modified ultrafiltration (MUF)

Reduce CPB circuit prime volume
● Use of smallest possible tubing length/diameter
● Use of smallest possible venous reservoir/oxygenator system
● Retrograde autologous priming (RAP)

Point of care testing (POCT) to identify coagulation defects
● ACT
● Protamine titration
● Thromboelastography (TEG)
● Platelet count, fibrinogen level, PT, aPTT

ACT, activated clotting time; aPTT, activated partial thromboplastin time; CPB, cardiopulmonary bypass; PT, prothrombin time.

1–3% of patients while postoperative cognitive dysfunction is far more common affecting upwards of 30–65% of patients at 1 month and 20–40% of patients at 6 months. The etiology of these neurologic complications is complex and involves the

interplay of several variables including cerebral emboli, global cerebral hypoperfusion, systemic inflammatory response, and genetic predisposition. The fact that the incidence of cognitive dysfunction and stroke following off-pump coronary artery bypass graft surgery (CABG) and on-pump CABG is not significantly different emphasizes the complex, multi-factorial nature of this problem.

Cerebral emboli

Both micro- and macroemboli are delivered to the brain during CPB despite the use of arterial and venous filters. There is concern that the increased CBF associated with pH-stat management can contribute to neurologic morbidity by increasing the embolic load to the brain and by inducing intra-cerebral steal of blood flow. This contention is unproven; nonetheless, α-stat management remains the standard during adult CPB.

Particulate macroemboli are generally composed of atheromatous or calcific debris from the aorta, cardiac valves, or great vessels. Microemboli can be gaseous or particulate. Particulate microemboli arise primarily from fat, marrow, bone wax, and other material in the pericardial well that are aspirated into the CPB circuit via cardiotomy suction. Gaseous microemboli arise from air that is introduced directly into the heart during open cardiac chamber procedures or from air introduced into the CPB circuit. Perfusionist interventions, specifically injection of drugs (and air) into the venous reservoir, and entrainment of air around the venous cannula introduce air into the venous reservoir that can transit the oxygenator and arterial line filter to reach the arterial circulation as microemboli.

Cerebral emboli are associated with neurocognitive deficits and stroke following cardiac surgery. The number of cerebral microemboli (microembolic load) delivered during CPB is related to the development of cognitive dysfunction occurring following CABG surgery. However, similar degrees of cognitive dysfunction occur following CABG and cardiac valve surgery despite the fact that the cerebral gaseous microembolic load is higher during valve surgery. This suggests that the type of cerebral microemboli may be a more important factor than the number of microemboli in the development of cognitive dysfunction. Lipid microemboli, such as those generated with use of cardiotomy suction, are particularly damaging to the cerebral microvascular endothelium and probably play a significant role in the genesis of microembolic cognitive dysfunction. Cerebral macroembolic load, as measured by the extent of aortic atheromatous disease (atheromatous burden), is associated with stroke following cardiac surgery. The role of macroemboli in the genesis of cognitive dysfunction is less clear.

Methods to reduce microemboli

A number of modifications to the CPB circuitry and surgical technique have been utilized to reduce particulate and gaseous microemboli. They are summarized below. Although none of these modifications has been conclusively shown to be of benefit in reducing neurocognitive deficits, each reduces the number of emboli detected by echocardiography or transcranial Doppler.

- Reduce perfusionist interventions and surgical field venous line manipulations to a minimum. The perfusionist should carefully remove air from all syringes prior to drug or flush administration. Hard shell venous reservoirs allow air to rise to the top possibly reducing the number of venous air emboli that reach the arterial circulation as compared to soft shell venous reservoirs.
- Diversion of cardiotomy suction to cell-saver or discarding cardiotomy suction to avoid contamination of the venous reservoir with particulate microemboli.
- Use of a gas diffuser to insufflate carbon dioxide into the surgical wound to displace air with more soluble and more easily absorbed carbon dioxide during open chamber procedures.

Methods to reduce macroemboli

Efforts to reduce macroemboli employ strategies to reduce dislodgement of atherosclerotic debris from the ascending aorta. These strategies as applied to CABG are summarized:

- Use of epiaortic ultrasonic scanning to identify aortic cannulation and aortic manipulation sites free of atheromata.

