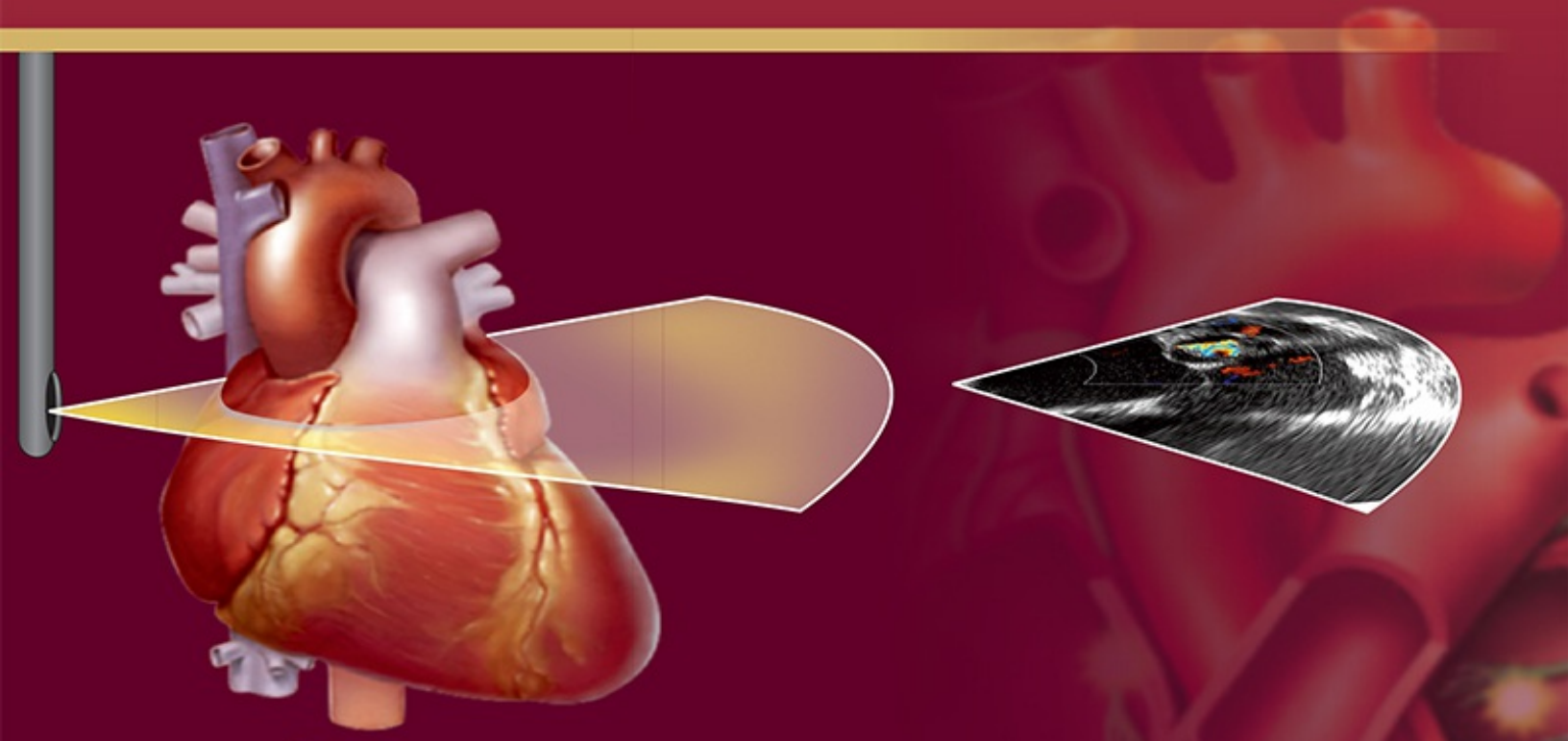
Clinical Practice of Cardiac Anaesthesia

Third Edition



Deepak K. Tempe

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Third Edition

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to
my parents
who have made me capable of
what I am today
and Anjali (my wife)
and Anuradha (my daughter)
who have made my life
so much more enjoyable

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Preface

The second edition of **Clinical Practice of Cardiac Anaesthesia** was published in 2004 and was received very well. It has been a long time, and the way medicine (especially cardiovascular science) has progressed, there has been a significant change in our understanding and practice of the subject. Thus, the need for a new edition has been in existence for quite sometime. However, revising and updating such a book single handedly is not an easy task. It is not only time consuming, but also physically and mentally tiring. One of the challenges of the book has been to provide the clinically relevant and latest important information without being too extensive. This involves reading quite a bit of recent literature and then filtering it and presenting it in a concise manner. I have tried my best to retain this uniqueness of the book, but some extra pages have been inevitably added.

At one time, I had almost given up the idea of revising the book, but there has been a continued all round pressure on me (from the anaesthesia and also some cardiac surgical residents!). In almost every conference that I attended, the residents queried, “When is the next edition coming?” So, in reality, it is the residents who have inspired me to undertake this job yet again.

A new chapter on cardiac physiology by Professor Neema has been added and all others have been updated to meet the current understanding and requirements of the subject. Some chapters such as haemodynamic monitoring, management of patients with coronary artery disease, blood management, neurological dysfunction, and cardiac patient undergoing noncardiac surgery have been made more comprehensive. Several new pictures of transoesophageal echocardiography have been added to make understanding of this complex subject easy. I believe that the third edition will meet the requirements of all the postgraduate students (cardiac and general anaesthesia), anaesthesiologists who are actively practicing cardiac

anaesthesia as well as those who frequently deal with cardiac patients undergoing noncardiac surgery.

As always, I enjoyed immense support from home and the work place, which is so vital for completion of such projects. All my residents were always helpful in collecting the clinical material (without knowing what it is meant for) and Dr. CS Joshi and Manoj Sanwal were particularly helpful in the proofreading.

Finally, I acknowledge the efforts of Mr. SK Jain, Mr. Varun Jain, Mr. YN Arjuna and Mr. Ashish Dixit from CBS Publishers & distributors (P) Ltd., New Delhi in publishing this ebook.

Deepak K. Tempe

Contents

Chapter 1: Preoperative Assessment of Cardiac Risk

The cardiac disease continues to be a major problem all over the world. In the developing countries, valvular heart disease (VHD) of rheumatic origin continues to constitute a major cardiac health care problem. In addition, during the last two decades, an increasing trend in the number of patients suffering from coronary artery disease (CAD) has been observed. The anaesthesiologist may be required to deal with such patients when they are subjected to either cardiac surgery or non-cardiac surgery. The preoperative assessment of these patients carries significance as it can be helpful in making recommendations concerning the cardiac risk in the perioperative period and providing a clinical risk profile that can be utilised for making the choice of an appropriate anaesthetic plan. In addition, the risk stratification may be useful for efficient assessment of new therapy and technology. Sometimes it may be necessary to alter the medical therapy to optimize the patient's condition before subjecting him to surgery.

Age

With the improvement in medical care and consequent increase in the life expectancy of the population, an increasing number of patients from older age group will be presenting for surgical procedures. In this context, the traditional cut-off value of 65 years dividing the elderly from non-elderly patients may no longer be valid, especially in view of the improved general health of the population. The prevalence of cardiovascular disease increases with age, and perioperative myocardial infarction (MI) is the leading cause of postoperative death in the aged.[1] It has also been shown that the response of the elderly heart to different forms of stress (exercise, catecholamine

stimulation) is depressed.[2] It has been shown that for patients undergoing coronary artery bypass grafting (CABG), the operative mortality is 11.8 percent for patients more than 90 years of age, 7.1 percent for those 80 to 89 years and 2.8 percent for those 50 to 79 years.[3] However, as the overall physiological status of an elderly patient might be affected by other associated diseases, it is difficult to evaluate age as an independent predictor factor. Nevertheless, age is considered an important factor for predicting the risk that has been found to increase with increasing age.

Body Size

Obese patients generally carry a higher statistical risk of death.[4] Some studies have shown the high-risk of morbid obesity in patients undergoing cardiac surgery,[5,6] while others have shown that low body weight or small body surface area is associated with increased risk.[7,8]

Sex

Female sex has been quoted as a risk factor for either morbidity or mortality.[9,10] Some studies, however, have examined both sex and body size in the same population and have shown that it is the small body size, and not sex, that increases the risk.[6,7,11] Without considering the body size, women do appear to be at a higher risk, as they commonly have smaller body surface area compared wilii men. In addition, a study has shown that the higher mortality rate that was observed in women after cardiac surgery was because of a higher baseline risk resulting from the presence of more concurrent risk factors.[12]

Previous Myocardial Infarction

As compared to the general population, the risk of developing perioperative MI is increased considerably in patients with previous MI (older than 1 month). Such re-infarctions occur postoperatively and silently, making them difficult to detect. In addition, the mortality associated with re-infarctions is also much higher. Recent preoperative MI is an important predictor and the risk of infarction exceeds 30 percent within 3 months, and it is 15 percent at 3

to 6 months and approximately 6 percent after 6 months of infarction.[13] However, it has been reported that the mortality rates were improved considerably when the patients were subjected to aggressive monitoring and management during the intraoperative and postoperative period.[14,15] Although, it is reasonable to believe that such monitoring and treatment modalities are likely to improve the outcome, the beneficial effects have not been confirmed. In any case, the management of MI has been revolutionised in the recent times so that these recommendations have a limited role to play. For instance, the importance of intervening time interval between MI and surgery may not be relevant in the current era of thrombolytics and angioplasty. Risk stratification should be performed during convalescence.[16] The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines[17] recommend coronary revascularisation in patients with stable angina having significant left main coronary artery stenosis, three vessel disease, or two vessel disease with significant proximal left anterior descending stenosis, high-risk unstable angina or non-ST segment elevation MI, or with acute ST-elevation MI. In patients in whom coronary revascularisation with percutaneous coronary intervention is appropriate, and non-cardiac surgery is required in subsequent 12 months, a strategy of balloon angioplasty or bare metal stent placement followed by 4 to 6 weeks of dual anti-platelet therapy is probably indicated. In patients who have received drug eluting coronary stents and who must undergo urgent surgical procedures that mandate discontinuation of thienopyridine therapy, it is reasonable to continue aspirin if at all possible and restart thienopyridine as soon as possible. For details, the reader should refer to the guidlines.[17]

In 2009, the first European Society of Cardiology guidelines on perioperative care were developed.[18] Like the ACC/AHA guidelines, the decision making process integrates clinical markers, early coronary evaluation, functional capacity, and the type of surgery involved.

In the developing countries, however, the treatment of acute MI in the form of thrombolysis, angioplasty and surgery may not be available to all the patients so that the earlier recommendations regarding the intervening time interval between MI and surgery should not be considered invalid in them.

Angina

Patients suffering from CAD can be identified by history of classical angina. The pain is of strangulating nature, often occurring with exercise, emotional stress or during meals and is relieved with rest. Anterior chest pain is most common, but may also present as left arm, neck and right arm pain. Other rare sites are chin, forehead and epigastrium. Typical duration of anginal pain is from 5 to 15 minutes. It is important to understand different types of anginal pain as they have different prediction of risk.

Stable angina

It is a substernal pain or discomfort that is precipitated by exercise, relieved by rest or nitroglycerin (NTG) or both in less than 15 minutes and is typically radiated to the shoulder, jaw or the inner aspect of the arm. It is a controversial predictor in non-cardiac surgical patients,[19] but the patient who develops dyspnoea on mild exertion is at a high-risk for developing perioperative ventricular dysfunction, myocardial ischaemia and possible MI. Such patients have a high probability of having extensive CAD, and additional monitoring or cardiovascular testing should be performed.

Angina can be frequently present in patients suffering from aortic stenosis (AS) in the absence of CAD. The reason for this is the increased left ventricular (LV) mass (concentric hypertrophy) as well as decreased coronary perfusion pressure. As AS commonly occurs in young patients in the developing countries (due to rheumatic fever), associated CAD is usually not present. Nevertheless, preoperative coronary angiogram may be performed in all patients with AS above 40 years of age to rule out associated CAD. The combination of AS and ischaemic heart disease (IHD) increases perioperative risk.[20]

Unstable angina

It may reflect cyclic coronary obstruction produced by an unstable thrombus associated with varying degrees of vasospasm and is defined as: (1) Newly developed angina occurring within the past 2 months; (2) Progressively worsening angina occurring with increased frequency, intensity or duration, being less responsive to medicine, and/or rest; or (3) Angina lasting longer than 30 minutes exhibiting transient unresponsiveness to standard therapeutic manoeuvres, including NTG and rest, and which is associated with transient ST-T wave changes without development of Q waves or diagnostic elevation

of enzymes. The presence of unstable angina has been associated with a high perioperative risk of MI.[21] Such patients should, therefore, be referred for further medical or coronary interventions before non-cardiac surgery.

Variant angina

It was described in 1959 by Prinzmetal and coworkers.[22] It usually occurs at rest and is not associated with exercise or emotional stress. These patients have a high incidence of arrhythmia and conduction abnormalities. Although, the perioperative risk in these patients has not been studied, the cardiac morbidity is likely to be higher in view of a higher incidence of arrhythmias.

It should be remembered, however, that the characteristics of an anginal pain have no relation to the anatomical lesions in the coronary arteries in terms of number of vessels involved or the degree of narrowing.

Silent Myocardial Ischaemia

Silent myocardial ischaemia is now recognised as an important predictor of cardiac risk. It has been shown that as many as 75 percent of episodes of significant ST depression are not accompanied by angina and occur at significantly lower heart rates (HR) than symptomatic episodes.[23] The mechanism of silent ischaemia and infarction is unknown, but sensory neuropathy has been labelled as the causative factor, particularly in the diabetics. These events can be detected by ambulatory (Holter) electrocardiography performed during normal daily activities in patients with CAD. There is however, some controversy regarding the utility of this technology in predicting the adverse outcome.[24]

Hypertension

IHD is commonly associated with hypertension. As a risk factor, hypertension is less today since the perioperative management of high blood pressure (BP) has improved. The degree of hypertension is more important and the risk of MI is increased in hypertensive patients, especially in the presence of hypercholesterolaemia, cigarette smoking and ECG abnormality Patients with untreated, poorly treated or labile preoperative hypertension are more likely to suffer perioperative BP lability, dysrhythmias, myocardial

ischaemia and transient neurological complications, thereby increasing the perioperative cardiac morbidity. However, some authors have demonstrated that such is not the case and the importance of preoperative hypertension as a risk factor for postoperative morbidity is controversial.[19]

As per the ACC/AHA guidelines, uncontrolled hypertension is considered as a minor clinical predictor i.e. it does not independently increase the perioperative risk.[17]

Diabetes Mellitus

Diabetes mellitus is a very common systemic disorder associated with CAD and has many important implications. It is considered to be an independent risk factor for preoperative cardiac morbidity. Painless Mis occur more frequently and the infarct size as well as the mortality is reported to be higher in diabetics.[25] In addition, it can also lead to diabetic cardiomyopathy, which by itself can increase the cardiovascular morbidity.[26] According to the ACC/AHA guidelines, diabetes is considered a clinical risk factor.[17] Therefore, diabetes should be considered a potential predictor of perioperative cardiac morbidity.

Cigarette Smoking

The adverse cardiovascular effects of cigarette smoking are well known and an increased risk of MI has been demonstrated in smokers.[27] Acute effects of smoking include increased coronary vascular resistance caused by direct vasoconstrictor effect of nicotine.[28] The myocardial oxygen consumption (MVO_2) may be increased by increasing the rate-pressure product. In addition, the decreased systemic oxygen transport caused by an increase in carboxyhaemoglobin levels can disturb the supply-demand balance. Chronic cigarette use can accelerate atherosclerosis by vasoconstriction, platelet aggregation and loss of endothelial integrity.[29] All these adverse cardiovascular effects, along with the well known detrimental effects of smoking on the respiratory system may increase the risk for cardiac morbidity in these patients.

Previous Cardiac Surgery

The increasing number of cardiac operations performed everyday has led to more patients returning for reoperation. The technical difficulties arising out of adhesions between the heart and surrounding tissues are well known. It has been observed that the tendency to scar formation is more in black as compared to the white population, and therefore, they are likely to have dense adhesions. Bleeding from the adhesions can be profuse and lead to increased blood transfusion requirements. In addition, difficult dissection may require excessive handling of the heart leading to arrhythmias and reduced cardiac output.

In valve replacement surgeries, inadequate mobilisation of the LV apex may impair the deairing of cardiac chambers before release of the aortic cross clamp leading to a higher risk of air embolisation. In addition, these patients are on anticoagulants such as warfarin, and unless the medicine has been discontinued for an adequate period (3 to 7 days), the postoperative bleeding can be increased further.

In general, the patients undergoing reoperation are sicker and carry a higher risk of morbidity and mortality. Previous CABG in patients undergoing non-cardiac surgery has been shown to improve the outcome, and the postoperative incidence of MI in these patients is reported to be 0 to 1.2 percent and mortality 0.5 to 0.9 percent. (MI, 1.1 to 6 percent and mortality, 1 to 2.4 percent in patients without prior CABG).[19]

Combined Procedures

Combined procedures such as CABG and valve replacement increase the operative mortality. Yadav et al[30] have examined the risk factors associated with early mortality in patients undergoing CABG and mitral valve replacement. Significant factors related to early death were, New York Heart Association (NYHA) functional class, urgency of surgery, valvular lesions secondary to an ischaemic event, increased pulmonary artery pressure (mean pulmonary artery pressure of > 30 mm Hg), low ejection fraction (< 40 percent) and low cardiac index. Likewise, patients undergoing aortic valve replacement combined with CABG are at risk for LV dysfunction that may adversely affect the postoperative outcome.[31]

Risk Indices

A number of risk indices have been reported for quantifying the overall risk. These include the American Society of Anesthesiologists (ASA) classification,[32] the NYHA classification[33] (Table 1.1), and the Canadian Cardiovascular Society (CCS) classification of angina.[34] In addition, Goldman et al[35,36] were the first to develop a multivariate risk index using prospective analysis of a large group of patients. Factors such as preoperative cardiac failure and the recent MI that were found to be associated with a high-risk were given a high score. Other factors such as hypertension and smoking were not found to be associated with increased risk and were, therefore, not included as risks. These were later modified by Detsky and Colleagues.[37] Subsequent indices showed similar performance in predicting cardiovascular risk.[38] However, Lee's revised cardiac risk index (RCRI) performed better than previous indices and was also validated.[39,40] The clinical risk factors include high-risk surgery, ischaemic heart disease, history of congestive cardiac failure, history of cerebrovascular disease, insulin therapy for diabetes, and a preoperative serum creatinine of more than 177 μmol/L. It is now incorporated into the ACC/AHA perioperative algorithm.[17] All these risk indices are useful in quantifying not only the preoperative cardiac status of the patient but also in estimation of the risk to which the patient is exposed. However, it should be remembered that the accuracy of these indices is controversial and not consistent. It has been shown that major risk stratification models do not predict perioperative outcome after CABG in patients with previous percutaneous intervention [41] Patients with previous elective percutaneous coronary interventions had increased perioperative mortality and higher rates of major adverse cardiac events as compared with patients without prior percutaneous coronary interventions.[40] It is suggested that the risk assignment should occur throughout the perioperative period (preoperative, intraoperative and postoperative) and the risk factors chosen for model inclusion should vary depending on when the assignment occurs.[42]

Table 1.1: New York Heart Association functional classification

Class I

Patients with cardiac disease but no limitation of physical activity. There is no undue fatigue, palpitation, dyspnoea or anginal pain on ordinary physical activity.

Class II

Patients with cardiac disease leading to slight limitation of physical activity. There is fatigue, palpitation, dyspnoea or anginal pain on ordinary physical activity, but they are comfortable at rest.

Class III

Patients with cardiac disease leading to marked limitation of physical activity. There is fatigue, palpitation, dyspnoea or anginal pain on less than ordinary physical activity, but they are comfortable at rest.

Class IV

Patients with cardiac disease leading to inability to carry out any physical activity without discomfort. Symptoms may be present even at rest. The discomfort is increased if any physical activity is undertaken

Some risk stratification methods more specific to cardiac surgery have also been described. One of the earliest reported methods identified poor ejection fraction (< 30 percent), unstable angina or recent MI, clinical evidence of heart failure, age greater than 65 years, severe obesity, emergency surgery, reoperation and other uncontrolled systemic disturbances as risk factors.[5] Patients are assigned to three risk levels: normal (no risk factor, mortality 0.4 percent), increased (one of the above factors present, mortality 3.1 percent) or high (two or more factors present, mortality 12.2 percent).

The Society of Thoracic Surgeons has developed a model for risk stratification based on more than 80,000 patients undergoing CABG.[43] Thirteen risk factors were identified among which, cardiogenic shock, renal failure and reoperation were labelled as those carrying significant risk.

Cardiac Status

The most important factor for predicting the outcome after surgery is the severity of cardiac disease. The clinician is constantly striving to accurately estimate the severity of disease by history, physical examination and performing several routine as well as specialised tests.

Congestive Heart Failure

Impairment of LV function can lead to an elevation of the pulmonary capillary pressure leading to the classical signs of dyspnoea. Occurrence of dyspnoea and its grading (NYHA classification) can be utilised for estimating the severity of LV dysfunction. However, it has been shown that physical signs may be absent in the presence of marked to severe elevation of LV filling pressure in chronic heart failure.[44]

The most frequent causes include hypertension, IHD, VHD and various cardiomyopathies. In VHD, the breathlessness is not related to LV dysfunction and in fact, may occur in the presence of normal or even supranormal LV function. For instance, in mitral stenosis (MS), the breathlessness is related to the degree of obstruction and the resulting increases in flow gradient across the mitral valve, and in AS it is related to the increased LV end-diastolic pressure (LVEDP) due to concentrically hypertrophied LV that has a poor compliance. Presence of dyspnoea, therefore, does not usually signify LV dysfunction in patients with VHD, unless the disease is in an advanced stage. The possibility of associated VHD in patients with IHD should also be considered, if dyspnoea is present. In fact VHD is an additional risk for a patient undergoing simultaneous CABG and valve replacement, especially for mitral regurgitation (MR) or AS.[20] The severity of symptoms is also related to the rapidity of onset of cardiac failure. Acute insults such as MI, may lead to severe symptoms even though only a small portion of the myocardium is damaged. In conditions that develop slowly such as aortic regurgitation (AR), AS, etc. there is time for compensatory mechanisms to develop and significant portions of the heart muscle may be impaired before symptoms appear.

In patients with CAD, clinical and radiological evidence of LV failure is associated with a poor prognosis.[45] Similarly, patients with ejection fraction of less than 40 percent are likely to have increased mortality. Preoperative

congestive heart failure (CHF) is identified as a risk factor and the presence of third heart sound and jugular venous distention are labelled as significant signs having prognostic value. Echocardiography should be performed in patients with CHF, results of which can suggest strategies for preoperative optimisation of cardiovascular status.