- Use of "no-touch technique" where the proximal ends of saphenous vein or radial artery grafts are "Y-ed" off an internal mammary artery graft to avoid a partial occluding (site-biting) clamp on the aorta.
- Use of "single cross-clamp technique" where proximal aortic graft anastomoses are constructed after the aortic cross-clamp is placed without use of partial occluding (site-biting) clamp on the aorta.
- Cannulation of the axillary artery, innominate artery or the distal aortic arch when atheromatous disease of the ascending aorta is severe and diffuse. Alternatively, DHCA can be used to replace the ascending aorta.
- Use of an aortic cannula with a deployable intra-aortic 120-μ filter to capture particulate emboli "sandblasted" or dislodged from the aorta by turbulent flow from the aortic cannula.
- Use of a longer aortic cannula to reduce turbulence in the aorta and potentially reduce creation of microemboli.
- Use of off-CPB technique in combination with a "no-touch technique".

Use of these strategies show promise in reducing stroke and cognitive dysfunction. It remains to be determined whether off-pump CABG per se results in better neurologic outcome as compared to on-pump CABG when appropriate measures to deal with an atheromatous aorta are utilized with each approach.

Cerebral hypoperfusion

Given what is known about cerebral autoregulation in adults, a mean arterial pressure (MAP) ≥ 50 mmHg on CPB is commonly targeted. Clear evidence supporting this target MAP during CPB is lacking however. There is no consistent link between a MAP < 50 mmHg on CPB per se and subsequent neurologic dysfunction. The combination of reduced MAP (<50–60 mmHg) on CPB and a large burden of aortic atheromata may increase the risk of CPB related stroke. Cerebral injury induced by macroemboli is presumably exacerbated by the reduced collateral perfusion accompanying hypotension. The neurologic sequalae of a reduced MAP during CPB in patients with cerebrovascular disease or with impaired cerebral autoregulation (elderly patients, hypertensive patients, diabetics, patients with prior strokes) has not been systematically investigated. Given the currently available data, maintenance of MAP ≥ 50 mmHg on CPB is reasonable and a higher target MAP (70–90 mmHg) is indicated for patients at high risk for neurologic dysfunction.

Pharmacologic interventions to improve neurologic outcome

A wide range of pharmacologic agents has undergone investigation as neuroprotective agents in adults undergoing cardiac surgery. To date, lidocaine, remaceamide (an NMDA antagonist), and aprotinin have shown the most promise. In retrospective analyses, high-dose aprotinin use has been associated with a reduced incidence of neurocognitive deficits and stroke following cardiac surgery. These conclusions require verification in placebo-controlled, randomized trials. The mechanism of aprotinin's neuroprotective effect is unknown. It may be due to its anti-inflammatory properties or to an associated reduction in cerebral microemboli as the result of the reduced use of cardiotomy suction and platelet transfusions. Lidocaine blocks voltage-dependent fast sodium channels, reduces cerebral metabolic rate, and reduces release of the excitatory neurotransmitters. Remaceamide blocks the effects of ischemia induced glutamate release on NMDA channels and thereby prevents the influx of calcium that exacerbates neuronal injury and death.

Renal function

Acute renal failure in adults following cardiac surgery is a major source of morbidity and mortality. The incidence and outcome in children is remarkably similar to adults. Approximately 13% of adults with a normal serum creatinine (<1.0 μmol/dL) have occult renal insufficiency defined as a creatinine clearance <60 mL/min. These patients have a risk (odds ratio of 2.8) for postoperative dialysis. This is similar to patients with mild renal insufficiency defined as a serum creatinine between 1.0 and 1.33 μmol/dL. Creatinine clearance can be

calculated using the Cockcroft–Gault equation:

C_{CR} (mL/min)

$= [(140 - \text{age}) \times \text{weight}]/(P_{CR} \times 72)$ for men;

C_{CR} (mL/min)

$= [(140 - \text{age}) \times \text{weight}]/(P_{CR} \times 85)$ for women.

Where C_{CR} = creatinine clearance, P_{CR} = serum creatinine in milligrams/deciliters (mg/dL), age in years, weight in kilograms (kg).

The etiology of renal failure following cardiac surgery and CPB is multi-factorial with both ischemic and direct nephrotoxic etiologies. Low flow, nonpulsatile CPB may produce renal perfusion pressures below the limit of renal autoregulation resulting in ischemia-reperfusion injury. This insult is exacerbated by CPB hemodilution. Although it is clear that CPB plays a role in the genesis of renal dysfunction following cardiac surgery, it is only one of multiple factors as evidenced by the fact that off-CPB cardiac surgical procedures do not have a lower incidence of renal dysfunction than on-CPB procedures. Atheromatous aortic emboli have been implicated in the genesis of renal failure as well. Mediators released as part of the systemic inflammatory response, particularly tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), produce renal microvascular changes that can result in tubular damage. Finally, many cardiac surgical patients will be exposed to nephrotoxic angiographic contrast agents preoperatively. It is important to point out that patients with pre-existing renal dysfunction are at no greater risk than patients with normal renal function for renal injury. However, patients with pre-existing renal dysfunction are at greater risk for acute renal failure and the requirement for renal replacement therapy following a given renal insult than patients with normal renal function.

A number of interventions commonly employed to prevent renal dysfunction following cardiac surgery and CPB particularly in high-risk patients are summarized:

- Prophylactic infusion of sodium bicarbonate (154 mmol/L at 3 mL/kg/h prior to angiographic contrast administration and at 1 mL/kg/h for 6 hours after administration) is probably superior
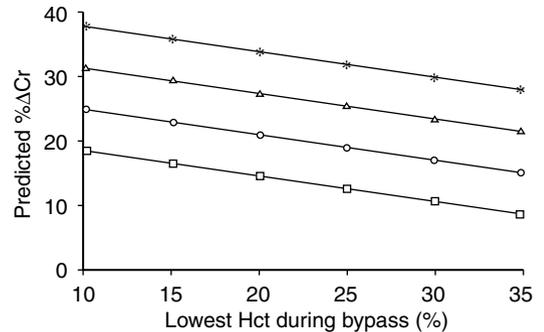
Fig. 13.2 The influence of intraoperative blood transfusion on the relationship between fractional change in creatinine (%ΔCr) and lowest hematocrit (Hct) on cardiopulmonary bypass. Parallel lines represent the number on units of packed red blood cells transfused intraoperatively: * = 9 units; Δ = 6 units; O = 3 units; □ = 0 units. Both low hematocrit on cardiopulmonary bypass and transfusion to treat the low hematocrit contribute to the development of renal dysfunction. (From Swaminathan M, *et al*. The association of lowest hematocrit during cardiopulmonary bypass with acute renal injury after coronary artery bypass surgery. *Ann Thorac Surg* 2003;**76**:789, with permission.)

to prehydration in preventing contrast medium-induced nephropathy.

- Preload and cardiac output should be optimized in both the pre- and post-CPB periods.
- A hematocrit <25% on CPB should be avoided, keeping in mind that PRBC transfusion to treat a low hematocrit increases the risk of developing renal dysfunction (Fig. 13.2). Strategies to avoid CPB hemodilution and transfusion are summarized in Table 13.2.
- Maintenance of CPB flow rates ≥ 2 L/min/m^2 and mean arterial pressure ≥ 50–70 mmHg are probably prudent in high-risk patients. A more important determinant than pump flow may be the product of pump flow and arterial oxygen content with a critical valve of 272 mL/min/m^2.
- No meaningful correlation between urine output on CPB and postoperative renal function has been demonstrated.
- Prophylactic administration of "low-dose" or "renal dose" dopamine (1–3 μg/kg/min) increases urine output but has not been demonstrated to improve or prevent perioperative renal dysfunction.

There is concern that prophylactic dopamine administration may not be benign given the fact that it is associated with release of markers such as β_2-microglobulin that are indicative of sub-clinical renal tubular injury. In addition, prophylactic dopamine administration may compromise splanchnic mucosal perfusion and predispose to development of postoperative atrial fibrillation.

• Prophylactic administration of low doses of the selective dopamine-1 receptor (D_1) agonist fenoldopam mesylate (0.01–0.03 µg/kg/min) may be renoprotective particularly in patients with pre-existing renal dysfunction. At higher dosages fenoldopam has a vasodilator profile similar to sodium nitroprusside.