Arrhythmias

These are usually benign in healthy patients, but their occurrence in patients with CAD signifies serious nature of CAD and ventricular dysfunction. Many patients with acute MI still die before reaching the hospital, presumably due to dysrhythmias, and complex dysrhythmias are one of the important factors that influence the prognosis in them.[46]

Frequent premature ventricular contractions increase the risk in patients with chronic IHD. Although, few data are available regarding preoperative arrhythmias as a risk factor, frequent premature atrial contractions, rhythms other than normal sinus or atrial fibrillation (AF) appear to be risk factors.[36] AF due to an enlarged left atrium (LA) is also common in patients suffering from mitral valve disease. Presence of AF signifies a long standing and more severe mitral valve disease.

ECG Abnormalities

ECG abnormalities excluding arrhythmias are considered as preoperative risk factors. ST-T wave changes and signs of LV hypertrophy are the commonest ECG abnormalities detected in patients with CAD. The predictive value of preoperative ECG is controversial. Carliner et al[47] found that an abnormal preoperative ECG was the only statistically significant independent predictor of adverse cardiac outcome. Whereas, Goldman et al have found that ECG abnormalities including old MI, ST segment or T wave changes, or bundle branch block were not significant risk factors.[36] In some valvular lesions such as AS, ST-T abnormalities signifying myocardial ischaemia can be present in the absence of CAD. The predictive value of ischaemic changes in preoperative ambulatory ECG is controversial. One study has claimed that positive finding for ischaemia (ST segment depression) is a predictor of cardiovascular morbidity peri and postoperatively,[48] while others have not been able to demonstrate the same.[49,50]

Priority of Care

The risk of operation may be influenced by emergency versus elective surgery.[6-8] The patient undergoing emergency surgery may have hypovolaemia, systemic vasoconstriction, acidosis or other physiological derangements. There may not be time for the usual careful preparation of the patient. The actual condition of the patient before operation is more important, as an emergency might mean a patient receiving cardiopulmonary resuscitation or may be undergoing a semi-elective or urgent procedure for left main coronary artery disease or mitral stenosis plus LA thrombus. With more experience and improvements in overall technique, the risk in patients undergoing emergency procedures is decreasing.

Preoperative Cardiac Tests

As a part of assessment of the cardiovascular disease, several tests are performed prior to anaesthesia and surgery. The anaesthesiologist may have to interpret and sometimes request these tests prior to anaesthesia. It is, therefore, necessary to have knowledge of the tests and be aware of their role in the preoperative assessment of the patient with cardiac disease.

Laboratory Tests

Some laboratory findings such as hyper-lipidaemia are predictive of CAD. In patients with cholesterol levels of less than 203 mg/dL, only 18 percent had angiographically documented CAD as against 80 percent in patients with cholesterol levels greater than 263 mg/dL.[51] Increased levels of low density lipoproteins are strong predictors of CAD and an inverse association has been demonstrated between high density lipoprotein (HDL) cholesterol level and CAD incidence. The incidence of CAD has been shown to be eight-fold higher in men and women with HDL cholesterol of 35 mg/dL or less as compared with men and women with HDL cholesterol of 65 mg/dL or greater.[52] Thus HDL cholesterol seems to provide protection from CAD. Triglycerides, however, are relatively unimportant for prediction of CAD. The perioperative risk associated with hypercholesterolaemia is not known.

The most important laboratory changes associated with myocardial ischaemia and infarction are cardiac enzyme elevations. The levels of

creatine kinase (CK), glutamic oxaloacetic transferase (GOT) and lactate dehydrogenase (LDH) are elevated. The isoenzyme of CK (MB) that is identified by electrophoresis reflects extraction from cardiac muscle. The CK MB level is a fairly accurate method of diagnosing acute MI and its serial measurements can be useful for predicting the infarct size.[53] GOT and LDH on the contrary are not specific enzymes and false positive readings can occur in patients with other non-cardiac diseases.

In general, the specificity and sensitivity of CK MB for MI are high, however, some drawbacks remain. For example, skeletal muscle content of CK MB (which is normally low) may be increased in patients with acute skeletal muscle injury (rigorous exercise) or chronic myopathies. Consequently, skeletal muscle injury occurring during surgery may increase postoperative concentration of CK MB, thus decreasing CK MB specificity for MI. In addition, the sensitivity of CK MB is limited to a short period as the increase persists for at most, 72 hours. Therefore, early and frequent measurements are necessary.

In this regard, cardiac troponins are relatively new markers that may prove to be more beneficial. With acute MI, plasma troponin concentrations (both troponin T and I) increase rapidly within 3 to 5 hours and continue to remain so for 5 days or more.[54] This allows for earlier detection of MI, as well as late diagnosis. Cardiac troponin I also offers greater specificity in patients with skeletal muscle disease or injury.[55] It has also been suggested that cardiac troponins may provide an insight into the preoperative risk stratification in patients with unstable angina undergoing CABG.[56]

B-type natriuretic peptides (BNP) have been shown to be independent predictors of cardiovascular events in noncardiac and vascular surgery. It has been shown that preoperative BNP levels can be used to independently predict cardiovascular events in the first 30 days after vascular surgery and to significantly improve the predictive performance of the revised cardiac risk index.[57] One study has shown that a preoperative BNP concentration of more than 87.5 pg/mL best predicted long-term all-cause mortality.[58]

In the developing countries, rheumatic fever is the most common cause of VHD. Repeated attacks of rheumatic fever are not unknown in these patients. Thus, patients subjected to valvular surgery should be investigated for evidence of endocarditis. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are almost always elevated during acute stages

of the disease. The surgical outcome in the presence of endocarditis may be compromised due to cardiac failure or increased risk of bleeding due to adhesions and friability of the tissues. Therefore, surgery should be delayed and endocarditis treated with aspirin and steroids, unless the valvular lesion warrants urgent surgery.

The chest radiograph

The routine postero-anterior (PA) and lateral radiographs of chest continue to be used extensively as a preoperative screening test. It provides useful information in both patients with CAD and VHD. Figure 1.1 shows the typical PA projection of the heart. The two boundaries of the heart (right and left) are in proximity with the respective lung fields. The right border of the heart is formed by the superior vena cava (SVC) and the right atrium (RA). The left border is formed by the aorta, the main pulmonary artery (PA), the LA appendage and the anterolateral border of the LV. RA enlargement can be detected by broadening of the right heart contour. The LA enlargement leads to displacement of the LA appendage laterally and the left bronchus upwards. In massive LA enlargements that can occur in some patients with mitral valve disease, the right border of the LA may overlap the right heart border giving an appearance of a double density (Fig. 1.2). Right ventricular (RV) enlargement is difficult to detect in the PA view except in conditions such as tetralogy of Fallot (TOF) where the left border may be formed by the RV with LV rotated posteriorly. On the contrary, LV enlargement can be easily detected using the PA view. In regurgitant lesions of the aortic and mitral valve, the long axis is elongated with downward and leftward displacement of the apex. In patients with CAD, both long and short axis enlargement leads to globular shaped heart. The cardiac valves are not normally visualised unless they are heavily calcified.

The lateral view of chest is most useful in detecting the RV enlargement, which is indicated by obliteration of the retrosternal space along the upper two-thirds of sternum (Fig. 1.3). It can also be useful in patients undergoing reoperation to know if the RV is adherent to the sternum.

Radiographic changes in valvular diseases

Individual valvular diseases can be differentiated with ease based on the radiographic presentation. In MS, LV size is normal, but LA, PA and RV enlargements are present. In MR, both LA and LV enlargement occur that

can further lead to pulmonary hypertension and RV enlargement. In AR, there is dilatation of the LV along with dilatation of the ascending aorta. The concentric hypertrophy of the LV in AS is not perceived radiographically. However, with advanced AS, LV dilatation and cardiomegaly occurs.

In patients with CAD, the chest radiograph provides useful information in the sense that cardiomegaly has been shown to be a specific predictor of low ejection fraction (< 0.40).[59]

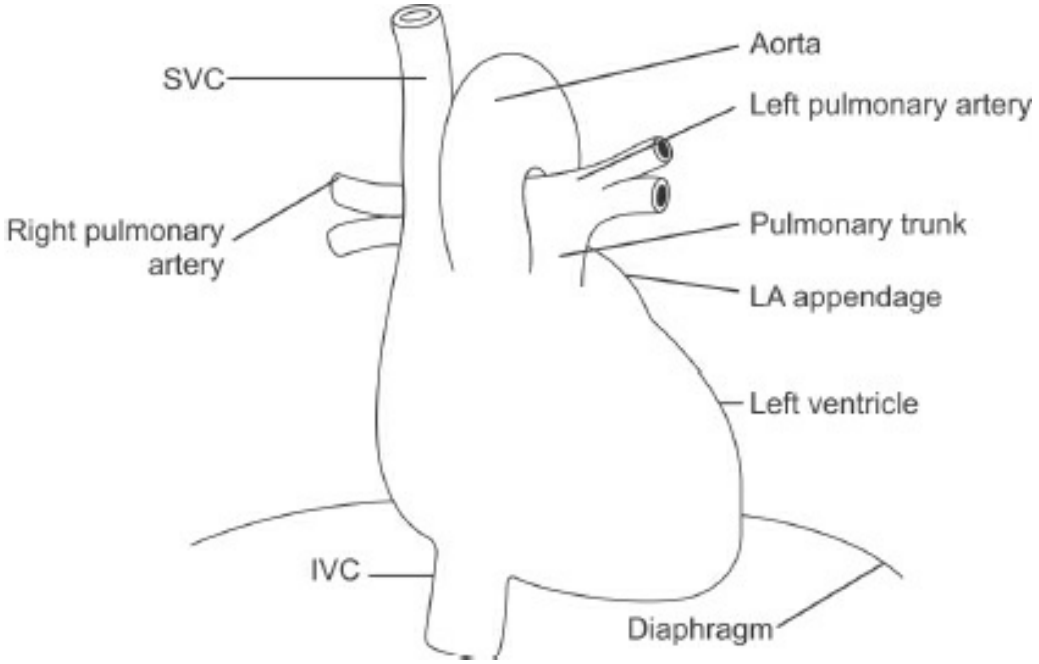

Figure 1.1A: Diagrammatic representation of the frontal projection of heart. (SVC: superior vena-cava, IVC: inferior vena-cava, LA: left atrium).

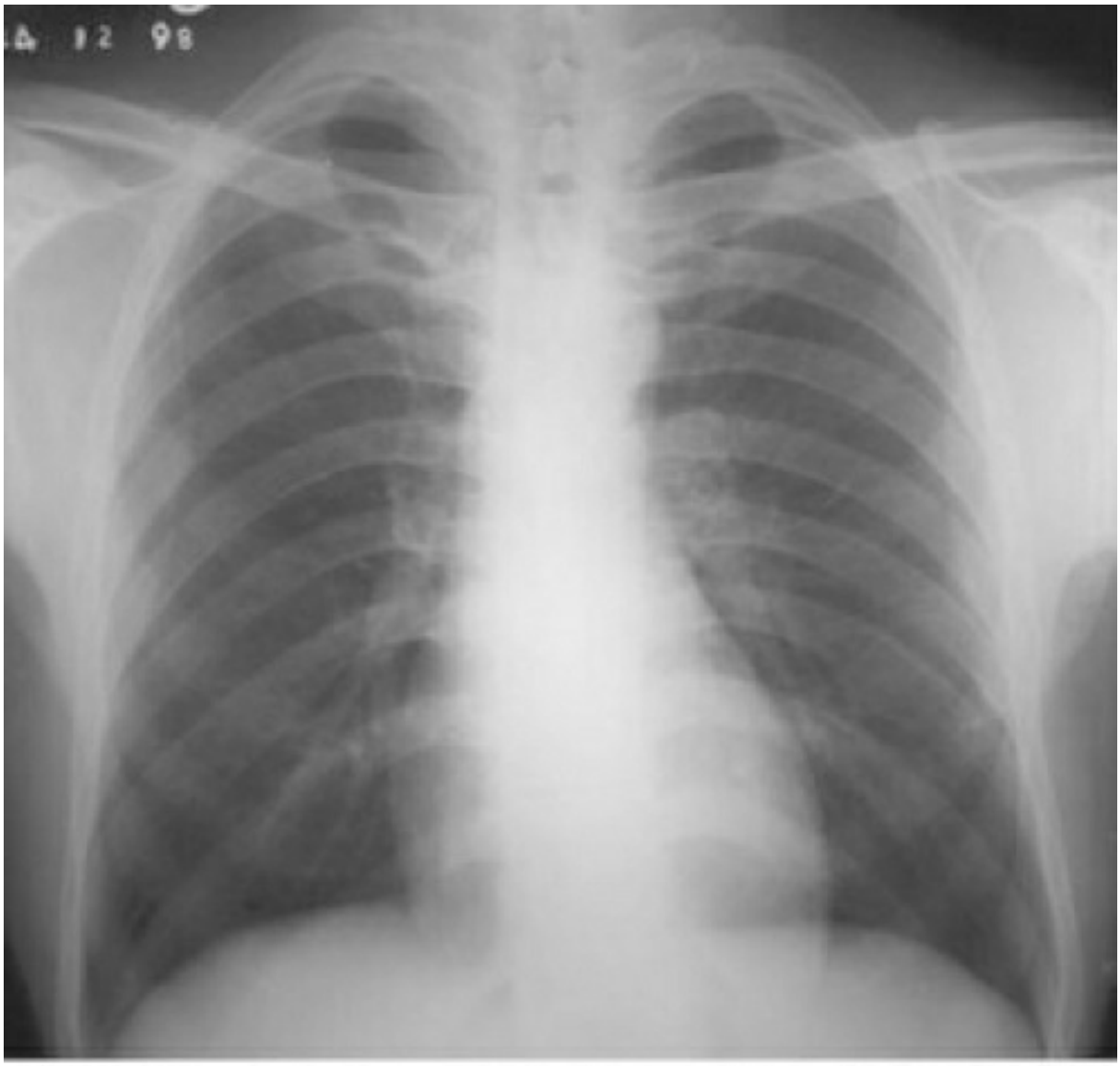

Figure 1.1B: Normal X-ray of chest postero-anterior view. The right border of heart is formed by the superior vena-cava and right atrium. The left border is formed by the aorta, main pulmonary artery, left atrial appendage, and anterolateral border of the left ventricle.

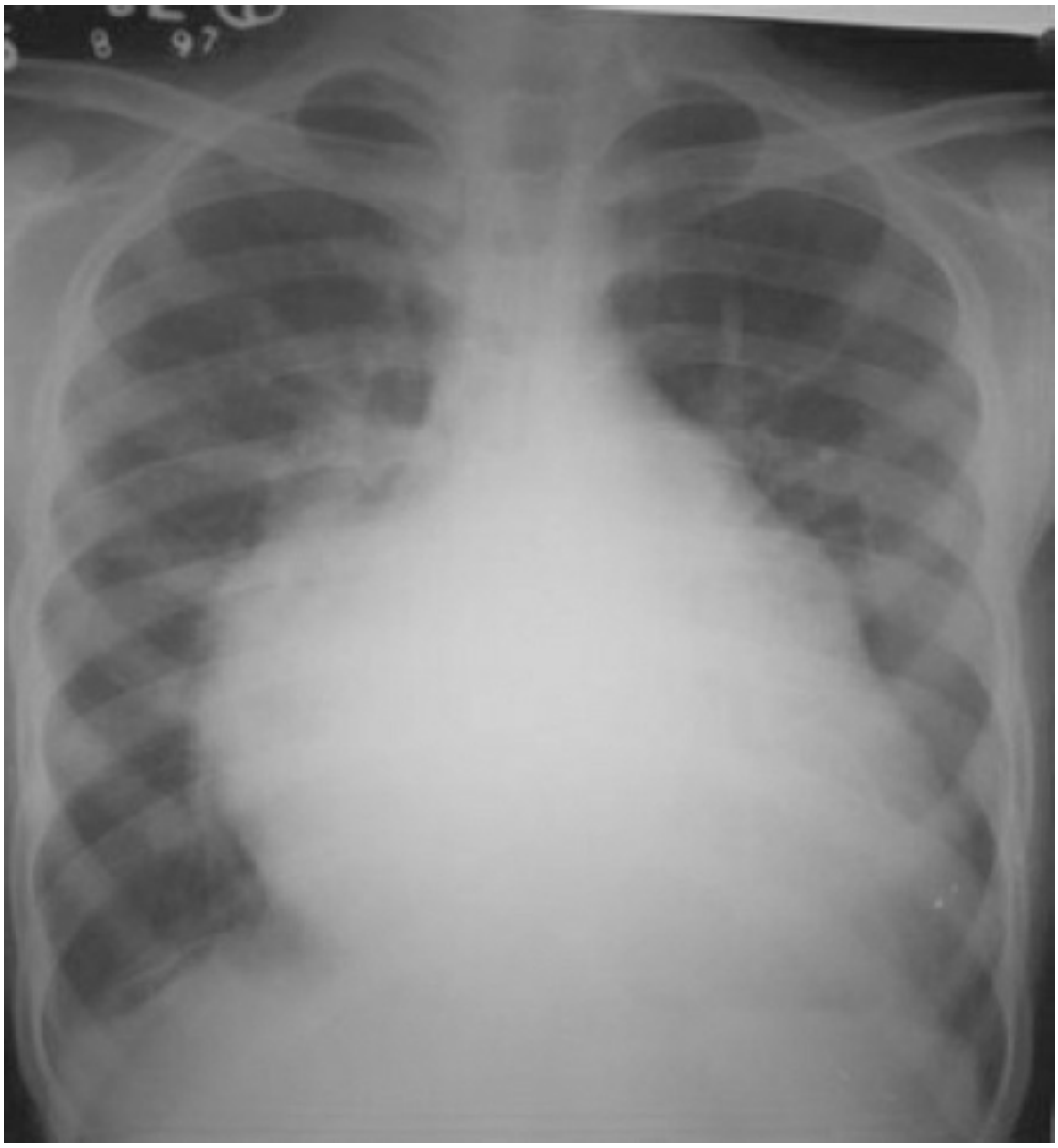

Figure 1.2: Massively enlarged left atrium producing double density of the right heart border.

In patients with cardiomyopathy, the degree of LV enlargement depends on whether the cardiomyopathy is dilational (moderate to marked LV enlargement), restrictive (mild LV enlargement), or hypertrophic (mild to moderate LV enlargement).

In addition to the size of cardiac chambers, the chest radiograph provides useful information by way of lung fields. The signs of CHF and pulmonary venous hypertension are useful in determining the cardiac status of the patient.

Chest radiography, thus provides a useful noninvasive method of estimating the cardiac function. However, it should be remembered that it

provides an indirect assessment and it is useful to correlate the radiological findings with other clinical findings in order to arrive at definite conclusions.

Electrocardiogram

The ECG is one of the most important preoperative tests for patients with cardiac disease, especially for patients with CAD. However, the resting ECG can be normal in 25 to 50 percent of patients with CAD[60] and in additional 25 percent of patients, the ECG may be difficult to interpret because of conditions such as left bundle branch block or Wolff-Parkinson-White syndrome. Also, ECG provides no information about the ventricular function and may be normal in the presence of severe CAD or VHD. ECG is typically utilised for detection of arrhythmias, conduction changes, myocardial ischaemia, injury and infarction. In patients with CAD, the occurrence of ST-T wave abnormalities may correlate with the severity of underlying heart disease, including the number of vessels involved and the presence of LV dysfunction.[61] In contrast, a normal resting ECG in patients with suspected or definite CAD is suggestive of a more favourable long term prognostic sign.[62]

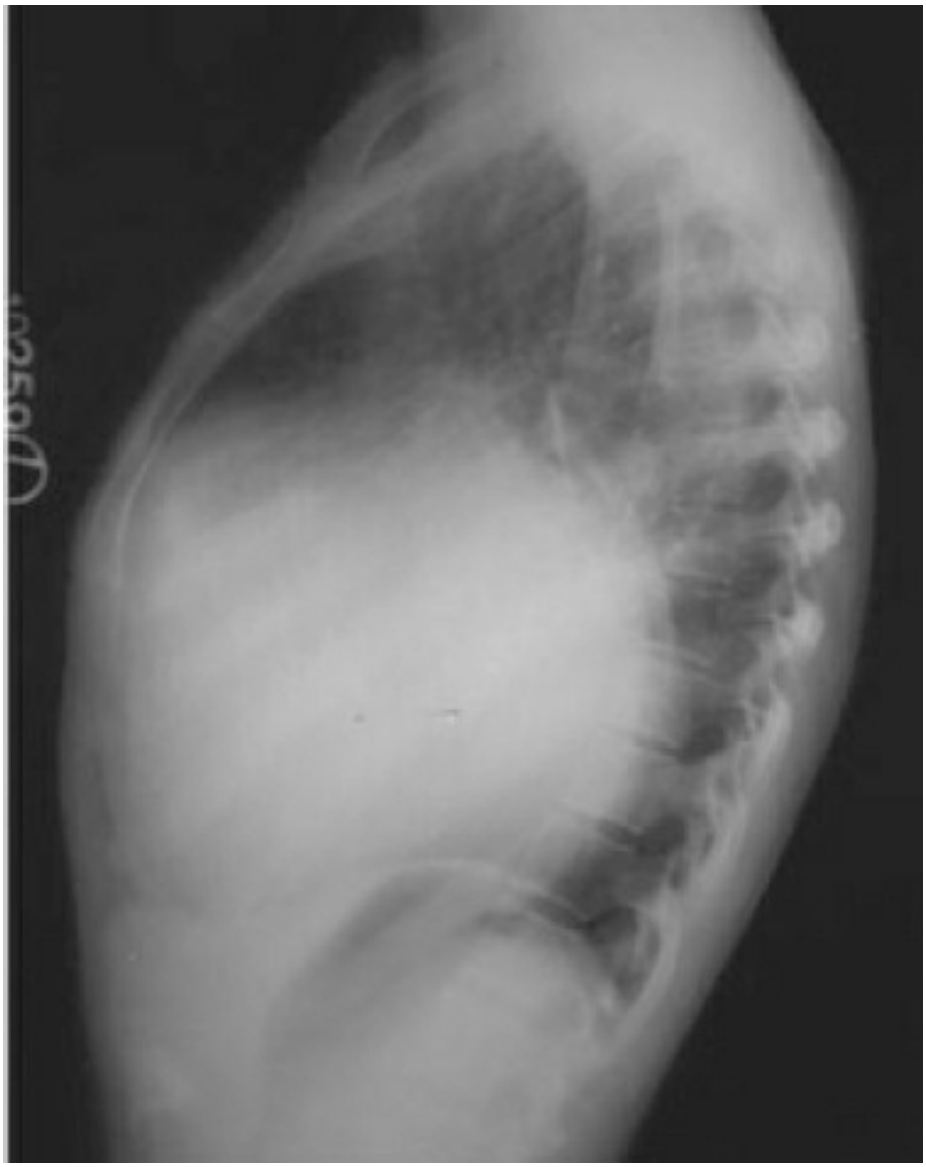

Figure 1.3: The lateral view of chest X-ray showing right ventricular enlargement causing obliteration of the retrosternal space.