• Diuretic administration (furosemide, mannitol) in conjunction with CPB increases urine output but is not renoprotective and may in fact be associated with an increased risk of serum creatinine elevation and acute renal failure due to part to the neuro-hormonal effects (renin–angiotensin–aldosterone) of preload reduction and hypovolemia.

Inflammatory sequalae of cardiac surgery and CPB

Cardiac surgery and CPB are known to be a potent stimulus for initiation of both pro- and anti-inflammatory responses. The balance of the elicited pro- and anti-inflammatory mediators determines the clinical manifestations of this response. A preponderance of anti-inflammatory mediators produces the compensatory anti-inflammatory response syndrome (CARS) while a preponderance of pro-inflammatory mediators produces the systemic inflammatory response syndrome (SIRS). SIRS is characterized by tissue and endothelial injury leading to enhanced capillary permeability (capillary leak syndrome) and transmigration of leukocytes into interstitial fluid with subsequent activation of sequestered leukocytes and amplification of the inflammatory process. The spectrum of SIRS induced responses range from tissue edema to end-organ dysfunction and failure. Immediate postoperative fever and leukocytosis is a common relatively benign manifestation of SIRS. Postoperative sepsis and SIRS is more likely in cardiac surgery patients who have reduced monocyte human lymphocyte antigen DR (HLA-DR) expression. This reduced expression is felt to be a manifestation of the relative predominance of anti-inflammatory stimuli over pro-inflammatory stimuli resulting in a state of immunoparesis.

The systemic inflammatory response associated with cardiac surgery and CPB is initiated by a variety of stimuli. Contact activation, heparin-protamine complexes, endothelial ischemia/reperfusion injury, and gut translocation of endotoxins have been implicated. Mechanical sheer stress, hemodilution, hypothermia, autotransfusion of unprocessed shed blood, and use of cardiotomy suction play a role. Genetic polymorphisms influence the response to initiating stimuli. The magnitude of the inflammatory response is enhanced in neonates, infants and small children due, in part, to the high circuit surface area to blood volume ratio as compared to adults.

Initiating stimuli induce the release of inflammatory mediators via a number of pathways as summarized in Fig. 13.3. The complement cascade is activated via both the classic and alternative pathway. Exposure of blood to the CPB circuit results in conversion of factor XII to factor XIIa with initiation of thrombin formation. In addition, factor XIIa leads to conversion of prekallikrein to kallikrein with production of bradykinin and alternative pathway activation (C3) of the complement cascade. This process is exacerbated by the fact that the CPB circuit lacks the endothelial cell surface inhibitors that normally limit C3 activation. Endotoxin and ischemia/reperfusion mediators also initiate complement activation via the alternative pathway. Activation of the complement pathway via the classical pathway (C1 and C4) occurs due to the presence of heparin-protamine complexes.

There is production and release of both pro- and anti-inflammatory cytokines from activated monocytes, macrophages, lymphocytes, and vascular endothelium. Cytokines are inflammatory mediators that can act on the cells that produced them (autocrine), on cells in the vicinity (paracrine) or systemically (endocrine). The intensity of the inflammatory response as measured by
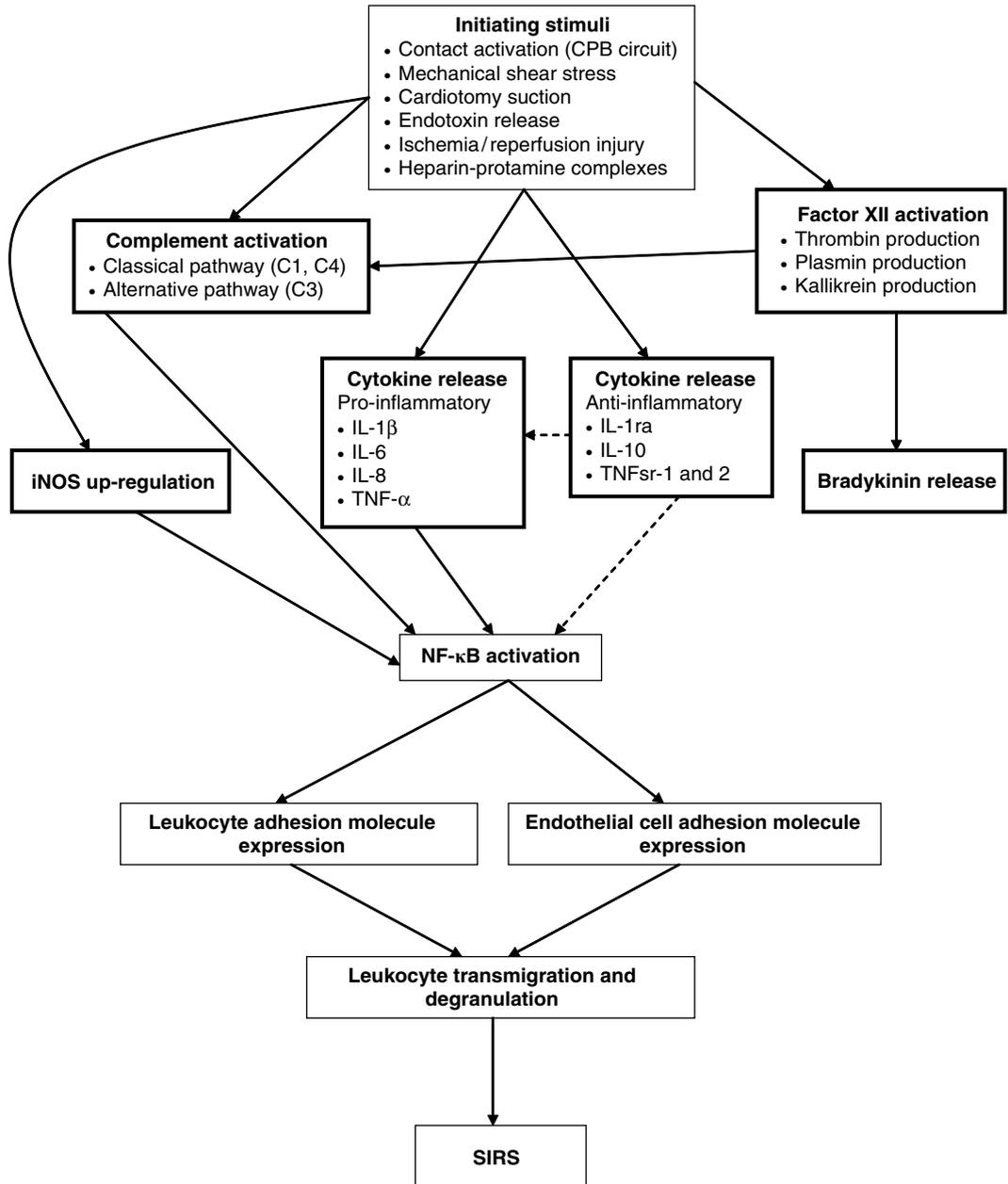
Fig. 13.3 Schematic of the inflammatory cascade associated with cardiac surgery and cardiopulmonary bypass leading to systemic inflammatory response syndrome (SIRS). Inflammatory mediators are in bold boxes. Solid arrow and line is stimulatory. Dashed arrow and line is inhibitory. CPB, cardiopulmonary bypass; IL, interleukin; iNOS, inducible nitric oxide synthase; NF-κB, nuclear factor-κB; ra, receptor antagonist; TNF, tumor necrosis factor; TNFsr, tumor necrosis factor soluble receptor.
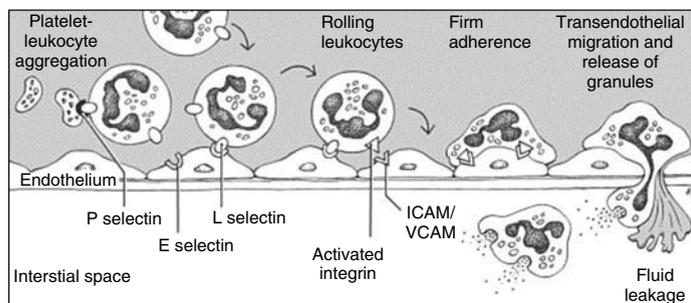
Fig. 13.4 Schematic of leukocyte–platelet–endothelial cell interaction leading to leukocyte margination, rolling, and adhesion. Transmigration of a leukocyte across the endothelial cell layer followed by leukocyte degranulation is illustrated. ICAM, intercellular adhesion molecule; VCAM, vascular cell adhesion molecule. (From Paparella D, *et al*. Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. *Eur J Cardiothorac Surg* 2002;**21**:232–244, with permission.)

pro-inflammatory cytokine levels such as TNF-α, IL-1β, IL-6, and IL-8 has been linked to the development of end organ dysfunction (myocardial, pulmonary, renal, hepatic) and sepsis in the perioperative period. Endothelial inducible nitric oxide synthase (iNOS) is up-regulated by the inflammatory process resulting in higher levels of NO. These higher levels result in increased vascular permeability and vasodilatation. Bradykinin release results in vasodilation and enhanced vascular permeability as well.