The earliest ECG change following ischaemia is usually the ST elevation. Later on there is diminution in the size of R wave and in transmural (full thickness) infarction, a Q wave begins to develop. Subsequently, the T wave becomes inverted, which persists after the ST segment has returned to normal. The Q wave appears within hours and the T wave inversion takes place within days. The T wave inversion becomes less marked in several weeks or months.

In contrast to transmural infarct, subendocardial infarction causes ST/T wave changes without Q wave or prominent ST elevation. This is

accompanied by the loss of R wave in the leads facing the infarct.

The ECG changes are best seen in the leads which face the infarcted area. For instance, in antero-septal infarction, abnormalities are found in one or more leads from V_1 to V_4, while anterolateral infarction produces changes in leads V_4 to V_6, AVL and I. Inferior infarction is best seen in leads II, III and AVE Infarction of the posterior wall of LV is not recorded in the standard leads by ST elevation or Q waves. The leads V_1 to V_4 may record reciprocal changes by way of ST depression and a tall R wave.

Exercise stress testing (Treadmill)

With exercise, the major determinants of MVO_2 such as HR and myocardial contractility are increased. The increased oxygen demand is met primarily by an increase in the coronary blood flow that is achieved by marked vasodilatation of the coronary vascular bed. Any impairment in this vascular reserve due to coronary obstruction or vasospasm may lead to myocardial ischaemia and its sequelae. In exercise stress testing, the myocardial work is progressively increased by graded physical exercise and the signs and symptoms of ischaemia, arrhythmias and pump dysfunction are simultaneously measured.

Currently, many treadmill protocols are available. They include those introduced by Bruce, Balke, Ellestad, Astand, Naughton and Sheffield. The most familiar of these, the Bruce protocol consists of 3 minute stages that have different grade and speed. Stage 1 has a speed of 1.7 miles/hour with a 10 percent grade. Patients with moderate CAD usually exercise to stages 3 and 4 before termination of the test because of symptoms or HR limitations. The principal indicator of ischaemia during exercise as well as immediate recovery period, is ST segment deviation. Three types of ST segment responses have been described.[63] The first type is characterised by ST depression occurring during the exercise period that reverts to normal during the early post-exercise period. In the second type, the ST depression worsens during the recovery period and indicates poor prognosis. The third type of response is ST segment elevation. The conventionally accepted criterion is a threshold elevation of 1.5 mm or more, regardless of the slope. In addition to ST segment response, changes in T wave or R wave, the occurrence of chest pain, alteration in HR, hypotension or arrhythmias are also considered.

Exercise stress testing is a noninvasive test that is useful in patients with

chest pain of unknown aetiology and for quantification and prognosis in patients with known CAD. It has a significant prognostic value when the ST changes of significant magnitude occur during early stages of the test (1 to 3), do not revert during recovery period, are associated with subnormal increases in HR or BP and are accompanied by angina or arrhythmias. It should be remembered, however, that negative tests do not imply absence of disease as many patients undergoing CABG have negative exercise stress testing results. Apart from the fact that the results of exercise stress test are valuable in offering the diagnosis of CAD, the anaesthesiologist should take note of the haemodynamic changes that are associated with ST segment deviation. In addition, the therapies used during exercise stress testing to reverse ischaemia should also be noted. These may help to set the guidelines regarding the dangerous HR and BP response during anaesthesia as well as the therapy that should be used to reverse intraoperative ischaemia. A few studies[64,65] have demonstrated that a positive ischaemic response and a low exercise capacity predict adverse outcome following non-cardiac surgery. It has been suggested that preoperative exercise stress testing should not be performed routinely in patients undergoing non-cardiac surgery, but should be reserved for patients who satisfy standard medical criteria for specialised testing, such as new, unexplained chest pain.[24]

The 6 min. walk test (6 MWT) has been shown to be a useful clinical tool to screen and risk stratify patients in departments where cardiopulmonary exercise testing (CPET) is not available. It has been shown that patients walking more than 563 meters in the 6 MWT do not routinely require CPET, those walking less than 427 meters should be referred for further evaluation, and in those walking more than 427 meters but less than 563 meters, the number of clinical risk factors and magnitude of surgery should be incorporated into decision making process.[66]

Echocardiography

The echocardiography is based on the principle of detection of reflected sound waves from the surfaces of the internal organs. Pulses of ultrasound waves with a frequency of 2.5 to 7.5 million cycles per second (MHz) are utilised in echocardiography. (Precordial echo: 2 to 3 MHz and transoesophageal echo (TOE): 3.5 to 5 MHz). Frequencies in this range provide the optimum penetration (10–25 cm) and resolution of objects

(objects 1 mm or less in size). When the ultrasound waves strike an interface of tissues of differing densities, a portion is reflected. The amount reflected is directly related to the difference in tissue densities. For instance, air in the LV appears as a brighter signal on the screen as it reflects a much greater portion of the transmitted ultrasound than the blood. The duration taken by the sound waves to bounce back to the transducer determines the location of the tissue. The longer a sound wave takes to bounce back, the greater is its distance from the transducer.

Echocardiography has undoubtedly become an important means of reliably and non-invasively assessing the cardiac function. The valvular function as well as the myocardial function is accurately assessed by this technique. The Doppler technique allows the detection of intracardiac shunts and valvular insufficiency and can estimate cardiac output (CO), valve gradients and intracardiac pressures.

M-mode echocardiography

A typical M-mode echocardiogram is shown in Figure 1.4. The tracing that is obtained by placing the transducer on chest wall represents the one dimensional view against time. The motion of valves, and linear dimensions of intracardiac and pericardial structures can be visualised. These views are useful in estimating the end-diastolic and end-systolic LV dimensions and calculation of ejection fraction. The LV dimensions can be useful in quantifying the LV enlargement. In AR a preoperative end-systolic diameter greater than 55 mm[67] and in MR a preoperative end-systolic diameter of more than 45 mm[68] are associated with adverse surgical outcome.

Two-dimensional echocardiography

Multiple views can be obtained by using phased array transducers that can be collated into a two-dimensional image. The two-dimensional picture helps to recognize anatomical and pathological landmarks. The operator can alter the angle and position of the ultrasound beam so that multiple cross-sectional images can be produced, helping to identify the anatomy of the heart and great vessels. Moreover, images are displayed in “real-time” on a monitor screen and can be recorded on a videotape or digital format. Two-dimensional echo enables the visualisation of valves and ventricular wall motion along with measurement of LV volumes (ejection fraction), areas and wall thickness. Figure 1.5 shows a typical 2-D echo using parasternal long

axis view. The other common views are parasternal short axis, apical (two chamber and four chamber), suprasternal (long axis and short axis) and subcostal views.

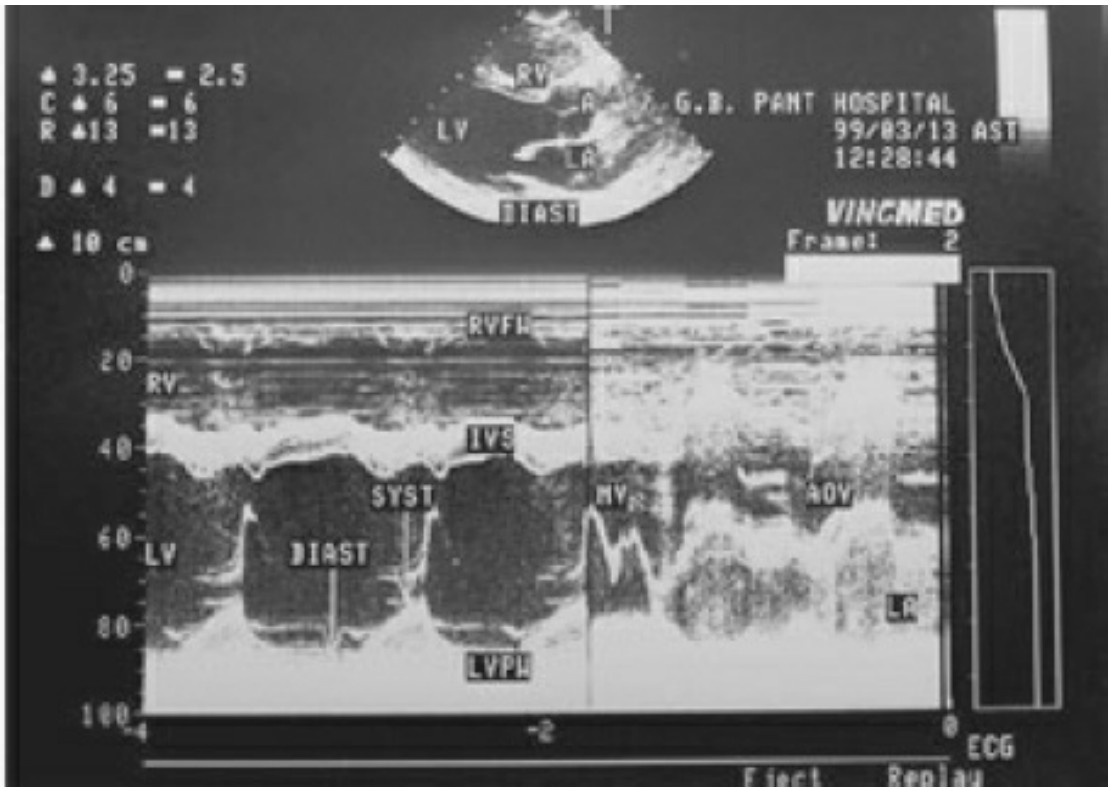

Figure 1.4: A typical M-mode echocardiogram (LA: left atrium, LV: left ventricle, RV: right ventricle, A: aorta, RVFW: right ventricular free wall, IVS: interventricular septum, LVPW: left ventricular posterior wall, MV: mitral valve, AOV: aortic valve).

Transoesophageal echocardiography

In this technique the transducer is placed at the distal end of the gastroscope that is passed into the oesophagus. As the transducer is close to the heart and the sound waves do not have to penetrate the chest wall or lung, very high quality images are obtained.

The simplest TOE probe has one phased array transducer. The ultrasound beam is oriented at right angles to the gastroscope to produce transverse imaging planes. In biplane transducers, a second transducer is mounted immediately proximal and at right angles to the first to provide a longitudinal imaging plane. In multiplane transducers, a single transducer is mounted on a rotating device that allows 0 to 180 degrees rotation of the transducer on its own axis. The whole assembly is housed within the tip of the gastroscope. The advances in technology have helped the manufacturers to produce

transducers that are small enough for use in infants and neonates.

The advances in Doppler technique have allowed for noninvasive estimation of morphology as well as function of valves, intracardiac shunts, intracardiac pressures and CO. As a preoperative test, precordial echocardiography provides a noninvasive and accurate method for estimating the overall cardiac performance. Of importance, is its value in the diagnosis of acute MI [presence of regional wall motion abnormalities, (RWMA)] when other technique such as ECG is inconclusive or uninterpretable. In VHD, it provides invaluable information in terms of valve size, degree of regurgitation, various chamber sizes, pressure gradients and degree of pulmonary hypertension. The severity of VHD can thus, be objectively assessed by echocardiography. In addition, it provides accurate assessment of the global ventricular function. Thus, it is helpful in deciding optimal preoperative management and perioperative monitoring and care. Its preoperative prognostic value is unknown. However, because preoperative ventricular dysfunction is associated with perioperative ventricular dysfunction, echocardiography can be potentially useful as it provides the information less invasively. More recently, stress echocardiography is being used as a preoperative test. The appearance of a new or worsened RWMA is considered a positive test and represents areas at risk for myocardial ischaemia. In this respect, dobutamine stress echocardiography has been found to be very useful.

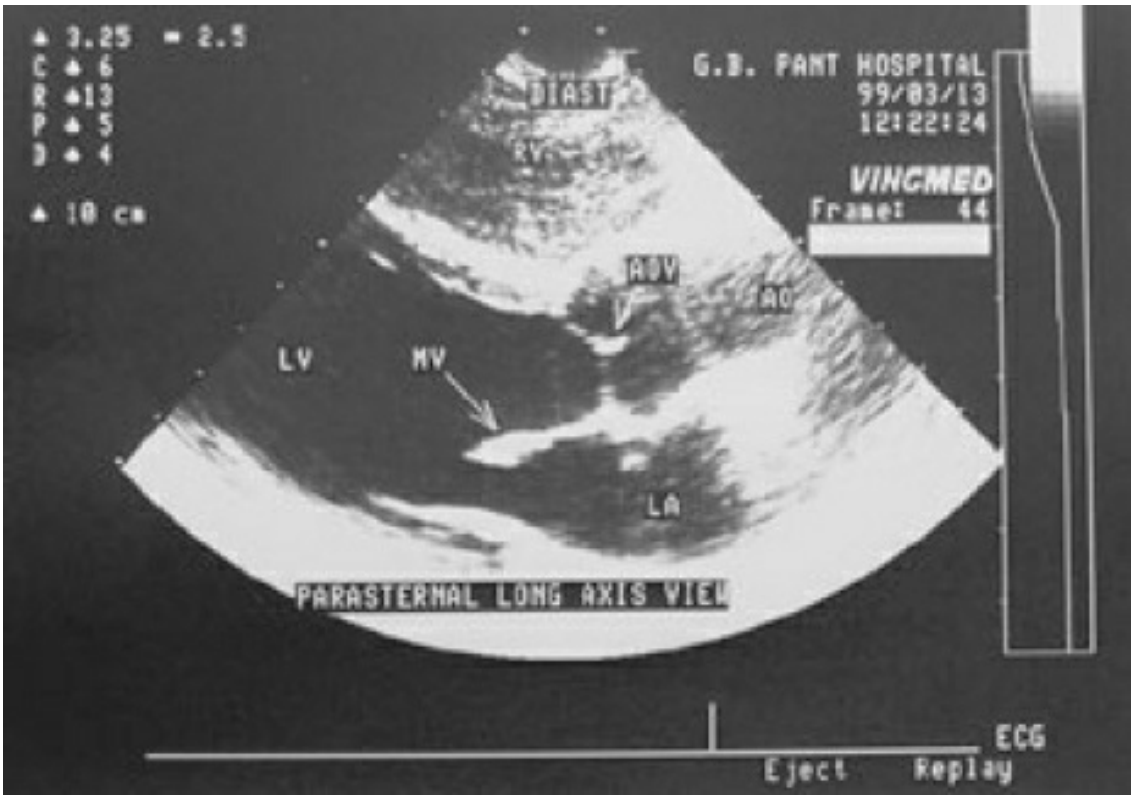

Figure 1.5: A typical 2-D echocardiogram showing parasternal long axis view (RV: right ventricle, LV: left ventricle, MV: mitral valve, LA: left atrium, AOV: aortic valve, AO: aorta).

Tissue Doppler

The tissue Doppler velocity of the mitral annulus is used for the assessment of LV function. The ratio of early transmitral blood flow velocity (as measured by colour Doppler) to early diastolic velocity of the mitral annulus by tissue Doppler (E/e') is an indicator of LV diastolic function and is relatively independent of the systolic function and rhythm abnormalities. The normal E/e' is less than 8. It has been shown that E/e' ratio of more than 15 is an independent predictor of composite endpoints of postoperative morbidity.[69]

Nuclear imaging

Nuclear imaging is now a safe and accurate method for assessment of myocardial perfusion and infarction, and ventricular function. The regional distribution of myocardial blood flow can be visualised using the radio-isotopes that accumulate proportional to the regional myocardial blood flow. Thallium-201 has been employed successfully for this purpose.

Recently, new technetium 99^m labelled compounds with better imaging characteristics and novel biological properties have been introduced. The relative distribution of myocardial blood flow can be visualised using these imaging agents. For the diagnosis of MI, two types of imaging exist: the myocardial scintigraphy (hot spot imaging) and perfusion scintigraphy (cold spot imaging).

The hot spot technique uses technetium 99^m pyrophosphate as the radionuclide. The infarcted segment of the myocardium that has a selective affinity for technetium is detected as a hot spot by the gamma camera. Normal tissue or areas of old infarction do not have affinity for technetium, and these areas are not visualised. The image can be detected after 12 to 16 hours following the event with maximum abnormality occurring from 48 to 72 hours. The intensity of the image returns towards normal within 5 to 7 days.

In perfusion scintigraphy or cold spot imaging, thallium-201 is used. The isotope is taken up by the areas of heart with normal perfusion and thus allows imaging of normal myocardium. Defects in the normal pattern (cold spots) represent areas of decreased perfusion as well as acute or old MI. The technique is useful in detecting the stress response of coronary circulation by obtaining scans during exercise or infusion of coronary vasodilator, dipyridamole. Because of rapid myocardial clearance rate of thallium-201, redistribution of thallium occurs quickly and allows visualisation of the reper-fusion process. Perfusion defects of the cold spots last for approximately 30 to 60 minutes with redistribution occurring during the next 2 to 3 hours. Repeat imaging is performed approximately 3 to 4 hours later. The initial perfusion defects that persist, indicate infarction or prolonged ischaemia, and those that disappear are indicative of reversible perfusion defect or transient myocardial ischaemia without infarction.

For the assessment of ventricular performance and wall motion indices, first-pass radionuclide angiography and gated blood-pool imaging is used. Thus, radionuclear imaging is useful in enhancing the preoperative assessment of MI and quantification of the ventricular function. The predictive value of preoperative radionuclear imaging has been studied in vascular surgery patients. Initial results suggested preoperative gated-pooled-determined ejection fraction of less than 0.35 as an independent predictor of perioperative cardiac morbidity.[70] More recently, however, it has been shown that there is no association between the redistribution defects and adverse

cardiac outcomes in patients undergoing elective vascular surgery.[71,72]

Pharmacological stress testing

Many patients with CAD are unable to perform exercise tests. Such patients who cannot exercise adequately can now be stressed by pharmacological agents. These techniques have been found to give results that are equivalent to exercise testing. Myocardial perfusion can be increased artificially by infusing the small vessel vasodilators, dipyridamole or adenosine. This is followed by thallium imaging to detect myocardial ischaemia. Areas of myocardium surrounding a coronary vessel (that has fixed stenosis) have small vessel vasodilation at rest to maintain normal resting flow. Such areas have a diminished hyperaemic response to vasodilator compared with normal myocardium. This leads to a relative defect in myocardial perfusion imaging at peak flow. In fixed defects, the decreased uptake persists whereas in reversible defects, later resting images reveal improved flow. Reversible defects are more likely to indicate myocardium at risk. The perioperative cardiac events occurring in patients undergoing non-cardiac surgery have been shown to be related to the size of jeopardised viable myocardium (myocardium at risk) determined by thallium imaging.[73] Abnormal scans are also useful to clinically select patients for therapeutic intervention such as revascularisation.

Dobutamine stress echocardiography is a newer technique that has rapidly established itself as a useful clinical tool. The coronary flow reserve is tested by increasing the heart rate by dobutamine infusion. A normal test result is defined as the absence of a new or worsening RWMA. The predictive value of dobutamine stress echocardiography is similar to dipyridamole thallium scintigraphy.[74]

Cardiac catheterisation

Cardiac catheterisation is the most important investigation that is undertaken in patients with CAD. Coronary angiography provides information about the coronary artery and the presence and pattern of atherosclerotic disease. For a cardiac surgeon, the coronary angiography helps to decide how many bypass grafts should be performed and where the distal anastomosis should be placed. Physiological information in terms of intracardiac pressures and CO can also be obtained. By knowing CO and ventricular filling pressure, i.e.

LVEDP, a reliable index of cardiac function can be derived. An increase in LVEDP (>15 mm Hg), is indicative of pulmonary congestion. Likewise, a sudden large increase in LVEDP (an increase of more than 5 mm Hg) during ventriculography (when the low oxygen containing contrast material displaces blood from coronary circulation) is indicative of transient episode of cardiac failure. Such information provides a rough estimate of the risk of similar episodes of altered cardiac performance during anaesthesia and surgery. In addition, LV angiogram can provide valuable information such as ejection fraction, LV volumes and the presence of associated MR.

The type of coronary artery lesion can be useful. According to one study, proximal left circumflex artery stenosis was an independent predictor of mid-term mortality, especially in patients with a history of heart failure.[75]

Cardiac catheterisation provides detailed anatomical information about the patient with complex congenital heart disease and contributes to the planning of surgical correction. The role of cardiac catheterisation in other simple congenital anomalies such as atrial septal defect, ventricular septal defect, TOF, etc. is now limited due to advances in the two-dimensional echo and colour Doppler techniques. It is rarely performed in situations where the echocardiography is not able to provide definitive diagnosis. Similarly, it is rarely performed in patients with VHD, as most of the information is obtained by echocardiography.[76] It is, however, indicated in patients with VHD before surgery to rule out associated CAD, especially in elderly patients. At many centres, coronary angiogram is routinely performed in patients more than 45 years of age. In the developing countries, however, rheumatic fever is still the commonest cause of VHD so that the patients are usually young and do not require coronary angiogram.

For patients undergoing non-cardiac surgery, cardiac catheterisation has a limited role, as alternative less costly and less invasive techniques are available to assess the ventricular as well as valvular function. However, it is perhaps indicated in patients with suspected left main or triple vessel disease or patients with unstable angina in whom revascularisation either with angioplasty or bypass surgery may be useful. Although, previously successful myocardial revascularisation appears to reduce the risk for subsequent non-cardiac surgery,[64,65] it is doubtful, if elective revascularisation should be performed prior to surgery. Since the risk of CABG itself often exceeds the risks of non-cardiac surgery, CABG is rarely justified simply to lower the

risk of non-cardiac surgery.[74] The current ACC/AHA guidelines endorse this view.[17] Therefore, routine angiography should not be performed in all high-risk patients undergoing non-cardiac surgery, but only in those patients who warrant revascularisation for medical reasons, independent of surgery.[24] In addition, relative urgency of the non-cardiac problem should also be considered.

ICU Admission Risk Assessment

Patient outcome is also influenced by the events in the operation theatre (OT). These may relate to the anaesthetic technique, adequacy of valve repair and myocardial protection. In other words, the OT events can alter the risk present (increase or decrease) that was based on preoperative status. Any other adverse events in the OT such as excessive surgical bleeding, difficulty in separating the patient from CPB, and use of intra-aortic balloon pump can change the outcome in a patient but cannot be predicted accurately at the time of preoperative evaluation. Therefore, assessment of the patient for the second time on arrival in the intensive care unit (ICU) may be necessary.

Acute Physiology and Chronic Health Evaluation (APACHE II) that was designed for general ICU patients has also been evaluated for cardiothoracic surgical patients.[77] APACHE III (refinement of APACHE II) has also been tested.[78] The independent predictors of outcome are the acute physiology score, age, emergency and reoperation status, number of grafts and sex of the patient. The most recent scoring system has identified seven factors at ICU admission that were independent predictors of morbidity and mortality outcome.[79] Amongst these, the use of intra-aortic balloon pump to separate the patient from CPB was the single most important predictor of poor outcome, followed by prolonged CPB time (> 160 min.).

In summary, the growing demands of improved outcome following cardiac surgery make it essential for each patient to undergo thorough perioperative evaluation. Preoperative cardiac complications are also an area of clinical interest and concern in patients undergoing non-cardiac surgery. Over the years, perioperative risk assessment has evolved significantly. A recent article has shown that postoperative survival following major elective abdominal surgery is influenced by reduced functional capacity even in the absence of cardiac risk factors.[80] It has also been shown that the use of a

routine preoperative cardiac assessment allows to obtain satisfactory perioperative results in patients undergoing abdominal aortic surgery.[81] Risk stratification of a patient is therefore important so that probabilities of the difficulties during the procedure as well as the outcome of surgery can be anticipated. By identifying the high-risk patient, it may be possible to alter the therapy or technique to reduce the risk. For instance, an appropriate method of myocardial preservation may be chosen in high-risk patients. This will not only be more cost-effective, but can also reduce the morbidity that is related to poor myocardial performance in the postoperative period. In addition, time may be spent preoperatively to improve the status of the patient by additional investigations and necessary therapy. Preoperative statins have been shown to provide protective effect in the perioperative period in terms of cardiac morbidity and mortality[82] as well as renal insufficiency[83] Most of the risk stratification has been described for patients risk stratification in patients undergoing valve suffering from CAD. There is a need to develop surgery or repair of congenital heart defects.

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Chapter 2: Anaesthetic Agents

The cardiac anaesthesiologist is expected to perform two important functions. First is to anaesthetise the patient and the second, to maintain normal or acceptable haemodynamics. No doubt, both the functions are important for any general anaesthetic, but in view of the deranged cardiovascular system of a cardiac patient, the maintenance of haemodynamics is especially important. Knowledge of the pathophysiology of underlying cardiovascular disease as well as understanding of the haemo-dynamic effects of various anaesthetic agents is therefore, important for the safe conduct of anaesthesia. In addition, understanding the interactions of the anaesthetic agents with cardiac medications such as beta adrenergic blockers, calcium channel blockers, etc. is also important. It is well known that there is no single agent or a technique that will meet all the requirements and will be the safest. Therefore, careful selection of the anaesthetic agents that will meet the requirements of anaesthesia (analgesia, paralysis, unconsciousness and attenuation of the stress response) as well as suit the underlying cardiovascular pathology is necessary. Indeed, there can be more than one way of meeting this goal, and perhaps, the choice is determined by the concerned anaesthesiologist.

This chapter describes the various anaesthetic agents with special reference to their cardiovascular effects. These effects can be used to tailor a general anaesthetic to an individual patient undergoing cardiac surgery.

Intravenous Anaesthetic Agents

Narcotics

Since the time Lowenstein[1] demonstrated the safety of high-dose morphine anaesthesia (up to 3 mg/Kg) in patients suffering from valvular heart disease

with virtually no cardiac reserve, high-dose opioid technique has been the mainstay of cardiac anaesthesia. It soon became apparent that morphine administered in such high doses provides adequate analgesia, but may expose the patients to awareness, especially in less critically ill patients.[2] In addition, hyperdynamic response (tachycardia and hypertension) to noxious stimulation may occur in patients having good myocardial function despite giving large doses of narcotics. This may increase the risk of myocardial ischaemia necessitating the use of beta adrenergic blockers and peripheral vasodilators in order to blunt the sympathetic response. It may also be necessary to suppress the sympathetic discharge by supplementing the narcotic base with hypnotics, volatile agents or nitrous oxide. Such a manoeuvre also helps to ensure absence of recall.

The respiratory depression as well as other prolonged effects of narcotics suited the anaesthetic technique, as elective ventilation in the postoperative period was an accepted practice. With the introduction of fast-track anaesthesia techniques,[3] lower doses of opioids are being used. The doses of opioids will also need to be restricted in patients undergoing closed heart procedures where prolonged ventilation in the postoperative period may not otherwise be required. More potent opioids having better cardiovascular stability than morphine, such as fentanyl, alfentanil and sufentanil have also been introduced.

The stress response including release of circulating catecholamines, Cortisol, growth hormone and antidiuretic hormone can be suppressed by fentanyl, alfentanil and sufentanil.[4-8] Although this suppression is dose related, it is not consistent and it may be preferable to add a hypnotic or an inhalational agent instead of further loading the patient with an opioid.

The commonly used induction doses and infusion rates of some opioids are shown in Table 2.1.

Table 2.1: Induction doses and infusion rates of the commonly used opioids.

Drug	***Induction dose***	***Infusion rate(60 Kg adult)***
Morphine	0.5 to 1 mg/Kg	15 to 20 µg/min
Fentanyl	20 to 40 µg/Kg	2 to 10 µg/min

Sufentanil	5 to 15 µg/Kg	1 to 2 µg/min
Alfentanil	80 to 200 µg/Kg	120 to 200 µg/min

Morphine

Morphine was the principal opioid used in the developing countries until recently. Now, fentanyl is gradually replacing morphine. The haemodynamic stability that can be achieved with morphine in cardiac patients was demonstrated by Lowenstein[1] in 1969. Induction of anaesthesia by slow administration of morphine (5 mg/min or less) generally results in stable haemodynamics, however, rapid infusion (10 mg/min or more) may produce hypotension that may require treatment.[1,9] Histamine release caused by morphine has been shown to be responsible for arteriolar vasodilatation.[10] A correlation between release of histamine and severity of hypotension after the administration of high doses of morphine has been demonstrated in patients undergoing coronary artery bypass grafting (CABG).[11] Pretreatment with histamine H_1 and H_2 antagonists can help to attenuate the cardiovascular response.[12] Some workers, however, believe that there is not enough histamine release after morphine to cause such hypotension.[13,14] Other mechanisms of hypotension are, direct dilatation of the capacitance vessels by inhibiting vascular smooth muscles,[15] and depression of the sympathetic ganglionic transmission.[16] Regardless of the mechanism, the underlying problem is a decreased systemic vascular resistance (SVR). Prevention of hypotension should include slow administration, and treatment should include appropriate volume replacement and head down tilt to the patient. Sympamomimetic agents (alpha and beta stimulants) can also be used.

There is little effect on the myocardial contractility with morphine in the dosage that are used in clinical practice. However, morphine may cause bradycardia, which along with decreased SVR can augment the degree of hypotension.[17] In such a situation, bradycardia should be reversed with an anticholinergic or sympathomimetic agent. In addition, muscle relaxant such as pancuronium that increases the heart rate (HR) can be used for intubation purposes.

Rarely, following large intravenous doses, muscle rigidity can develop[18] that can impede positive pressure ventilation. This particular problem is not a

major concern for the anesthesiologist as during induction of anaesthesia, patients are generally breathing high oxygen concentration so that desaturation of oxyhemoglobin is delayed. In addition, rigidity can be relieved within 1 to 2 minutes by administration of a muscle relaxant.

The induction of anaesthesia usually requires 1 to 3 mg/Kg of morphine depending upon the patient's clinical condition. Larger closes may be necessary in patients having reasonable cardiac reserve. Since respiratory depression may occur before the loss of consciousness, ventilatory assistance may be required. It is a usual practice to use morphine in the dose of 0.5 to 1 mg/Kg for induction of anaesthesia. Thiopental and benzodiazepines are also administered in order to accomplish this reduction in morphine dosage as well as to ensure amnesia. In sick patients, hypotension is avoided by administering morphine slowly and using incremental bolus doses of thiopental while constantly monitoring the blood pressure (BP). Currently in cardiac surgery, morphine is mainly used as a premedicant, and for providing intraoperative and postoperative analgesia by intrathecal or epidural route.

Fentanyl

Fentanyl is a synthetic phenylperidine belonging to the 4-anilo-piperidine series. Fentanyl was introduced initially as Innovar (combination of droperidol and fentanyl in a ratio of 5:1) in 1960s and its use in cardiac anaesthesia was first reported in 1978.[19] It is now freely available in the developing countries and widely used in clinical practice.

It is more lipid soluble than morphine and achieves its full effect in 2 to 3 min. after intravenous injection. However, it has a shorter duration of action than morphine. In man, it is 60 to 80 times more potent than morphine. It also provides better cardiovascular stability and the haemodynamics are usually stable during induction of anaesthesia with larger doses of fentanyl (> 50 μg/Kg).[4,20] There is no direct effect on the myocardial performance[21,22] and direct intracoronary injection of fentanyl in concentrations up to 240 ng/ml produced no changes in the myocardial mechanical functions.[23] Fentanyl has little effect on the vascular smooth muscles or histamine release.[14] Consequently, there is no significant decrease in SVR.[24] However, bradycardia is commonly observed following fentanyl administration.[25] The bradycardia can be accentuated by administration of muscle relaxants such as vecuronium and hence, if bradycardia is severe, pancuronium should be

preferred. In addition, anticholinergic or sympathomimetic agents may be used, if necessary. Rarely, fentanyl may cause severe hypotension which might necessitate inotropic support.

Other adverse effects of fentanyl are muscle rigidity and seizure like activity. Rigidity is rarely observed after small bolus doses administered to awake patients but is more common after large bolus doses that are used for induction of anaesthesia.[26]

Haemodynamic response to surgical stress (intubation, skin incision, sternotomy) can be blunted with fentanyl. However, the response is not consistent and depends largely on the myocardial performance. Patients with normal myocardial function may respond to surgical stress despite maintaining high plasma levels of fentanyl. On the contrary, patients with poor myocardial function will not manifest a hyperdynamic response. Therefore, if large doses of fentanyl become ineffective in controlling the haemodynamic response, supplementation with nitrous oxide, benzodiazepine and/or inhalational agent may be necessary.

The induction dose of fentanyl is 50 to 100 μg/Kg, but higher doses up to 150 μg/Kg have been used in patients undergoing CABG in an attempt to control the mean arterial pressure (MAP).[4] With growing interest in early postoperative extubation, even lower doses (10 to 20 μg/Kg) in combination with isoflurane or propofol are being utilised. The plasma concentration of fentanyl decreases rapidly due to distribution from the plasma to tissues after bolus injection of moderate doses (up to 10 μg/ Kg) making it a short acting agent. Giving larger initial doses of fentanyl convert it from a short acting to a long acting drug. With the larger dose, the distribution phase is completed before the fentanyl concentration declines to threshold levels so that the duration of action becomes dependent on the decrease in concentration during the much slower elimination phase.[27] The dose of fentanyl should be titrated according to the response and needs of the patient to avoid accumulation. It is desirable to progressively decrease the successive doses at regular intervals. Continuous infusion of fentanyl for cardiac surgery has also been used to maintain anaesthetic fentanyl plasma concentration throughout surgery. A priming dose of 2.4 μg/Kg/min. for 20 min. in combination with a simultaneously started and maintained infusion of 0.3 μg/Kg/min. has been reported to produce plasma fentanyl concentration between 20 and 27 ng/mL (10 to 30 ng/mL are sufficient to provide stable haemodynamics) and

effectively eliminate the need for supplements.[28] Haemodynamic stability during fentanyl infusion can be further enhanced by the use of computer assisted mechanical drug delivery systems.

In children, it has been shown that a balanced anaesthetic containing fentanyl 25 to 50 μg/Kg is sufficient to obtund haemodynamic and stress responses to the prebypass phase of surgery.[29]

Sufentanil

Sufentanil is a fentanyl analogue with a potency five to ten times that of fentanyl and with a similar short duration of action.[30] Like fentanyl, it does not cause histamine release and both provide similar haemodynamic stability during induction of anaesthesia. Due to its increased potency, a greater haemodynamic stability during cardiac surgery is expected. Some authors showed that sufentanil provided better control of intraoperative haemodynamics,[31,32] while others did not find a marked difference.[33] It has been used in a wide range of doses (0.25 to 25 μg/Kg), but doses of 5 to 15 μg/Kg are commonly employed in cardiac surgery.

With the advent of fast-track cardiac surgery, some cardiac anaesthesiologists believe that the goal should be to administer minimal dose for the shortest possible time to improve recovery. Consequently, the induction dose can be decreased to as low as 1 μg/Kg followed by the maintenance dose of 1 μg/Kg/hour in the form of an infusion. Such a reduction in dosage will however, require concomitant use of some other anaesthetics such as propofol or inhalational agents. It has also been given intrathecally in combination with morphine with a target controlled infusion of propofol to achieve the goals of fast-track cardiac surgery.[34] Bolus doses used for anaesthetic induction can lead to severe bradycardia and asystole, especially when used with vecuronium or succinylcholine.[35,36] In general, all narcotics tend to cause bradycardia and it is not uncommon to use pancuronium as the muscle relaxant of choice following induction to counter the bradycardia and attain better haemodynamic stability.[37,38] Although, this holds true for patients undergoing CABG who are on preoperative beta-blockers, it may not be true for patients undergoing valve surgery who tend to have faster heart rates, especially those who have atrial fibrillation. In such patients, therefore, pancuronium may not be an appropriate choice for muscle relaxation.

Alfentanil

Alfentanil is another fentanyl analogue that is very short acting and shows about one fifth the potency of fentanyl. Its maximum effects are achieved in 90 seconds after intravenous administration. The rapid rate of elimination makes it suitable for use by continuous infusion, during the maintenance of anaesthesia and for pain relief in the intensive care unit (ICU). It can be used as a bolus dose of 80 to 200 µg/Kg followed by an infusion of 2 to 12 µg/Kg/min. However to meet the requirements of fast-track cardiac surgery, smaller doses (15 µg/Kg bolus for induction followed by 15 µg/Kg/hour for maintenance) have also been used. A sedative-hypnotic such as propofol should be combined with this regimen. Its haemodynamic effects have been found to be similar to those of fentanyl and sufentanil in patients undergoing valve surgery[39], but it has been shown to cause haemodynamic instability and myocardial ischaemia in patients undergoing CABG.[40] Alfentanil and sufentanil can be combined to minimise the side effects of each compound. Alfentanil can be followed by sufentanil because of their different onset times (1 to 2 min. for alfentanil, 4 to 6 min. for sufentanil) to achieve better blunting of the circulatory responses to tracheal intubation.[41]

Remifentanil

Remifentanil is an anilidopiperidine derivative. It is 19 times more potent than alfentanil in humans. It undergoes extensive hepatic and extrahepatic breakdown by nonspecific tissue and blood esterases. It has a very rapid onset of action comparable to that of alfentanil. The cardiovascular effects are similar to those observed with fentanyl analogues. The fast decay in plasma concentrations, even with high dose and long infusion times, ensures a rapid recovery. This, however, necessitates early requirement of postoperative analgesics, which should be considered before the remifentanil is discontinued at the end of surgery. It is well suited for fast-track cardiac surgery and is given best as a short infusion in the dose of 1 to 2 µg/Kg/min. for induction of anaesthesia. The anaesthesia can be maintained with an infusion at the rate of around 1 µg/Kg/min. It has been shown to provide safe and stable operating conditions and facilitate earlier tracheal extubation as compared with sufentanil.[42] The postoperative analgesia can be effectively provided with remifentanil infusion using patient controlled analgesia [43] or intrathecal morphine.[44] Further, it can be safety used for short procedures

such as chest drain removal in the intensive care unit.[45]

Buprenorphine

Buprenorphine is classified as agonist-antagonist opioid that is agonist at one opioid receptor subtype and/or antagonist at another receptor subtype. It is a useful analgesic for general use, particularly in view of its relatively low risk of causing respiratory depression. However, it has never gained popularity in cardiac anaesthesia. This is mainly due to its inability to attenuate cardiovascular and hormonal responses to surgical stimulus.[46] In addition, its onset of action is slow, its peak effect may not occur until 3 hours, and the duration of action is prolonged (> 10 hours).

Other Narcotics

Meperidine, hydroxymorphone and oxymorphone that are widely used for analgesia can be used as anaesthetic agents during cardiac surgery in a manner similar to that of morphine or fentanyl. Meperidine is similar to morphine and can be used as a primary anaesthetic agent. However, its use is not recommended as it causes frequent cardiovascular depression [47] It can also cause neurotoxicity due to its metabolite normeperidine that is a central stimulant. In addition, it occasionally can cause tachycardia. Due to these limitations, meperidine is not preferred in cardiac patients.

In summary, the high-dose opioid technique is still popular in patients undergoing cardiac surgery. However, whether opioids can adequately anaesthetise a patient is questionable. High doses of opioids are capable of producing intense analgesia and unconsciousness, but it is generally accepted that they are incapable of producing adequate state of anaesthesia. Additionally, opioids alone may not be sufficient to prevent haemodynamic responses to sternotomy and aortic dissection. In clinical practice, therefore, opioids are generally combined with benzodiazepines, nitrous oxide, inhalational agents and propofol.

Barbiturates

Thiopental

Since its introduction in 1934, this ultrashort acting barbiturate has survived the test of time and has become the most widely used induction agent. The

rapid awakening from thiopental has been related to its rapid redistribution. However, awakening may be delayed in older patients. It is a direct myocardial depressant and also causes increased venous capacitance leading to hypotension and reflex tachycardia.[48] These haemodynamic changes, however, can be minimised by administering it slowly or by an infusion. The cardiovascular effects of thiopental are similar in healthy patients or those who have compensated heart disease. The increase in HR can be potentially deleterious in patients with coronary artery disease (CAD), because of the increase in myocardial oxygen consumption (MVO_2). It is also obvious that if given in hypovolemic patients, it can lead to a significant decrease in cardiac output (CO) and MAP. In addition, histamine release and anaphylactoid reactions are possible with thiopental administration.[49]

Thiopental can be used safely for induction of anaesthesia in normal patients and in those who have compensated heart disease. However, rapid bolus injection must be avoided and caution be exercised in hypovolemic patients or patients having ventricular dysfunction and valvular disease.

The usual induction dose of thiopental is 2.5 to 4.5 mg/Kg, but age, gender and lean body mass should be considered for calculation of the doses. In clinical practice of cardiac anaesthesia, thiopental is rarely used as the sole induction agent. It is generally combined with opioids and benzodiazepines. Small increments of bolus doses of thiopental (25 to 50 mg) can be used to control the hypertensive response that may be observed during intubation. In addition, thiopental has been used for cerebral protection during cardiopulmonary bypass (CPB), especially if a haemodynamic compromise has occurred during the operation. However, this practice is no longer in use. It has been shown that thiopental in the dose of 3–5 mg/Kg produces only a short duration of incomplete burst suppression.[50]

Methohexital

Methohexital is an ultrashort acting methylbarbiturate. It is more potent than thiopental and has similar actions and uses. The cardiovascular depression produced by methohexital in patients who have cardiac disease is similar to that of thiopental. Methohexital, thus does not provide any cardiovascular advantage over thiopental.

Benzodiazepines

Diazepam used to be the only benzodiazepine available in the developing countries until recently. Midazolam has now been introduced. The other intravenous benzodiazepine in clinical use is flunitrazepam. Diazepam, lorazepam and flunitrazepam are similar in that they are insoluble in water and require organic solvents to form solutions. The resultant pH range of 6.6 to 6.9 can cause pain and thrombophlebitis.[51] In contrast, midazolam is water soluble and does not cause thrombophlebitis or pain on injection. The mechanism of action of benzodiazepines in the central nervous system is by potentiation of the inhibitory effect of gammaamino butyric acid (GABA) on neuronal transmission.[52] All benzodiazepines have hypnotic, anticonvulsant, muscle relaxant, amnesic and anxiolytic effects.

Diazepam

Diazepam is used as an induction agent in some centres in the dose of 0.3 to 0.5 mg/Kg over 5 to 15 seconds.[53] The haemodynamic stability, amnesic property and smooth induction are the properties that are responsible for its usage. Its ability to maintain cardiac index (CI), despite producing decrease in MAP and HR can be especially desirable in patients suffering from CAD as it leads to a decrease in MVO_2.[54] Its use in patients suffering from mitral valve disease and pulmonary artery hypertension (PAH) has been shown to significantly decrease the PAH and pulmonary vascular resistance (PVR) while mamtaining the CO.[55] However, it may not be safe in patients suffering from severe mitral stenosis (commonly seen in the developing countries) who are vasoconstricted and cannot tolerate reductions in preload. The vasodilatation produced by diazepam can lead to severe decrease in BP and CO. It is also not well tolerated by patients suffering from constrictive pericarditis.[56]

Diazepam combined with opioids can produce more precipitous haemodynamic changes leading to decrease in CO, stroke volume (SV) and MAP.[19,57] A significant decrease in MAP and SVR may occur if diazepam is followed by fentanyl.[57]

Diazepam can be used for induction of anaesthesia in patients having cardiac disease. The amnesic action is especially desirable. However, it should be avoided in patients having hypovolemia or cardiac tamponade. In addition, it must be used with caution when combined with opioids. The other undesirable features include, pain on injection, thrombophlebitis,

variability of response among individual patients, the long half-life and the tendency for accumulation of the drug with repeated administration in elderly patients and those who have liver disease. It is perhaps, due to these drawbacks that it is not a popular agent for induction of anaesthesia. It is generally combined with opioids in the dose of 5 to 10 mg for adults in order to avoid the awareness that may occur with opioid alone. However, diazepam has been replaced by midazolam in most settings.

Midazolam

Midazolam, a water soluble benzodiazepine was synthesised in the United States in 1975.[58] It is unique because of its speed of onset, short duration of action and rapid clearance.[59] These properties make it an ideal agent for induction of anaesthesia. However, if used as the main anaesthetic agent, continuous infusion is necessary for long procedures. In addition, adjuvant analgesic drugs are required to block the response to noxious stimuli because midazolam is not an analgesic. Although, the haemodynamic effects of midzolam are similar to diazepam,[60,61] midazolam causes greater decrease in MAP which may be due to more negative inotropic effect.[53] It is also suggested that midazolam affects the capacitance vessels more than does diazepam.[62] Sedation with midazolam (0.05 mg/Kg) in patients undergoing cardiac catheterisation is devoid of any haemodynamic effects.[63]

Midazolam can be used safely with almost all the anaesthetic agents. The combination of midzolam and fentanyl is commonly used for induction and maintenance of general anaesthesia during cardiac surgery without adverse haemodynamic consequences.[64] However, significant hypotension may sometimes occur with combination of fentanyl and midazolam, and caution should be exercised. Due to its rapid onset and haemodynamic stability, if used alone, it seems to be an ideal agent for short procedures such as cardioversion or cardiac catheterisation, and automatic internal cardioverter defibrillator (AICD) implantation. It is also useful whenever neuropharmacological properties of a benzodiazepine are required rapidly and for a brief period of time.

Etomidate

Etomidate is moderately lipid soluble and has a rapid onset (10 to 12 seconds) and a brief duration of action similar to thiopental and metho-

hexital.[65,66] The very short duration of hypnotic effect of etomidate is probably a result of its rapid distribution in peripheral tissues. Its effects on haemodynamics are less detrimental, as there is minimal myocardial depression and no increase in HR.[67,68] The recommended induction dose is 0.3 mg/Kg. Since the hypnotic effect is brief, additional analgesia and hypnotic drugs must be administered.