Production of these inflammatory mediators leads to induction of nuclear factor κB (NF-κB), the transcription factor responsible for expression of both endothelial and leukocyte adhesion molecules (selectins and integrins). These molecules promote the margination, rolling, adhesion, and transmigration of leukocytes through the endothelium into the extravascular space (Fig. 13.4). Degranulation of leukocytes releases elastase and myeloperoxidase that lead to tissue damage. Release of cytokines by these leukocytes further escalates the inflammatory response. In addition, once NF-κB is induced it up-regulates cytokine production.

A number of different approaches aimed at effective attenuation of SIRS following cardiac surgery have been investigated (Table 13.3) but none have proven uniformly effective. This is not surprising considering the multi-mediator nature of the systemic inflammatory response. A multi-modal approach will likely be needed. Nonetheless, the two most commonly employed drug therapies are aprotinin and glucocorticoids.

Table 13.3 Therapies to modulate the systemic inflammatory response to cardiac surgery and cardiopulmonary bypass (CPB).

Avoidance of CPB
- Off-pump coronary artery bypass grafting (OPCAB)

Modification of the CPB circuit
- Use of biocompatible CPB circuits:
a Covalent heparin binding coating
b Phosphorylcholine coating
c Poly 2-methoxyethylacrylate coating
d Siloxane/caprolactone oligomer coating
- Normoxic rather than hyperoxic CPB
- Avoidance of cardiotomy suction
- Avoidance of unwashed autotransfusion

Selective digestive decontamination
- Nonabsorbable oral antibiotics (polymyxin E, tobramycin, amphotericin B)

Hemofiltration on CPB
- Continuous ultrafiltration (CUF)
- Modified ultrafiltration (MUF)
- Dilutional ultrafiltration (DUF)
- Zero-balance ultrafiltration (ZBUF)

Leukocyte depletion
- Use of leukodepleted blood or leukocyte filters

Complement inhibition
- C5 monoclonal antibody (pexelizumab)
- C1-esterase inhibitor
- C4A rich plasma administration to C4A-deficient patients

Free radical scavengers – antioxidants
- Allopurinol
- Mannitol
- Ascorbic acid (vitamin C)
- α-Tocopherol (vitamin E)

Serine protease inhibitors
- Aprotinin

Glucocorticoids
- Methylprednisolone
- Dexamethasone

CPB, cardiopulmonary bypass.

High-dose aprotinin regimens producing plasma levels $\geq 30\,\mu g/mL$ (215 KIU/mL) inhibit CPB-induced kallikrein production. Kallikrein is responsible for production of bradykinin and for activation of the complement system both of which play a prominent role in the genesis of SIRS. Kallikrein is also responsible for production of plasmin, an additional source of complement activation. Aprotinin at lower plasma levels is also capable of directly inhibiting plasmin. Aprotinin also plays an important role in attenuation of SIRS through inhibition of up-regulation of pro-inflammatory adhesion molecules such as the integrin CD11b. Multi-level inhibition of the leukocyte-endothelial cell adhesion cascade by aprotinin inhibits leukocyte transmigration through vascular endothelium. Aprotinin is also capable of inhibiting cytokine-induced production of iNOS.

Glucocorticoids reduce inflammation via a number of mechanisms. They inhibit NF-κB, the main transcription factor of genes for inflammatory proteins and also increase the transcription of many anti-inflammatory proteins such as IL-10- and IL-1-receptor antagonist. In addition, glucocorticoids decrease endotoxin release and leukocyte adhesion molecule (CD 11b) expression. The optimal timing, dosage, and formulation of glucocorticoid administration remain to be determined.

Suggested reading

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