It has been shown to provide excellent anaesthetic conditions with minimal haemodynamic disturbances when used in combination with an opioid.[69] However, its use has been limited by concerns about its inhibition of steroid synthesis.[70] Etomidate offers no real advantage over most other induction agents, but it may be considered in emergency situations where rapid induction is essential, such as patients with hypovolaemia, cardiac tamponade or low CO.

Ketamine

Ketamine is a phencyclidine derivative and its anaesthetic actions differ markedly from barbiturates and other central nervous system depressants. Its effect has been labelled as 'dissociative anaesthesia'.[71] Ketamine provides rapid hypnosis and profound analgesia, however, respiratory and cardiovascular functions are not depressed much in comparison to other anaesthetic agents. In fact, it stimulates the cardiovascular system leading to increases in HR, CI, SVR, BP and pulmonary artery pressure (PAP). All these changes result in an increase in MVO_2,[72] and therefore, make it unsuitable for use in patients undergoing CABG as well as valve surgery. The increase in PVR in patients with mitral valve disease as well as congenital heart disease is especially undesirable.[73,74] However, a number of pharmacological methods have been used to block the ketamine induced tachycardia and systemic hypertension. These include propranolol (beta-blockade) and phenoxybenzamine (alpha-blockade)[75] verapamil,[76] benzodiazepines,[77,78] and dexmedetomidine.[79] Nevertheless, ketamine is not a popular agent in adult cardiac surgery except in those patients who have decreased blood volume, uncompensated congestive heart failure or cardiac tamponade, who depend on sympathetic activity for the maintenance of cardiovascular function. It is also used for induction of anaesthesia in paediatric patients, partly because of its haemodynamic effects and partly because it can be administered intramuscularly.[80] Ketamine (2 mg/Kg

intravenous or 4 to 6 mg/Kg intramuscular) in combination with heavy premedication has been used as the anaesthetic for paediatric cardiac cafheterisation at some places without much problem.[81] However, such a technique prolongs emergence time.

Undesirable increases in MVO_2, and PVR, as well as disturbing psychotomimetic activity (vivid dreams, hallucinations or emergence phenomenon) have limited the use of ketamine in cardiac anaesthesia practice.

Propofol

Propofol is one of the most recent intravenous anaesthetic agents to be introduced into clinical practice.[82] It is available as 1 percent solution in 20 mL glass ampoules, 50 and 100 mL vials, and in 50 mL prefilled syringes. It is a rapidly acting intravenous anaesthetic agent that is formulated in a soyabean emulsion. The brevity of action and rapid recovery with propofol has led to its extensive usage in short surgical procedures, especially day-care surgery. The short duration of action is due to rapid redistribution and elimination. Propofol causes decrease in BP that is accompanied by decrease in SVR. Systolic BP decreases by 15 to 40 percent following intravenous induction with 2 mg/Kg and maintenance infusion of 100 µg/Kg/min.[83] The decrease in BP is associated with a decrease in CI, stroke volume index and SVR.[84] Despite a significant decrease in MAP, propofol can lead to a decrease in HR.[85] Some authors have demonstrated an increase[86] or no change in the HR.[87] It has also been shown to decrease myocardial contractility.[88,89]

Due to these haemodynamic effects, propofol may not be suitable for induction of anaesthesia in patients undergoing open-heart surgery. However, it can be used in low dosage along with morphine, fentanyl or midazolam to accomplish fast-track cardiac anaesthesia. It is customary to use propofol in the dose of 30 to 50 µg/Kg/min. in such a situation. Its merit of rapid recovery after cardiac surgery and in the intensive care unit is well demonstrated.[90,91] It can also be used in the cardiac catheterisation laboratory in combination with an opioid for short procedures such as electrophysiological studies and AICD implantation.

Propofol is now readily available, but it should not be used indiscriminately. It must be remembered that the cardiovascular depressant

properties may be harmful in patients having impaired myocardial contractility or those having low fixed CO. Two cases of complete heart block after its use have also been reported.[92]

Dexmedetomidine

Dexmedetomidine is the pharmacologically active D-isomer of medotimidine and is a highly selective, specific and potent alpha-2 adrenoreceptor agonist. It has sedative effects and can reduce the volatile anaesthetic requirements. The exact mechanism of action is not known but is considered to involve an action at both presynaptic and post-synaptic alpha-2 adreno-receptor in the central nervous system. It causes modest decrease in the BP and HR. It, thus seems that it can be used as an adjunct to anaesthetic agents (opioids/inhalational agents) to reduce their requirement and improve haemodynamic stability. The alpha-2 adrenergic agonists have the potential to inhibit opioid-induced rigidity. Therefore, dexmedetomidine may be used as an adjunct with high-dose opioid technique. It can be used in the dose of 2.5 μg/Kg for premedication and 0.2 to 0.7 μg/ Kg/hour infusion for adjunctive purposes.

Muscle Relaxants

The use of muscle relaxants is an integral part of an anaesthetic technique. The neuromuscular blocking agents have differing cardiovascular effects and duration of action. These differences allow the anaesthesiologist to choose a suitable muscle relaxant in order to match the cardiovascular needs of a patient. This choice is based mainly on the haemodynamic effects during induction and prebypass period. The use during CPB is empirical as the pharmacokinetics of muscle relaxants during CPB is confusing and steady-state drug plasma levels are very difficult to obtain.

Until recently, succinylcholine, d-tubocurarine and pancuronium were the only muscle relaxants available in the developing countries, with pancuronium being the most widely used agent. With the recent introduction of agents such as atracurium, vecuronium and rocuronium, the cardiac anaesthesiologist has a wider choice to select an agent that is best suited for his patient.

The intubating dose and clinical duration of action of the commonly used

muscle relaxants are shown in Table 2.2.

Table 2.2: Intubating dose and duration of action of muscle relaxants.

Drug	*Intubating dose*	*Duration (min)*
Succinylcholine	1 mg/Kg	5 to 10
Pancuronium	0.08 to 0.12 mg/Kg	60 to 120
Atracurium	0.5 to 0.6 mg/Kg	30 to 45
Vecuronium	0.15 to 0.2 mg/Kg	45 to 90
Rocuronium	0.6 to 1 mg/Kg	35 to 75
Cisatracurium	0.15 to 0.2 mg/Kg	40 to 75

Succinylcholine

Succinylcholine is a depolariser and leads to cardiac arrhythmias during anaesthesia. Bradycardia is a major haemodynamic effect of succinylcholine. The development of cardiac arrhythmias is a clinical manifestation of generalised autonomic stimulation, and sinus bradycardia, junctional rhythms and ventricular arrhythmia ranging from unifocal premature ventricular contractions to ventricular fibrillation have all been documented.[93]

The bradycardia is due to stimulation of cardiac muscarinic receptors in the sinus node,[94] and appears more commonly after a second dose of the drug given approximately 5 min. after the first.[95] It can be readily reversed by atropine. The depolarising nature of the drug leads to release of potassium from the skeletal muscles that may encourage ventricular arrhythmias.[96] Due to these drawbacks, its use in cardiac anaesthesia is limited and perhaps used by some anaesthesiologists for provision of paralysis for intubation, if difficult intubation is anticipated.

d-Tubocurarine

The major drawback of this muscle relaxant is a decrease in SVR leading to

hypotension.[97] The degree of hypotension depends on intravascular volume, and depth of anaesthesia. The hypotension may be accompanied by tachycardia secondary to baroreceptor reflex or histamine release.[98] Due to these limitations, d-tubocurarine is not used in cardiac anaesthesia.

Metocurine

Metocurine is produced by methylation of d-tubocurarine and has cardiovascular effects similar to those of d-tubocurarine, but to a lesser extent. The major haemodynamic response is slight decrease in SVR. It has not been accepted widely in cardiac anaesthesia practice.

Pancuronium

Pancuronium enjoyed wide acceptance mainly due to the fact that the muscle relaxants that were available earlier such as gallamine and d-tubocurarine were known to produce haemodynamic disturbances. Compared to these agents, pancuronium certainly appeared to be a very attractive alternative. However, pancuronium increases the heart rate by blocking the cardiac muscarinic receptors[99] and indirectly stimulating sympathetic nerve endings.[100] Increases in HR, CO and BP can raise the myocardial oxygen demand and may not be suitable for patients undergoing CABG. However, it is a commonly used muscle relaxant for CABG surgery.[101,102] This may be due to the fact that the vagal effects of anaesthesia and certain surgical stimuli that are concealed by the vagolytic effect of pancuronium, are exposed by other neuromuscular blocking agents. In addition, beta-adrenergic blockade, and bradycardia associated with the commonly used high-dose narcotic anaesthetic technique can attenuate, in part the tendency of pancuronium to produce tachycardia. Nevertheless, some investigators have cautioned against using pancuronium because it can cause significant increase in HR and myocardial ischaemia.[103] Its longer duration of action is a potential disadvantage in the setting of fast-track cardiac surgery. Although, pancuronium has mostly been studied in patients undergoing CABG, its haemodynamic effects have been found to be similar in patients undergoing valve surgery.[104] The tachycardia can be especially undesirable in patients suffering from valvular disease who have a higher basal HR due to atrial fibrillation. It is used in the dose of 0.1 to 0.15 mg/Kg for intubation purposes.

Atracurium

Atracurium is degraded by hydrolysis or by Hofmann elimination and has a duration of action intermediate in the spectrum of muscle relaxants. Hofmann elimination is a chemical process that results in the loss of positive charges by molecular fragmentation to laudanosine (a tertiary amine) and monoquatemary acrylate. These breakdown products have no neuromuscular and little or no clinically relevant cardiovascular activity. Laudanosine has central nervous system stimulating properties, but adverse effects are unlikely in clinically used doses of atracurium. The short duration of action suggests that it should be used as an infusion during cardiac procedures. There are no significant haemodynamic changes with atracurium, when used in doses of less than 0.6 mg/Kg.[105,106] However, doses more than 0.6 mg/Kg may cause a decrease in SVR, which may be related to histamine release.[107,108] It has generally been found to be suitable for use in cardiac anaesthesia.[109] As atracurium does not increase the HR, the bradycardia often associated with high doses of narcotics is unopposed, a fact that can be used effectively in those patients who have higher basal HR or in those who have their ischaemia related to HR. It has been shown that the bradycardia is accompanied by a decrease in CI in patients undergoing valve surgery.[104] The histamine release caused by atracurium is dose-dependent and correlates with the degree of HR and MAP changes. However, in clinical practice, this histamine release is minimal and significantly less than that produced by tubocurarine.[110] These changes can be abolished by either slowing the rate of injection of atracurium to 75 seconds or by intravenous pretreatment with Hj and H2 blockers.[111] It is used in a dose of 0.5 to 0.6 mg/ Kg for intubation purposes.

Vecuronium

The margin between the neuromuscular blocking dose of vecuronium and the dose producing cardiovascular and autonomic effects is very wide.[112] Consequently, there are no major cardiovascular effects associated with the administration of vecuronium even in large doses (up to 0.3 mg/Kg).[113,114] The drug does not seem to block the sympathetic ganglion, cardiac muscarinic receptors or to stimulate histamine release. As with atracurium, when vecuronium is given with high-dose opioids, bradycardia secondary to

the opioids is manifested. Sometimes, the bradycardia can be dangerous and even may lead to asystole.[115] The bradycardia maybe desirable in order to reduce the MVO_2 and the risk of myocardial ischaemia. However, it may be undesirable in patients who have low fixed CO such as severe valvular lesion or poor left ventricular (LV) function. The duration of action of vecuronium is similar to that of atracurium. It is metabolised primarily in the biliary and hepatic systems and to a lesser degree in the renal system. Therefore, unlike atracurium, vecuronium is dependent on liver and kidney functions for degradation. It is used in the dose of 0.1 to 0.2 mg/Kg for intubation purposes.

Rocuronium

Rocuronium is a non-depolarising steroidal analogue of vecuronium. Its effects are similar to vecuronium, but it produces good intubating conditions almost as quickly as succinylcholine. However, it lacks succinylcholine's brevity of action. Its duration of action is similar to vecuronium when administered in equipotent doses. Most studies have indicated a relative lack of haemodynamic effects, but mild increases in HR may be noted. It has also been shown to decrease PAP[116] and thus, appears to be a useful agent for patients undergoing cardiac surgery. In a comparison with pancuronium, it has been shown to be associated with reduction in tracheal extubation times as well as residual neuromuscular block.[117] It is used in a dose of 0.6 to 1 mg/Kg for intubation purposes.

Mivacurium

Mivacurium is a non-depolarising relaxant that is very short acting, but has a slower onset time than succinylcholine and rocuronium. Like succinylcholine, it is deactivated by plasma cholinesterase. Due to its short duration of action, it needs to be administered in a continuous infusion form in patients undergoing open-heart surgery.

There is substantial decrease in cholinesterase activity during CPB. The reduction in cholinesterase activity is attributed to some irreversible enzyme inactivation caused by CPB, rather than by haemodilution or hypothermia.[118] This, however, does not cause a clinically relevant prolongation of mivacurium neuromuscular block.[119]

Mivacurium can cause histamine release, which is dose-dependent leading to a decrease in BP. There is not much effect on the HR. The histamine release can be minimised by slower rate of administration (30 to 60 seconds). The intubating dose of mivacurium is 0.15 to 0.25 mg/Kg. It has been used in cardiac surgery in the dose of 0.15 and 0.2 mg/Kg and has been shown to be associated with transient hypotension and erythema.[120] However, if mivacurium is injected over 60 seconds period, no haemodynamic changes were observed in patients with documented coronary artery disease undergoing non-cardiac surgery.[121]

Cisatracurium

The major pathway for elimination of cisatracurium appears to be Hofmann elimination. It is approximately four times as potent as atracurium with an approximate ED95 value of 0.05 mg/Kg. Cisatracurium has a slightly slower onset of action than atracurium when given in equipotent doses. Intubation may be carried out within 90 to 120 seconds with a dose of 3 to 4 times the ED_{95} (0.15 to 0.2 mg/kg).[122] The clinically effective duration of block varies with the dose and ranges from 15–30 min. It has a predictable and fast rate of spontaneous recovery. The rate of infusion is about 1 μg/kg/min. but, more refined infusion protocols with different rates of infusion, before, during and after CPB have been proposed with the purpose to reduce postoperative neuromuscular blockade. [123] Like atracurium, cisatracurium does not depend an liver or kidney for its removal and does not accumulate even in renal on hepatic failure. Studies on animals have shown a wide separation between the neuromuscular blocking dose and doses that affect the autonomic nervous system. It has no significant cardiovascular and histamine like effects and its cardiovascular stability has been demonstrated in healthy adults as well as in patients with cardiovascular diseases.[124,125] It has been found to be suitable for fast-track cardiac surgery. [126]

Pipecuronium

Pipecuronium is a long acting steroidal non-depolarising neuromuscular blocking agent. The most important advantage of pipecuronium over pancuronium is that it is relatively free of circulatory effects. However, some decrease in HR may be observed which is related to unopposed bradycardia inducing effect of narcotics or anaesthesia. Perfect intubating conditions as

well as haemodynamic stability can be achieved by administering about 3 times the ED_{95} dose (i.e. 0.1 mg/Kg) of pipecuronium.[127,128] Pipecuronium, thus, seems to be well suited for cardiac anaesthesia.

Alcuronium and Fazadinium

Alcuronium resembles metocurine in pharmacological and cardiovascular profiles. It leads to little release of Mstamine and weakly blocks sympathetic ganglia at high doses. Fazadinium increases HR in a manner similar to pancuronium. However, there seems to be no major advantage of these drugs over the currently available relaxants.

In summary, vecuronium and atracurium along with opioids decrease the HR and might be advantageous in patients with higher baseline HR. Rocuronium provides excellent intubating conditions with a faster onset of action. It also causes a mild increase in HR and is beneficial in patients with slower baseline HR, especially regurgitant valvular lesions. Cisatracurium in quite promising with its lack of haemodynamic effects, quick recovery pattern and metabolism via Hofmann elimination, but has longer onset time.

Nitrous Oxide

Nitrous oxide has been used as an adjuvant to general anaesthesia for a long time. The insolubility of nitrous oxide results in rapid awakening and its combination with potent volatile anaesthetics or narcotics decreases their dose requirements. The use of nitrous oxide has declined mainly due to the fear of expansion of air emboli.[129] Many centres have discontinued the use of nitrous oxide, while at others, nitrous oxide is combined with narcotics until shortly before CPB commences, following which it is discontinued.

Nitrous oxide is not a potent anaesthetic and its cardiovascular effects appear minimal.[130] However, it is a direct depressant of the myocardium and its use following high doses of opioids leads to decrease in CO and BP.[131] Although, its haemodynamic effects have been mostly studied in patients suffering from CAD, it has been shown to have similar effects in patients undergoing valve surgery.[132,133] In addition, its ability to increase PVR is of particular concern in patients with PAH.

In all these studies, nitrous oxide has been used in combination with some other anaesthetic, either opioid or volatile agent. Nevertheless, the use of

nitrous oxide has declined in cardiac surgery mainly due to the fear of expansion of air emboli following CPB. This also may be related to the introduction and ready availability of agents such as fentanyl, midazolam, propofol, isoflurane, desflurane and sevoflurane. Those who still use nitrous oxide should restrict its use following CPB in all patients, and during prebypass period in patients who have poor LV function or increased PVR.

Volatile Anaesthetic Agents

Volatile agents are complete anaesthetic agents, in the sense, that each potent volatile anaesthetic can be used without supplementation to provide appropriate levels of amnesia and analgesia. The volatile agents can also supplement muscle relaxation. However, their use as the sole anaesthetic is limited by their effects of myocardial depression and vasodilatation, when used in higher concentration that are necessary to suppress the sympathetic responses to noxious stimuli. Therefore, volatile agents are used along with opioids so that they can be used in smaller concentration and their myocardial depressant effect is minimised. Most cardiac anaesthesiologists prefer an anaesthetic technique that consists of a base of a relatively high-dose narcotic supplemented with low concentrations of volatile anaesthetic agents. In addition to being a valuable supplemental agent to provide unconsciousness along with an opioid based anaesthetic technique, volatile agents can be used to increase the anaesthetic depth temporarily in anticipation of a strong noxious stimulation and to control hypertension and tachycardia. The amnesic property of volatile agents may be useful to prevent awareness. New evidence suggests that volatile anaesthetics at clinical concentrations may also be useful in protection against perioperative myocardial ischaemia, by a mechanism that is independent of effects of myocardial oxygen balance.[134]

In the developing countries, halothane has enjoyed a wide acceptance and popularity so far, but with the introduction of isoflurane, sevoflurane, and desflurane, the cardiac anaes-thesiologists can be a little more selective.

Halothane

The introduction of halothane in 1956 really was a major advance. It is non-flammable, non-irritant and stable in soda lime. It has relatively low solubility coefficients resulting in a fairly rapid onset and recovery. It is

potent with minimum alveolar concentration (MAC) of 0.75 percent. It produces a dose-related decrease in myocardial function. In human volunteers, it has been shown to decrease BP, which is due to concomitant decreases in SV and CO.[135] The HR and SVR do not change significantly. Similar effects are seen in children.[136] Halothane appears to have minor coronary vasodilating action in humans having normal coronary circulation as well as those with CAD having normal or abnormal LV function.[137-139] The decrease in coronary blood flow that may be observed is related to a decrease in the BP and MVO_2.[140] Because of its ability to decrease myocardial oxygen demand, it may be beneficial during periods of myocardial ischaemia if coronary blood flow is maintained.[141]

Halothane also has important electrophysiological effects. These primarily include increase in refractoriness within atrioventricular as well as accessory pathways. However halothane has the least effect compared to enflurane and isoflurane.[142-144] Frequent atrioventricular junctional rhythms may be observed during halothane anaesthesia. Halothane sensitises the myocardium to catecholamines and may lead to the development of arrhythmias.[145,146] These arrhythmias can be easily treated by oxygenation and discontinuation or substitution of halothane. Its major disadvantage is the fact that around 20 percent of the dose is metabolised by the liver by oxidative and reductive pathways. Halothane metabolites are probably responsible for the genesis of a rare but potentially fatal condition, halothane hepatitis. In the developing countries, the use of halothane has considerably declined in cardiac anaesthesia. Its low price is perhaps the only attraction for those few anaesthesiologists who use it.

Isoflurane

Isoflurane is more heavily fluorinated than halothane, so it is more stable chemically. It has rapid onset and recovery characteristics. It is hardly metabolised, so toxic effects on liver and kidneys are unlikely.

It causes a dose-dependent decrease in BP, mainly by decreasing the SVR. The CO is maintained or decreased marginally.[147] The increase in HR produced by isoflurane compensates for the decrease in SV, thereby maintaining the CO. It does not destabilise the heart rhythm even in the presence of adrenaline.

Coronary Steal

The presence of obstruction in the coronary artery leads to vasodilatation in an effort to maintain coronary blood flow across the lesion. However, as the obstruction increases (> 90 percent), the vasodilatation is maximal and no further dilatation is possible. Thus, if a coronary artery provides blood to two or three distal branches and one of them is tightly narrowed, administration of a vasodilator may cause preferential vasodilatation of the normal vessels leading to a relative increase in blood flow to the area of heart that is supplied by the normal anatomy. This causes relative decrease in blood flow to the area of heart supplied by the stenotic vessel. This phenomenon is known as coronary steal (Fig. 2.1).

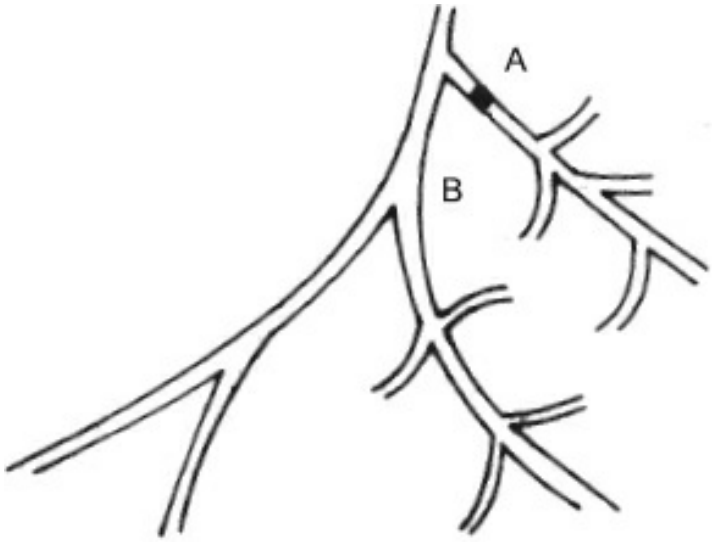

Figure 2.1: The coronary vessel A has developed stenosis, so that the vessels distal to the stenosis are maximally dilated. In addition, collaterals develop between the lschaemlc and the adjacent nonischaemic zone supplied by vessel B. When vasodilatation occurs, e.g. during exercise, it occurs mainly in the non-ischaemic zone (vessel B) leading to decrease in pressure In the nonlschaemic zone. The flow across the high resistance collateral vessels Is reduced leading to coronary steal.

Isoflurane was in the midst of controversy regarding its potential to cause coronary steal. Animal experiments have demonstrated that isoflurane is a coronary vasodilator and interferes with coronary autoregulation.[148,149] The possibility that dilating effect on normal coronary vessels might steal blood away from the diseased vessels, and cause myocardial ischae-mia was extensively investigated. The data derived from these studies revealed conflicting results. Some studies clearly demonstrated both regional and transmural maldistribution of myocardial blood flow during isoflurane,[150] whereas others could not document maldistribution in coronary blood

flow.[151] It also appeared at this time that the associated alterations in the haemodynamics such as hypotension or tachycardia were necessary to cause maldistribution of coronary blood flow. It was shown that myocardial blood flow distribution was not altered by isoflurane when systemic haemodynamics were controlled at awake levels.[152] However, the use of isoflurane in patients with CAD became controversial when it was suggested that 1 MAC of isoflurane can lead to ischaemia in the presence of normal systemic haemodynamics.[152] Its usage declined further when Becker[153] in an editorial, strongly recommended that the safest course is to avoid isoflurane in patients with known CAD. Several outcome studies performed subsequently showed that isoflurane is not associated with higher cardiac morbidity or mortality than other volatile agents or opioid regimens.[154-158] However, in all the studies isoflurane was used as an adjunct to opioids so that the concentration of isoflurane used was minimal and may not have been enough to cause coronary dilatation.

Since at present there is no evidence, which clearly demonstrates that isoflurane causes coronary steal and that it is responsible for increased morbidity in patients with CAD, isoflurane has become the favoured volatile agent for most anaesthesiologists.

Enflurane

The haemodynamic effects of enflurane are remarkably similar to those of halothane. Enflurane produces dose-dependent myocardial depression[159,160] that is readily reversible with time by lowering the inspired concentration. Enflurane, however, sensitizes the myocardium to catecholamines to a lesser degree as compared with halothane.

It has been shown to produce coronary vasodilation leading to decreased coronary perfusion pressure and MVO_2.[161] However, there were no metabolic or ECG signs of ischaemia despite a decrease in the coronary perfusion pressure.

Enflurane is metabolised producing fluoride ions which may be toxic to kidneys, if prolonged administration is performed.

Sevoflurane

Sevoflurane offers an acceptable aroma and also the incidence of bradycardia

or arrhythmias and hypotension is less as compared with halothane. These properties along with a low blood and tissue solubility (that allow for rapid equilibration between the inspired and alveolar concentrations) makes sevoflurane a preferred inhalational agent for induction of anaesthesia in children. Its use in cardiac surgery is increasing due to its favourable haemodynamic effects and cardioprotective properties. It produces less sympathetic activation as compared with desflurane.[162] It decreases SVR, arterial BP and CO in a dose-dependent fashion with a tendency to lower HRs, which can be an advantage in most patients with ischaemic heart disease.[163] Sevoflurane participates in the preconditioning cascade leading to beneficial effects on intraoperative myocardial function after CPB.[164] This effect might influence the long-term morbidity and mortality after CABG.[165]

Animal studies have shown that sevoflurane does not cause coronary steal. Prolongation of QT interval has been reported without any evidence of adverse clinical effects.[166] Its potential adverse effects on renal function have been shown to be of little significance in normal clinical use.[167] The haemodynamic stability, cardioprotective properties and acceptable aroma make it an ideal inhalational agent for patients undergoing cardiac surgery.

Desflurane

The cardiovascular effects of desflurane are similar to isoflurane. There is a dose-dependent decrease in BP due to decrease in SVR, but there is no significant increase in HR. The sympathetic excitation associated with desflurane might lead to undesirable increase in HR and BP.[168] However, in clinical practice, the haemodynamic effects of desflurane have been found to be similar to isoflurane without any difference in clinical outcome.[169] Like sevoflurane, desflurane provides direct protection from ischaemic myocardial damage. Multicentre, randomised clinical trials have demonstrated that desflurane could reduce the postoperative release of cardiac troponin-I, the need for inotropic support, and the number of patients requiring prolonged hospitalisation after CABG.[170] However, similar beneficial effect of desflurane has not been demonstrated in patients undergoing mitral valve surgery.[171] Further, one report has shown that desflurane is associated with higher incidence of atrial fibrillation after surgery.[172]

In summary, all volatile anaesthetics have cardiac depressant effects that decrease the myocardial oxygen demand. This may improve the myocardial

oxygenbalance during ischaemia. In addition, recent evidence has clearly demonstrated that they also have direct protective effect from ischaemic myocardial damage. Thus, volatile agents should form a part of anaesthetic plan in patients undergoing cardiac surgery.

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Chapter 3: Physiology of the Cardiovascular System

The heart along with its vascular system constitutes cardiovascular system. The ‘heart’ is a muscle pump designed to pump blood through the vascular system in a rhythmic manner. In fact it consists of two pumps, the left heart and the right heart. Each heart has two pumps a minor pump (atrium) and a major pump (ventricle). Atria generate low pressure and serve to prime the respective ventricles, which are the main pumps that generate force to propel blood in systemic and pulmonary circulations. Special conduction mechanisms in the heart transmit action potential throughout the heart muscle to cause simultaneous rhythmic beat of the two hearts; therefore, the two hearts function in phase and in parallel. The vascular systems (the arterial and the venous), aptly help the heart in optimizing its output in tune to the metabolic requirement. This chapter provides an overview of the various components of the cardiovascular system. The aim of this chapter is to describe understanding of cardiovascular physiology from anaesthesia point so that the practicing anaesthesiologists can make appropriate decisions while managing cardiac issues in patients undergoing surgery under anaesthesia. For the detailed knowledge of cardiovascular physiology, one should refer to a standard textbook of medical physiology.

Cardiac Muscle

The basic muscle unit of the heart is ‘myocyte’. The muscles of the heart are of three types namely atrial muscles, ventricular muscles and the specialized muscles. The specialized muscles are excitatory, exhibit rhythmicity, varying rates of conduction and provide excitatory pathway that control rhythmic heartbeat.[1] The atrial and the ventricular muscles are similar to skeletal

muscles except the fact that when excited, their duration of action potential and contraction is much longer. The cardiac muscle is a syncytium of many heart muscle cells such that when one of these muscle cells is excited, the action potential spreads to all the muscle cells. The muscles of atria are separated from that of respective ventricles by fibrous tissue that surrounds the atrioventricular (AV) valve openings between the atria and the ventricles. The fibrous tissue does not allow conduction of the atrial muscle potential to the ventricular muscle.[2] Instead, the excitation is conducted by way of a specialized conduction system called A-V bundle. This division of the muscles of the heart into two functional syncytium namely atrial and ventricular syncytium allows the atria to contract ahead of ventricular contraction and serve to prime the respective ventricles.[1]

The action potential in the ventricular muscle averages about 120 mV. The membrane potential in cardiac muscle on excitation rises from –80 mV to + 20 mV. The membrane potential remains depolarised for about 0.2 sec in the atrial muscle and for 0.3 sec in the ventricular muscle; therefore, the action potential curve shows a plateau (Fig. 3.1). The presence of plateau causes cardiac muscle contraction to last 15 times longer as compared to skeletal muscle.[1] The action potential is caused by two types of channels namely the fast sodium channels and the slow calcium channels also called as calcium-sodium channels. The initial action potential is caused by sudden opening of a large number of fast sodium channels, which allow tremendous number of sodium ions to enter inside the cell; the action potential is sustained (plateau) by opening of the slow calcium channels which allow entry of calcium as well as sodium ions.[1] The calcium ions that enter during this phase play a vital role in muscle contraction. During action potential plateau, the membrane permeability to potassium ions is greatly decreased but at the end of plateau, the membrane permeability to potassium ions greatly increases which returns the membrane potential to its resting level.

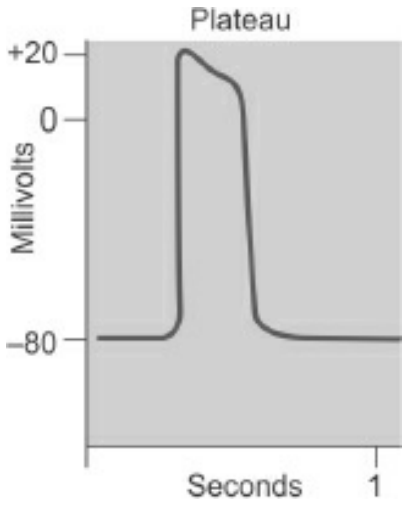

Figure 3.1: Diagrammatic representation of the action potential graph.

Rhythmical Excitation of the Heart

The excitatory and the conduction system of the heart (Fig. 3.2) consist of sinus node (Sinoatrial node; SA node), the internodal pathway that carries the impulse from the SA node to the A-V node, the A-V bundle (Bundle of His) which carries the impulse from the atria to the ventricles, and the left and right bundles and Purkinje fibres which carry the impulse to all parts of the ventricles. The conduction delay at A-V node ensures that the atria contract before the ventricles and serve as the primers of the respective ventricles. The fast conduction down the Purkinje fibres allows all portions of the ventricles to contract simultaneously to generate most effective pressure in the ventricular chambers.

Impulse normally generates in the SA node; however, the A-V node, the Purkinje fibre, and even the atrial and ventricular muscles can generate impulse but the impulse so generated is abnormal. The SA node generates impulses at a rate of 70–80/min., the A-V node and the Purkinje fibres can generate impulses at a rate of 40–60/min. and 15–40/min. respectively provided they are not stimulated by the SA node or any other outside source. Since the discharge rate of SA node is faster than the A-V node and the Purkinje fibres, the SAnode functions as the natural pacemaker of the heart. Apparently, the conduction system and the pacemaker function of the SAnode are designed to achieve adequate volume priming of the ventricles but at a lowest mean pressure in the atria and the downstream venous system. The surface recording of the electrical activity of the heart including

conduction system, and the atrial and ventricular muscles results in electrocardiogram (ECG).

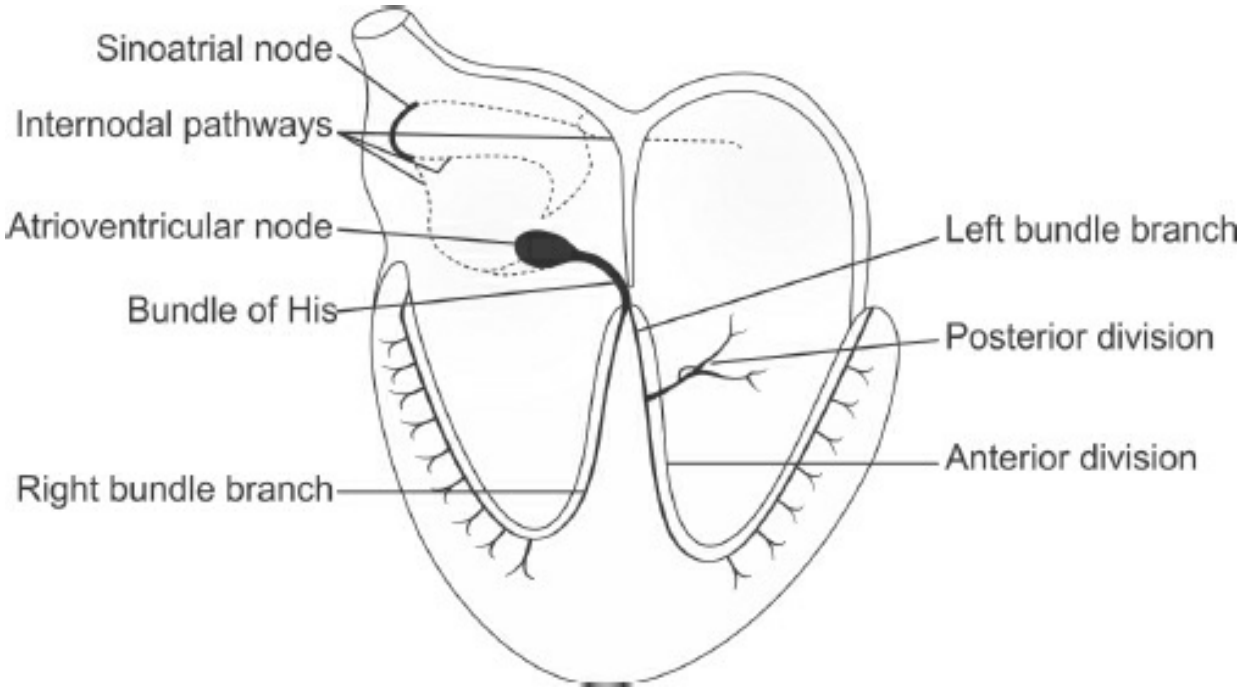

Figure 3.2: Showing cardiac conduction pathway.

Electrocardiogram

The normal ECG (Fig. 3.3) is composed of a 'P' wave, a 'QRS' complex and a 'T' wave; the 'P' wave and 'QRS' complex are caused by electrical depolarisation of atria and ventricles, respectively. The 'T' wave represents repolarisation of the ventricles.

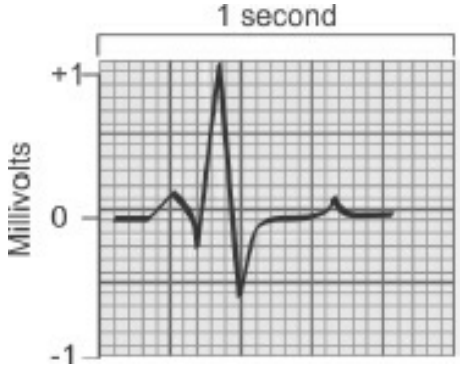

Figure 3.3: Shows normal ECG

Duration and voltage of complexes and

intervals

The proximity of the surface electrode to the heart decides the voltage of the complexes, consequently, ECG recorded from the chest leads show larger voltage and the standard limb leads show smaller voltage. The ‘QRS’ voltage recorded from the chest leads can be as great as 3–4 mV and the one recorded from the limb leads is usually 1 mV. The voltage of the ‘P’ wave is usually between 0.1 and 0.3 mV and that of the ‘T’ wave is between 0.2 and 0.3 mV. The time interval between beginning of the ‘P’ wave and the beginning of the ‘QRS’ complex is described as PR interval and denotes time between initiation of excitation of atria to the initiation of excitation of ventricles; the normal PR interval is 0.12 second to 0.16 second. The contraction of ventricle lasts almost from the beginning of the ‘QRS’ complex (beginning of ‘R’ if ‘Q’ wave is absent) to the end of ‘T’ wave. The interval is known as QT interval and measures around 0.35 second.

Cardiac Cycle

The cardiac cycle is the rhythmic repetition of mechanical activity of different chambers of the heart and composed of events that start from the beginning of one heartbeat to the beginning of the next heartbeat. For understanding the cardiac cycle, it is important to simultaneously learn the electrical activity of the heart represented by ECG and the mechanical changes (volume and pressure) occurring in various chambers of the heart (Fig. 3.4). The cardiac cycle consists of a period of relaxation called diastole during which ventricles fill with blood and a period of contraction called systole during which ventricles eject blood in the pulmonary and systemic circulations. For simplicity, the mechanical changes occurring on the left side including left atrium and left ventricle are described; however, the mechanical changes that occur during cardiac cycle on the right side are similar in volume but differ in the pressure changes.

Pressure changes in the left atrium during cardiac cycle

The SA node initiates electrical depolarisation and mechanical contraction of the atria which is followed by ventricular depolarisation by a delay of l/10th

of a second and its contraction. The mechanical contraction of atria (atrial systole) serves to prime the ventricle ahead of its contraction. Atrial systole is followed by its relaxation (atrial diastole). At a heart rate of 72/min. each cardiac cycle consists of about 0.8 second; atrial systole lasts for about 0.1 second; the remaining about 0.7 second is atrial diastole during which it receives pulmonary venous blood. A normal left atrial pressure (LAP) waveform trace consists of 3 peaks (‘a’, ‘c’, and V) and 2 descents (‘x’ and ‘y’) (Fig. 3.4). The ECG serves as a useful marker to discern its components.[3] The mechanical events in atria are always delayed relative to the electrical events in the ECG. The ‘a’ wave represents atrial systole, follows the ECG ‘P’ wave, and occurs in late ventricular diastole. The atrium then begins to relax, leading to a decline in the atrial pressure. The V wave, a transient increase in the atrial pressure begins with ventricular contraction caused by the bulging of AV valve in the atrium. The ‘c’ wave is an early systolic event, follows ventricular depolarisation (QRS complex) and represents beginning of isovolumic ventricular contraction (described later). The ‘c’ wave continues as ‘x’ descent and is caused by the continuing relaxation of the atrium and the descent of the floor of the atrium during ventricular ejection. The V descent is followed by V wave caused by the filling of the left atrium and occurs during late systole. At the end of systole, the ventricle relaxes and the ventricular pressure decreases, the point at which ventricular pressure decrease below LAP, the mitral valve opens and the LAP decreases precipitously and appears as ‘y’ descent on LAP waveform trace. It follows that in the presence of mitral valve insufficiency, the mitral regurgitation will begin with the ventricular contraction, and continue through ventricular systole and the ‘c’, ‘x’, and V waves will be replaced by a single positive deflection.

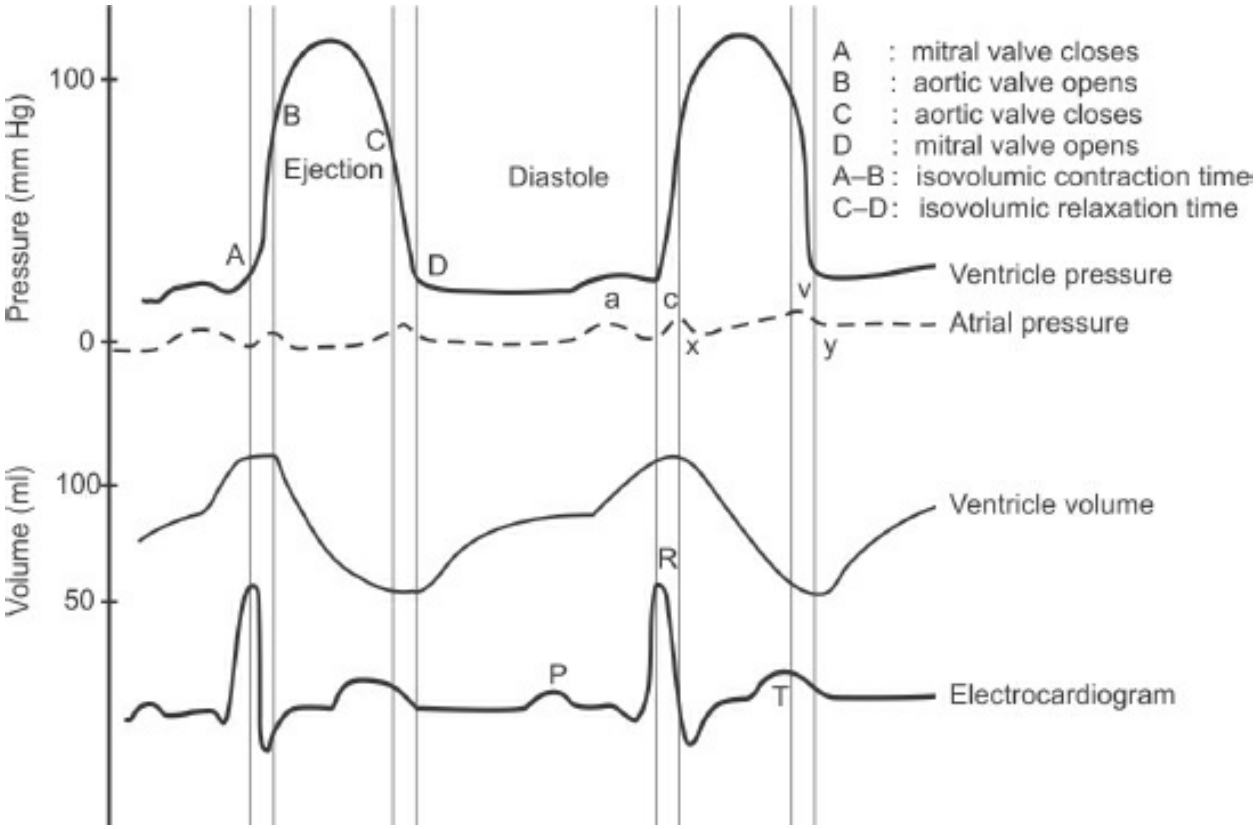

Figure 3.4: Shows changes in LV volume and LA pressure timed with ECG, for details, refer to the text (This is a diagrammatic representation and not an actual figure).

Pressure and volume changes in the left ventricle during cardiac cycle

The ventricular contraction follows the 'QRS' complex of the ECG. With the beginning of ventricular systole, the ventricular pressure increases which causes closure of the mitral valve; continuing ventricular contraction further increases the ventricular pressure which opens the aortic valve against the pressure in the aorta. The period from the closure of the mitral valve to the opening of the aortic valve, is described as 'isovolumic contraction time' (IVCT), as there is no change in the volume of the ventricle during this time. Once the ventricular pressure increases above the aortic pressure, the ventricle begins to eject blood and about 70 percent blood is ejected during first third of the ejection period and the ventricular volume decreases abruptly. The ventricular volume continues to decrease during the remaining 2/3rd ejection period. At the end of systole, the ventricle begins to relax and ventricular diastole starts. As soon as the ventricular pressure decreases

below the aortic pressure, the blood in the aorta pushes back the aortic valve to the closed position. The ventricle continues to relax and once ventricular pressure decreases below the atrial pressure, the mitral valve opens and blood begins to fill the ventricle. During the period from the time of closure of aortic valve to the opening of mitral valve, there is no change in the ventricular volume, there is only decrease in the ventricular pressure, this period is described as ‘isovolumic relaxation time’ (IVRT).

The ventricular filling starts after opening of the mitral valve and about 80–90 percent ventricular filling occurs within the first third of the diastolic period. The relationship between ventricular volume and pressure describes the compliance of the left ventricle. During middle third of the diastole, very little volume increase occurs, finally, the atrial systole occurs in the late diastole when the ventricle reaches to end-diastolic volume and pressure. In an adult, the left ventricular volume at the end of diastole (end-diastolic volume) measures about 110 to 120 mL and the ventricular volume at the end of systole (end-systolic volume) measures about 40–50 mL. The fraction of end-diastolic volume that is ejected during systole is described as ejection fraction. When the heart strongly contracts, the end-systolic volume can decrease to 10–20 mL, whereas when large amount of blood flows in to the ventricle the end-diastolic volume can increase up to 150–200 mL.

The changes in volume and pressure that occur during each cardiac cycle of systole and diastole in the ventricle can be represented by a pressure-volume loop or pressure-volume relationship. Figure 3.5 describes the pressure-volume relationship under normal conditions. The phase 1 (A-B), horizontal up-sloping line along the ‘X’ axis, shows volume change from end-systolic to end-diastolic volume and the accompanying change in pressure. The straight up line along the ‘Y’ axis, phase 2 (B-C), shows change in pressure from end-diastolic pressure till aortic valve opening and represents IVCT. The phase 3 along the ‘X’ axis (C-D) shows change in the ventricular volume from end-diastolic to end-systolic volume and represents ventricular ejection phase. Lastly, the straight down line along the ‘Y’ axis, the phase 4 (D-A), shows change from end-systolic to the LV diastolic pressure at which mitral valve opens and represents IVRT. The area inside the loop provides a rough index of energy used to eject blood or stroke work. The shape of the loop changes with changes in ventricular load, compliance, and ventricular contractility. The changes in volume and pressure in various cardiac diseases can be represented on pressure-volume loops. Each valvular

lesion imposes its own unique set of variables on the left and right ventricular mechanics. Indeed, the signature of pressure-volume relationship of each valvular heart disease is typical and may predict severity of different valvular diseases.

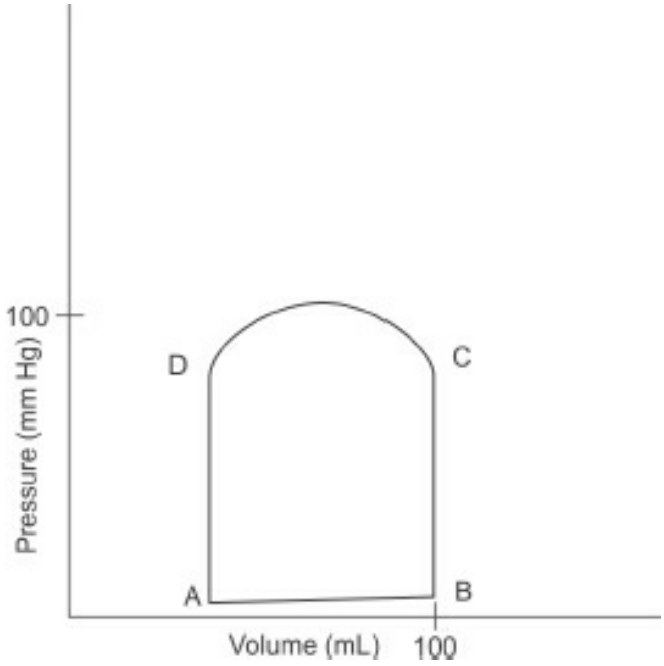

Figure 3.5: diagrammatic representation of the normal left ventricular pressure-volume loop. Refer to the text for details.

Saturation in various cardiac chambers and flow profile across various valves

The measurement of saturation in various chambers of the heart and flow across the various valves can be performed in the evaluation of congenital heart disease, valvular heart disease and evaluation of myocardial functions. The oxygen saturation in the right heart is below 75 percent whereas in the left heart it is > 98 percent. The figures 3.6 and 3.7 show saturations and pressures in various chambers in a normal heart. The flow profile is streamlined across the various valves and is usually below 1 m/second. The figures 3.8 and 3.9 show velocity flow profile across aortic valve and mitral valve as obtained by Doppler interogation on transoesophageal echocardiography. The flow across various diseased valves for example mitral stenosis, aortic stenosis, etc. and abnormal communication between the left and right ventricles are turbulent and the flow velocity increases above 1 m/sec.

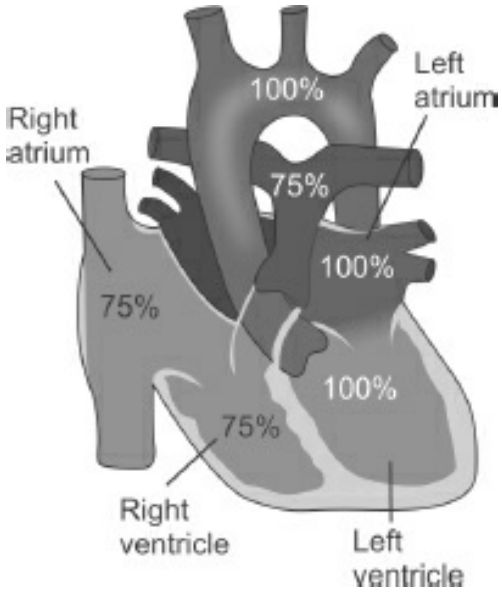

Figure 3.6: Shows oxygen saturation in various cardiac chambers

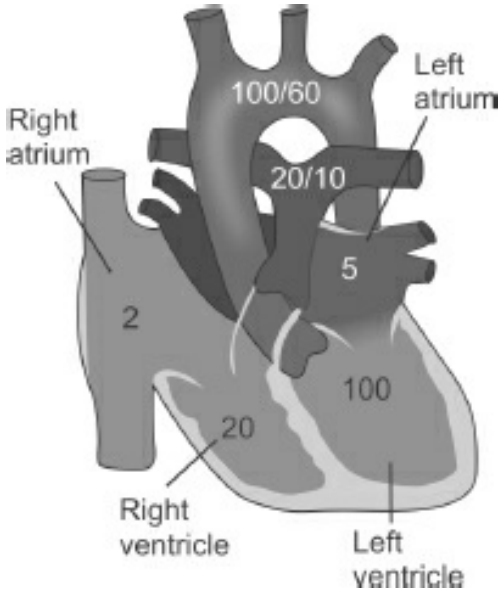

Figure 3.7: Shows pressures (mm Hg) in various cardiac chambers.

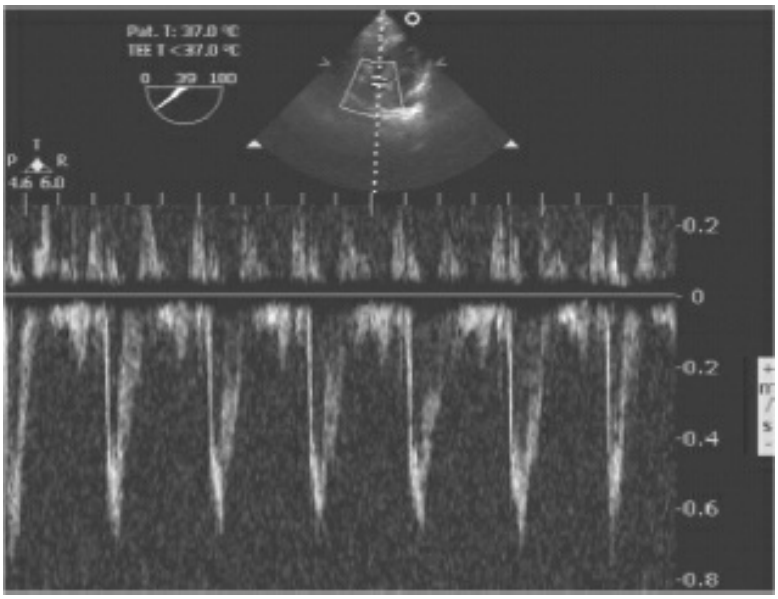

Figure 3.8: Pulsed Doppler flow across the normal aortic valve in deep trans-gastric view

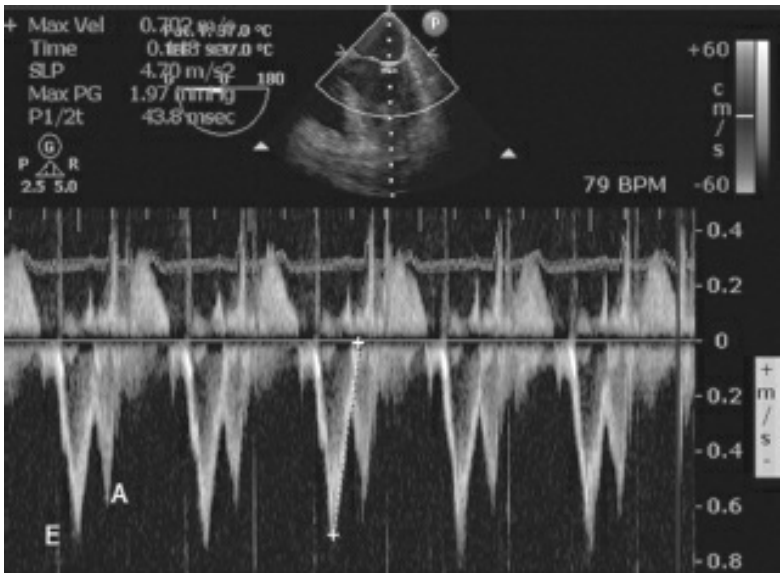

Figure 3.9: Pulsed wave Doppler flow velocity across the normal mitral valve in mid-oesophageal 4-chamber view. (E: early filling. A: late filling due to atrial contraction).

Role of the Cardiovascular system

The cardiovascular system supplies oxygen and nutrients to various organs, collects gaseous and other metabolites from tissues and transports them to lungs, liver, and kidney for their final disposition. However, during anaesthesia, the oxygenation function of the cardiovascular system is considered most important, which depends on the cardiac output and its

distribution to various tissues. The magnitude of cardiac output and its distribution to various organs in a healthy individual is highly regulated and tuned to meet metabolic requirements of various tissues. For example, during muscular exercise, the cardiac output in a healthy adult can increase from 5 L/min. to 20–25 L/min. (4–5 times), and its distribution to exercising muscles can increase from a basal flow of 4 mL/min./100 gm to 80 mL/min./100 gm.[4] The blood flow through myocardium during rest and muscular exercise can vary from 75 mL/min./100 gm to 400 mL/min./100 gm.[4] The distribution of cardiac output in health through an organ is locally regulated; the increases in the blood flow through an active organ or exercising muscles occur because of vasodilatation. The increased flow through an active organ instantly results in increases in venous return to right atrium and consequently returns to left heart, which increases the stroke volume and the cardiac output.

In healthy individuals, during muscular exercise in spite of vasodilatation, there is no decrease in the systemic arterial pressure rather there can be an increase in the arterial pressure. Autonomic nervous system mediated arterial constriction in less active tissues, an increase in heart rate, and an increase in the circulating blood volume secondary to mobilization of stored blood from venous reservoirs because of venoconstriction increases cardiac output which not only maintains but often further increases the systemic arterial pressure. A few organs such as brain and kidney are endowed with the mechanism of ‘preferential and constant blood flow’ that is “autoregulation” and continue to get its share of cardiac output over a wide range of mean arterial pressures. During stress or haemorrhagic or hypovolaemic shock, various systemic regulatory mechanisms ensure priority distribution of cardiac output to vital organs such as brain, heart, and liver at the cost of other tissues and organs.

At this point, it is important to conceptualize what an increased cardiac output means and what changes could result in an increased cardiac output. In simple words, an increased cardiac output means higher rate of circulation of the same or increased blood volume. The circulation of the blood volume can be increased by an increase in the performance of the pump, and/or by a decrease in the systemic vascular resistance against which the heart pumps, provided the driving pressure remains unaffected (Table 3.1). The foregoing description describes four important components of the cardiovascular physiology that regulate the cardiac output, 1] the central pump “heart” and determinants of its performance, 2] the mechanisms that tune the cardiac output to metabolic requirement, 3] the various regulatory mechanisms that

ensure distribution of the cardiac output to vital organs during stress, and 4] the local regulations that control peripheral distribution of the cardiac output.

Table 3.1: Factors and the associated mechanisms that increase the cardiac output

a. Increased pump performance—Increased heart rate and myocardial contractility
b. Increased circulating blood volume—Mobilization of blood from venous system
c. Decresaed systemic vascular resistance—Peripheral vasodilatation
d. Sustained or increased systemic arterial pressure—Increased sympathetic activity

The central pump "heart" and the determinants of its performance

The heart pumps blood in the systemic and pulmonary circulation with each stroke. The cardiac output (total stroke volume over one minute) equals the product of stroke volume and the heart rate. An increase in the stroke volume or the heart rate or both increases the cardiac output. However, beyond a certain limit, an increase in the heart rate decreases the diastolic filling period of the heart and limits the increase in the stroke volume and the cardiac output. Similarly, the stroke volume cannot increase beyond the end-diastolic volume which is limited by the pericardial restrain. Like a mechanical pump, the capability of the heart is subject to the inherent quality of its performance, and the extraneous and the internal forces. The inherent quality and the internal and extraneous forces that determine the stroke volume are myocardial contractility, preload, and the afterload. The heart rate and rhythm are the two other factors that affect the cardiac output.

Myocardial contractility

The myocardial muscles (myocytes) have an inherent quality of spontaneous contraction. Within the physiological limits, the force of contraction of the cardiac myocytes increases as the load applied increases. The quality is described as Frank-Starling mechanism[1] and graphically represented by ventricular function curves as relationship between the atrial filling pressure and the ventricular output or by the relationship between mean ventricular

filling pressure and ventricular stroke volume (Fig. 3.10). The force of contraction of cardiac myocytes is directly related to the initial fibre length or fibre stretch; within the physiological limits, greater the initial fibre length, greater the force of contraction.[1] The volume of the ventricle at the end of diastole represents the end-diastolic fibre length the "preload" of the myocytes. The heart is endowed with an instant inbuilt mechanism to increase its performance if the preload is increased. Therefore, within the physiological limits, the heart pumps all the blood that comes to it without allowing excessive damming of blood within the veins.[1] Apart from increase in the preload, the myocardial performance can also be increased by an increase in the sympathetic activity and by hypertrophy of the heart muscle. By increasing the preload alone, the cardiac output can increase up to 2 and a half times; sympathetic stimulation can further double the cardiac output to 5 times the normal. In a trained athlete, the cardiac output on exercise can increase up to 7 times the normal.[4]

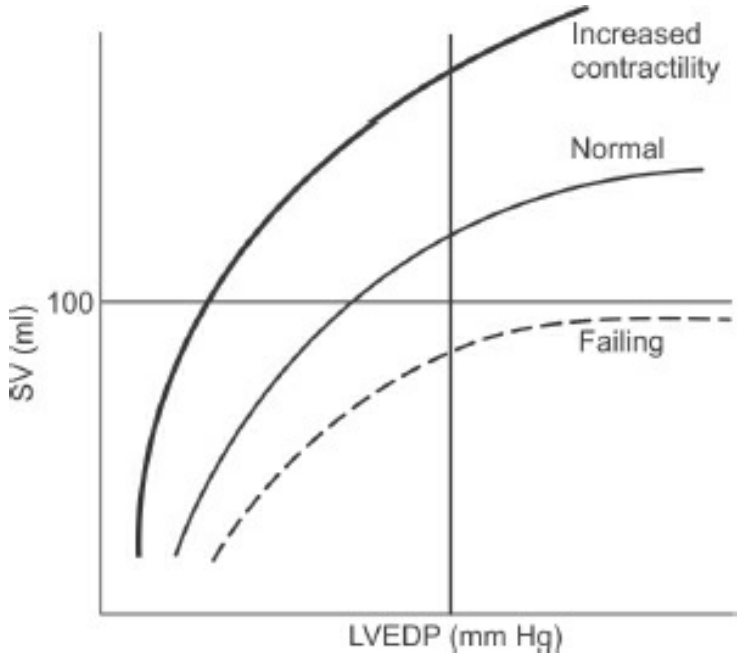

Figure 3.10: Diagrammatic representation of the Frank-Starling relationship. (SV: stroke volume, LVEDP: Left ventricular end-diastolic pressure)

Preload

The volume of the ventricle at the end of diastole the "end-diastolic volume" represents the end-diastolic fibre length of the myocytes. In clinical practice, measurement of the end-diastolic volume the "preload" is not always

available; however, its surrogate, atrial filling pressure is available for monitoring. Consequently, the central venous pressure (CVP) and the pulmonary capillary wedge pressure (PCWP) are considered indicators of the end-diastolic fibre length and described as preload of the right and left ventricles. However, these indicators are affected by various factors such as volume and compliance of these chambers, inter-ventricular dependence, ventricular hypertrophy, afterload to the respective ventricles, pericardial restrain, etc. Presently, the absolute values of the CVP and the PCWP are less relied. As described earlier, the myocardial performance is instantly increased as the preload increases; therefore, it is important to discuss the factors that affect the preload. The preload (venous return) to the heart can be increased in 4 different ways: 1] by peripheral vasodilatation, 2] by sympathetic activity induced increase in the venous tone and venous return and decrease in splanchnic arterial blood flow, 3] by mobilizing stored blood from venous reservoirs, and 4] by transfusion of blood or plasma or by infusion of colloids or crystalloids.

Peripheral vasodilatation

The peripheral vasodilatation is the mechanism that increases the flow to various organs/tissues where metabolic activity is increased. When vasculature of an organ dilates, the main artery supplying the organ can become the limiting factor; however, release of endothelial derived relaxing factor (EDRF) from the arteries and arterioles of microcirculation in response to rapid flow of blood through them causes a secondary increase in the dimensions of the upstream arterial blood vessels and decreases resistance in them. According to Hagen-Poiseuille equation [($Q = \pi r^4 \Delta p/8L\eta$) where Q is the flow rate, Δp is the driving pressure, r is the radius of the vessel, L is the length and η is the viscosity of the blood], it is evident that if the diameter of a vessel is doubled, the flow through it can increase by sixteen times the basal value (the radius is raised to power 4 in the equation). The increased peripheral flows instantly result in increased venous return and cardiac output. However, it should be realized that the driving pressure should remain constant. A decrease in the pressure can decrease the flow.[5] However, reflex increase in heart rate and vasoconstriction secondary to baroreceptor reflex and sympathetic stimulation in response to decreased arterial pressure ensures recovery of the arterial pressure to normal.[6]

The relationship between arterial pressure and cardiac output with and

without intact sympathetic system (sustained or increased arterial pressure) is shown in figure 3.11. In situations of peripheral vasodilatation associated with increased metabolic activity, the driving pressure is sustained by increases in sympathetic activity and stroke volume. Beriberi, anaemia, arteriovenous fistula, hyperthyroidism, are the chronic clinical situations in which the cardiac output is increased by peripheral vasodilatation.[7] In these situations, the increased cardiac output is associated with other changes also such as increased blood volume and decrease in viscosity.

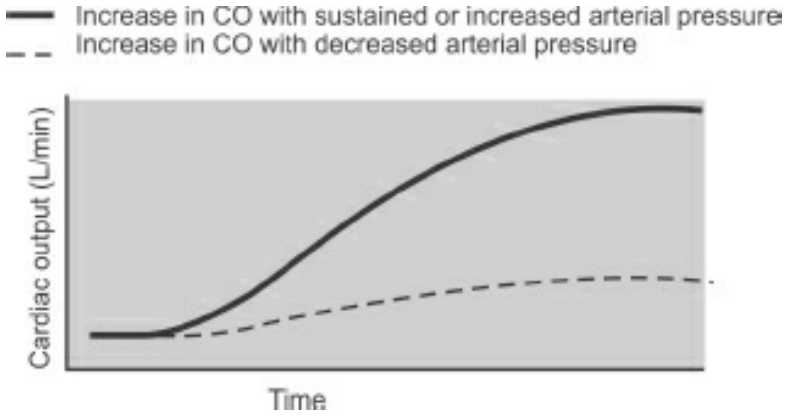

Figure 3.11: Shows relationship between the arterial pressure and cardiac output (CO) with and without intact sympathetic system (see the text for details).

Role of the venous system

The main functions of the venous system are to return blood to the heart from the periphery and to serve as capacitance vessels to maintain filling of the heart.[8] The veins contain approximately 70 percent of the total blood volume and are 30 times more compliant than arteries that means their capacity increases or decreases based on the blood volume available. Therefore, changes in blood volume within the veins are associated with relatively small changes in venous pressure.[8] Because of very high compliance, a small increase in venous pressure can immediately result in mobilization of a large volume of blood in to the circulatory system. Thus the venous system serves as a reservoir of blood that easily changes volume in it to maintain the filling pressure in the right heart.[8]

The blood volume contained in the venous system can be considered to exist as the stressed volume and the unstressed volume. The concept is simple and explained as follows - when a distensible closed system is filled with gas/fluid, the pressure measured in the system remains zero until the walls in the system begin to stretch, the volume just before the beginning of the

stretch is unstressed volume and determines the reserve volume available for mobilization. The volume above the unstressed volume is the stressed volume which raises pressure in the system and determines the driving pressure. For the cardiovascular system, this pressure is described as mean circulatory filling pressure (MCFP).[7]It follows that a change in the distensibility (tone) can significantly change the stressed and unstressed volume.

An increase in the tone would result in an increase in stressed volume and pressure in the system, and a decrease in tone would result in an increase in unstressed volume and a decrease in the pressure in the system. The change in the venous capacity is controlled by changing the venous tone, which is controlled by the sympathetic activity. An increase in the sympathetic activity augments the venous tone, decreases the venous capacity, the unstressed volume, and increases the stressed volume, the MCFP and the venous return (preload) to the heart. Conversely, a precipitous decrease in venous tone decreases the stressed volume and the MCFP which can severely compromise the venous return and might result in cardiovascular collapse and cardiac arrest.

The venous system can be considered a two compartment model, the splanchnic venous system and the systemic venous system.[9] The splanchnic venous system joins the hepatic vein which drains into the inferior vena-cava. The splanchnic vessels receive approximately 25 percent of the cardiac output and contain approximately 20 percent of total blood volume, and play a major role in the compensatory mechanisms. The splanchnic venous system is highly compliant; therefore, a decrease in flow in the system secondary to a decreased arterial flow through splanchnic vessels results in a decrease in the splanchnic venous pressure. To re-establish the pressure gradient for venous flow to occur from splanchnic venous system to right atrium, a decrease in venous pressure results in a passive decrease in the venous capacity that results in mobilization of blood and increased venous return. Thus, in the splanchnic venous system a decrease in arterial flow initially passively results in mobilization of stored blood and an increase in venous return to the heart. Once the pressure gradient is re-established, the splanchnic venous return becomes equal to splanchnic arterial inflow.

Conversely, the flow in the systemic veins follows the changes in the arterial flow. The active mobilization of the splanchnic venous blood is further regulated by adrenergic receptors present in the splanchnic veins and hepatic veins by varying the venous tone and resistance within the liver and

hepatic veins. The sympathetic system stimulation results in splanchnic venoconstriction and a decreased capacity of splanchnic venous system and mobilization of blood from splanchnic venous system in to circulation. Activation of α-adrenergic receptors within the liver and hepatic veins increases resistance,[10,11] whereas activation of β2-adrenergic receptors decreases it.[10,12] The decreases in resistance to venous flow within the liver and/or hepatic veins would facilitate the blood flow and volume shift from splanchnic vasculature to the inferior vena-cava and right atrium, thereby increasing the venous return. Thus, the administration of pure α-adrenergic agonists could result in a decrease in venous capacity and an increase in stressed volume and venous pressure thereby increasing venous return.[12-19] However, activation of α-adrenergic receptors also could be associated with an increase in resistance within the liver and hepatic veins, which would impede the blood flow and shift of blood volume from the splanchnic system into the systemic circulation.[18,20-25]

In conditions of normovolaemia and a relatively small degree of α-adrenergic receptor activation, a decrease in the venous capacity probably plays a prominent role in shifting volume from splanchnic vasculature. However, in conditions with congestive heart failure and/or a high degree of α-adrenergic receptor activation, sequestration of blood volume within the liver decreases venous return and may prevent aggravation of congestive heart failure. These observations have bearing on anesthesia management. Induction of anaesthesia results in inhibition of sympathetic activity and decrease in systemic arterial pressure by systemic vasodilatation. However, in patients with congestive heart failure, inhibition of sympathetic activity within the liver and hepatic veins can enhance the venous return and aggravate congestive heart failure. Therefore, if a patient with congestive heart failure develops cardiovascular decompensation due to inhibition of sympathetic activity, the patient would be better managed with a drug having a combination of both α and β2-adrenergic activity. The β2-adrenergic activity will help heart to cope with increased preload whereas α-adrenergic activity will restore the systemic vascular resistance and systemic arterial pressure. In conditions with hypovolaemia, the combination of α and β2-adrenergic agonists may facilitate the shift of blood volume from the splanchnic system into the systemic circulation more effectively than α-adrenergic agonists alone. Such a combination would lead to a decrease in venous capacity, mobilization of unstressed volume and a decrease in

resistance to venous outflow from the splanchnic system. Apparently, treatment of acute hypotension with α-adrenergic agonists is appropriate in presence of normovolaemia whereas in presence of hypovolaemia and congestive heart failure, treatment with combination of α and β2-adrenergic agonists is logical. Because of the mechanisms described, a healthy adult can mobilize about 500-700 mL blood into the circulation from splanchnic venous system.

Mobilization of stored blood

Alarge amount of blood is stored in the liver and splanchnic venous system and is available for mobilization. Because of stored blood, a healthy adult can easily donate about 500 ml blood without affecting the circulating- blood-volume. It is well known that at the beginning of running or other athletic activity, the abdominal muscles become taut and contracted which squeeze large amount of blood in to the circulation which increases the venous return, the circulating blood volume and the cardiac output. Additionally, the exercising muscles exert pumping effect on veins and squeeze blood towards the heart. During intense muscular exercise, the splanchnic blood supply is drastically reduced which results in mobilization of blood in to circulation as explained earlier. At the end of exercise, reverse actions occur and the cardiac output returns to basal level.

Transfusion or infusion of fluids

The infusion of colloids/crystalloids or transfusion of blood or plasma instantly results in an increase in the preload and the cardiac output. However, one may ask why an increase in CVP secondary to an infusion of fluid increases cardiac output despite the increased downstream pressure which is expected to decrease the venous return. The increases in cardiac output secondary to increased preload and myocardial contractility results in an increase in stressed volume and MCFP, which is at least equal or larger than an increase in CVP and maintains larger pressure gradient and achieves higher venous return with subsequent increases in cardiac output.[8] However, because of various mechanisms such as storage, excretion, distribution in to tissue spaces, etc. the circulating blood volume returns to basal level over a period of few hours and the cardiac output returns to basal level. It should be appreciated that volume administration increases cardiac output if the patient is hypovolaemic else, the increase in cardiac output is temporary and it

returns to basal level as soon as the administered volume is redistributed.

Afterload

The afterload is a relatively difficult concept to follow. It is described as the instantaneous stress sustained by the ventricle while emptying into the systemic or pulmonary circulation. Mathematically, the afterload is expressed as P X r/2h (where 'P' indicates pressure in the system, 'r' the radius of the heart and 'h' the myocardial wall thickness). It is evident that as the ventricle empties into the circulation, the ventricular size decreases, its diameter decreases and the stress sustained decreases. However, because of emptying of the blood in the vascular system, the impedance to ventricular ejection increases by a variable amount depending on the resistance, compliance and the stiffness of the vascular system (systemic or pulmonary) and run off of blood in the distal circulation. It is also clear that an increase in the preload and systemic vascular resistance increases the afterload. The myocardial hypertrophy observed in patients with hypertension, aortic stenosis, etc. decreases the myocardial stress and the afterload; however, it increases oxygen demand of the myocardium. The left ventricle is six times more muscular and is designed to perform pressure work against high systemic vascular resistance, Therefore, increasing the pressure in the aorta/arterial system does not decrease the cardiac output until the mean arterial pressure rises above about 160 mm Hg. In other words, at normal range of mean arterial pressure (80–140 mm Hg), the cardiac output is determined by the amount of blood entering into the ventricles (preload) and the myocardial contractility. However, a decrease in peripheral vascular resistance facilitates flow and increases the cardiac output provided the systemic arterial pressure is maintained. Vasodilatation is the major mechanism that increases the cardiac output during exercise. Contrary to the left ventricle, the right ventricle is a relatively thin walled structure and is designed to perform volume work against low resistance pulmonary circulation. Therefore, right ventricular dysfunction is a possibility, if right ventricular afterload increases.

Peripheral (Local) determinants of distribution of cardiac output

The blood flow to a peripheral organ is determined by its level of metabolic activity. The enormity of the adjustment can be understood from the fact that

in the resting state when the metabolic activity of muscles is very low, the blood flow is only 4 mL/min./100 gm of muscle but during exercise, when the metabolic activity of muscles increases 60 fold, the blood flow increases 20 times to 80 mL/min./100 gm of muscle. Evidently, the cardiac output increases or decreases according to the requirement of various peripheral tissues. Since the change in blood flow is required locally, it is logical that the regulation of blood flow should also occur at the tissue level. The experiments have shown that the blood flow to each tissue is regulated at the minimal level such that tissue's requirement is exactly met. By controlling the local blood flow in such an exact way, the tissues never suffer from nutritional deficiency, yet the workload on heart is kept at a minimum.

The blood flow to an organ is determined by the driving pressure (the difference between mean arterial pressure and the venous pressure) and the resistance to that flow. The relationship is explained by Hagen-Poiseuille equation $Q = \pi r^4 \Delta p/81\eta$. The relationship is applicable for Newtonian fluids; although blood is Non-Newtonian, the equation provides an easy understanding of the dynamics of blood flow. From the equation, it is evident that the vessel diameter is critical to flow and a small increase in diameter can increase the flow significantly. Indeed, the local variation in flow is controlled by changes in arteriolar tone and diameter; an increase in diameter with a steady pressure increases flow and a decrease in diameter decreases flow.

The microvasculature (Fig. 3.12) of each organ is organized to serve that organ's need. The main artery after entering the organ divides in to small arteries and then in to arterioles, metarterioles and finally capillaries emerge from the metarterioles. The capillaries are composed of a single layer of endothelial cells and allow free exchange of nutrients, metabolites and gases between tissues and blood. The microcirculation consists of arteriole, metarte-riole, and capillaries. Blood usually does not flow continuously through the capillaries. Instead the flow is intermittent and turns on and off every few seconds or minutes and is known as vasomotion. The control of flow through capillaries is affected by contraction and relaxation of the smooth muscles of arteriole, metarteriole and the precapillary sphincters. The most important factor that affects the degree of opening and closing of metarterioles and precapillary sphincters is the concentration of oxygen in tissues; when the rate of oxygen use increases such that tissue oxygen decreases the intermittent flows occur more often and for a longer period.

Mechanisms of blood flow control

Whenever the availability of oxygen to the tissues decrease, the blood flow through the tissues increases. The decrease in the availability of oxygen to the tissues can be secondary to various reasons such as hypoxia of high altitude, ventilation-perfusion defects of lung, defect of oxygen utilization at tissue level, or an increase in oxygen consumption due to an increase in metabolic rate. There are two basic theories for the regulation of local blood flow-the vasodilator theory and the oxygen lack theory. Additionally, catecholamines, pH; lactic acid, prostaglandins, bradykinin, acetylcholine, etc. all can directly or indirectly affect the vascular tone and the diameter.

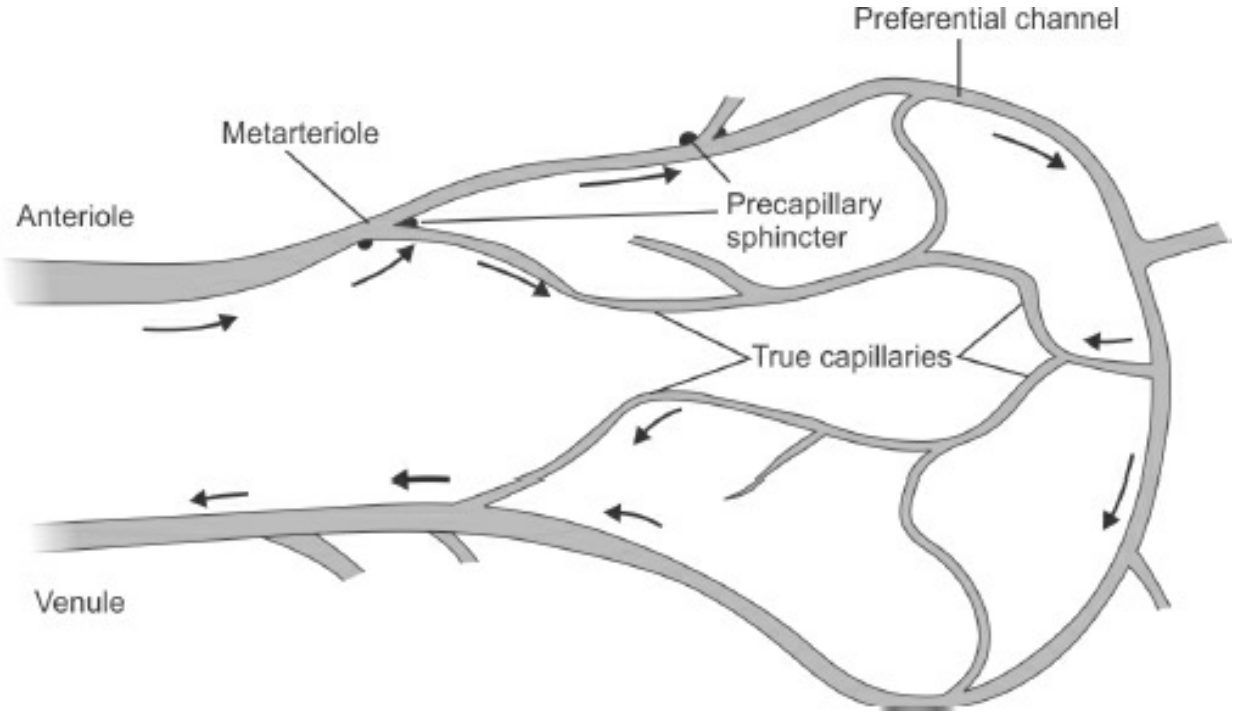

Figure 3.12: Shows schematic diagram of microvasculature with arterioles, meta-arterioles, venuies and precapillary sphincters.

Vasodilator theory

According to this theory, the greater the rate of metabolism, greater the formation of a vasodilator substance; the vasodilator substance is believed to diffuse through the tissues to precapillary sphincters, arterioles, and met-arterioles to cause dilatation. The substances that are believed to cause dilatation are adenosine, carbon dioxide, adenosine phosphate compounds, histamine, potassium ions, and hydrogen ions. Most of the vasodilator theories assume that vasodilator substance is released from the tissues in

response to oxygen deficiency. However, the major issue with the vasodilator theories is that it has been difficult to prove that sufficient quantities of any single vasodilator substance are formed in the tissues to cause all the measured increase in blood flow in states of increased tissue oxygen demand or decreased tissue oxygen.

Oxygon lack theory or the nutrient lack theory

Oxygen and other nutrients are required as metabolic substrates to maintain vascular muscle contraction; therefore, it is reasonable to believe that blood vessels would dilate if there is lack of oxygen and other nutrients. Similarly, an increase in tissue metabolism will theoretically cause decreased availability of oxygen and nutrients to the muscles in local vessels and would cause local vasodilatation.

Mechanism of increase in cardiac output during exercise

Haemodynamic response to exercise is a beautiful illustration of how the different vascular beds respond in opposite directions to fulfill the changing requirements of the body for blood volume and oxygen delivery redistribution. The mechanisms responsible for such haemodynamic adjustments involve different responses of the arteries and arterioles in the muscles versus the splanchnic system. During muscular exercise four important basic changes take place: 1] contraction of abdominal muscles, 2] muscle pump effect on veins of exercising muscles 3] vasodilatation in the exercising muscles, and 4] sympathetic stimulation. These changes distribute major proportion of the cardiac output towards exercising muscles and just enough proportion of the cardiac output towards inactive tissues. The contraction of the abdominal muscles squeezes blood from liver, and splanchnic venous system into the inferior vena-cava thereby increasing venous return to the right ventricle which in turn increases preload of left ventricle. Additionally, exercising muscles squeeze (muscle pump) blood out of the muscles towards the heart and increase venous return. Since heart is endowed with an inbuilt capability to increase its performance (Frank-Starling mechanism), the increased venous return instantly leads to an increased stroke volume. Increased venous return also increases the heart rate by 10–20 percent. Increased heart rate and venous return can increase the cardiac output by two and a half times.

The vasodilatation within the exercising muscle secondary to a local accumulation of vasodilating metabolites (lactate, adenosine, and other

compounds) and from adrenergic receptor activation leads to increase in flow in the muscle, a decrease in arteriovenous pressure gradient and a significant increase in MCFP, venous return and cardiac output (as explained earlier). Sympathetic stimulation increases heart rate, augments myocardial contractility, increases venous tone, and maintains systemic arterial pressure. However, in exercising muscles, local vasodilating mechanisms (metabolites) override sympathetic vasoconstriction. An increase in sympathetic discharge during exercise leads to splanchnic arterial vasoconstriction leading to a decrease in flow, pressure, and volume within the splanchnic veins and an increase in venous return and cardiac output (as explained earlier). Sympathetic discharge also constricts vasculature in non-exercising muscle and other tissues, helping to increase arterial pressure and MCFP, also increasing venous return and cardiac output.

During moderate muscular exercise, splanchnic blood flow is maintained; however, with vigorous exercise because of increasing sympathetic stimulation, the splanchnic blood flow decreases. Evidently, the sympathetic nervous system primarily maintains the systolic arterial pressure and based on priority, regulates the blood flow to various organs. During exercise, splanchnic blood flow can decrease from 1,500 mL/min. to 350 ml/min. Splanchnic oxygen consumption is preserved by an increase in the arterio-venous oxygen difference in this region, which increases from 4 mL to 17 mL of oxygen/100 mL of blood.[26] The total muscle blood flow can increase from approximately 1,000 mL/min. at rest to almost 22,000 mL/min. and oxygen uptake of almost 4 L/min. Arterio-venous oxygen difference in the muscle increases to 18 mL of oxygen/100 mL of blood, which represents approximately 90 percent oxygen extraction.[27] Indeed, because of the changes described, the cardiac output can easily increase by 4–5 times during muscular exercise and in trained hearts it can increase up to 7–8 times.

Summary

The cardiovascular system is designed to fulfill the varying nutritional and oxygen requirements of various tissues of the body. In general the various functional components of the cardiovascular system such as heart rate, cardiac rhythm, preload, myocardial contractility, venous return, afterload etc. function in the most efficient way possible and generate the cardiac output which is just sufficient to meet the whole body requirement. Various

systems such as central nervous system, autonomic nervous system, venous system, humoral factors, etc. take part in regulating the cardiac output to meet the requirement. In health, the local/peripheral tissue requirement of nutrition and oxygen regulates the magnitude and distribution of the cardiac output; however during stress, central control dominates and ensures cardiac output distribution to vital organs at the expense of less active tissues.

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Chapter 4: Haemodynamic Monitoring during Cardiac Surgery

Patients undergoing cardiac surgery have abnormal cardiovascular physiology. Naturally therefore, they are more prone to develop haemodynamic instability during surgery. The extent of the haemodynamic disturbances is likely to be related to the nature and severity of cardiovascular disease. The cardiac anaesthesio-logist should make every effort to minimise these disturbances. He should choose the anaesthetic agents that are most suitable for a particular condition. In addition, if the haemodynamic disturbances do occur, he should use appropriate pharmacological agents either in bolus or infusion forms so that normal or acceptable haemodynamics is restored. Accurate assessment of the cardiovascular function is extremely important in order to be able to execute this aspect of his duty. This is made possible by haemodynamic monitoring of the essential physiological parameters during cardiac surgery. The extent of haemodynamic monitoring in an individual patient depends upon the gravity of the cardiovascular disease, with more extensive monitoring being required for sicker patients. Although difficult to prove, it is reasonable to believe that appropriate haemodynamic monitoring is likely to reduce the incidence of cardiovascular complications leading to improved outcome.

A vast range of monitoring devices is currently available. Some of these devices are completely noninvasive, such as an electrocardiogram (ECG) and pulse oximeter, whereas others are more invasive such as pulmonary artery catheter (PAC). In an experienced hand, there are few complications related to the invasive monitoring and therefore, they are used liberally in critically ill patients. However, the anaesthesiologist must have enough knowledge to

understand the interpretation of these complex data, so that maximum benefit is derived from them.

Standard monitoring that is generally employed in patients undergoing cardiac surgery includes ECG, invasive blood pressure, central venous pressure (CVP), urinary output, temperature, pulse oximetry, capnography and intermittent arterial blood gas analysis. However, PACs, cardiac output (CO) measurements along with mixed venous oximetry and transoesophageal echocardiography (TOE) are being increasingly used. Some of the more recent monitoring tools include continuous CO measurements by different techniques such as pulse contour analysis.

Electrocardiogram

Continuous monitoring of ECG is routinely performed in almost all types of surgery. In cardiac surgery, it is of exceptional value and permits instantaneous identification of rate, rhythm and ST segment abnormalities. Not only the diagnosis, but also the efficacy of corrective treatment can be judged. The cardiac anaesthesiologist relies heavily on the “on-line” information obtained from the ECG to make important decisions during cardiac surgery. He has a special advantage of looking at the heart to confirm his “on-line” diagnosis of some of the arrhythmias such as atrial fibrillation (AF), atrioventricular (AV) blocks and AV dissociation.

A standard bipolar lead II which measures differences in potential between the right arm and the left leg is utilised to differentiate ventricular from supraventricular arrhythmias. This is so because its axis parallels that between the sino-atrial (SA) and AV nodes, hence, the P wave is larger and easier to identify. Myocardial ischaemia of the inferior wall can be detected by ST segment depression in lead II, but the more common anterior and lateral wall ischaemia may be missed. Selecting a lead near the cardiac apex (V5: left fifth interspace at the anterior axillary line) is necessary to detect the anterior or lateral wall ischaemia.[1]

Arrhythmias

Cardiac arrhythmias are one of the most frequent cardiovascular abnormalities that occur during perioperative period. In fact, the cardiac anaesthesiologist can observe a wide spectrum of cardiac arrhythmias during

the immediate period following the release of aortic cross clamp when the myocardium is recovering from ischaemic insult and trying to regain normal sinus rhythm.

Conduction system anatomy

The action potential originates in the SA node, which is located at the right atrial sulcus terminalis and traverses via a discrete specialised tissue pathway to the ventricular myocardium (Fig. 4.1). The orifices of superior vena cava, inferior vena cava, the fossa ovalis, and ostium of the coronary sinus divide the atrium into muscle bundles. The impulse travels more rapidly through these thick atrial muscle bundles. The impulse is conducted rapidly down to AV node that is located in the triangle of Koch, which is formed by the tendon of Todaro, tricuspid valve annulus, and the ostium of the coronary sinus.[2] The conduction velocity through the AV node is only 20 to 25 percent of that through the atria. This mechanism permits completion of the atrial conduction before ventricular activation.

The bundle of His originates at the inferior margin of the AV node. It divides into the right and left bundle branches at the upper margin of the muscular interventricular septum (IVS). The right and left bundles divide further into the Purkrnje system. The right bundle supplies the IVS near the apex and the right ventricle (RV). The rest of the IVS and the left ventricle (LV) are supplied by the left bundle. The conduction velocity through the bundle of His and Purkinje system is very rapid and this assures rapid synchronous activation of the ventricles. The normal conduction of impulse through this pathway results in a normal sinus rhythm (Fig. 4.2). The conduction system has some safety features. The atria and ventricles are electrically insulated by fibrous rings and the electrical conductivity is established only via the AV node-His bundle region. The AV node functions as a protective barrier delaying the AV conduction and controlling the ventricular rate.

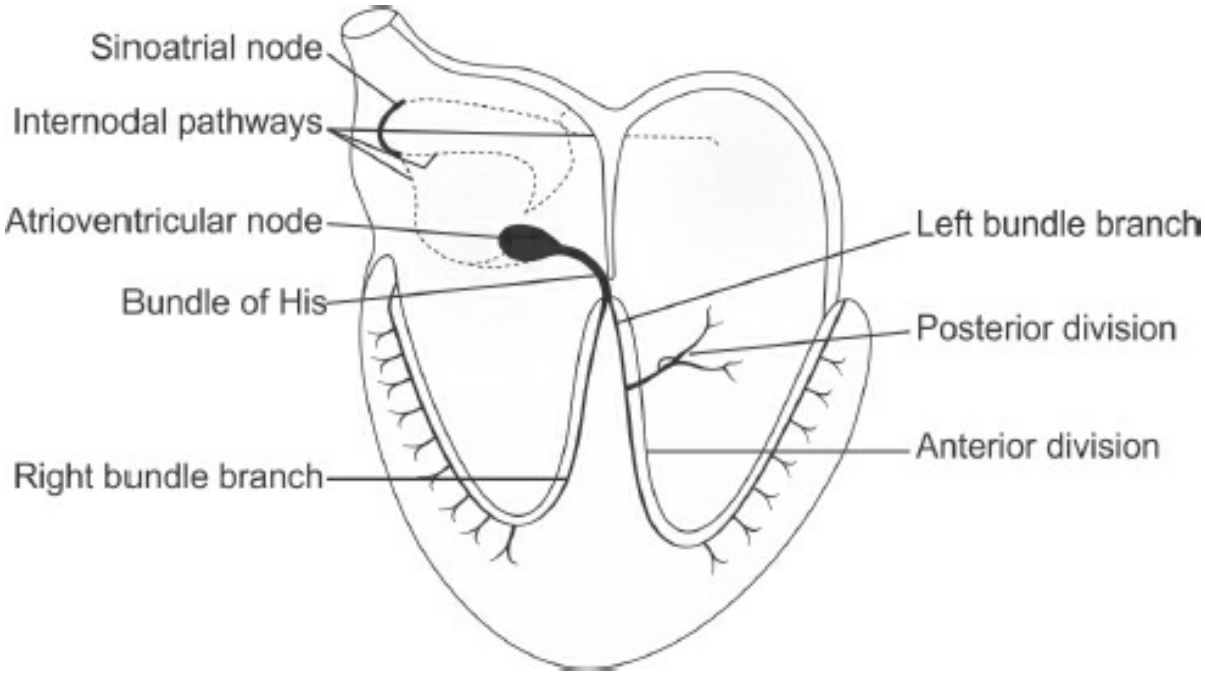


Figure 4.1: Diagram showing cardiac conduction system.

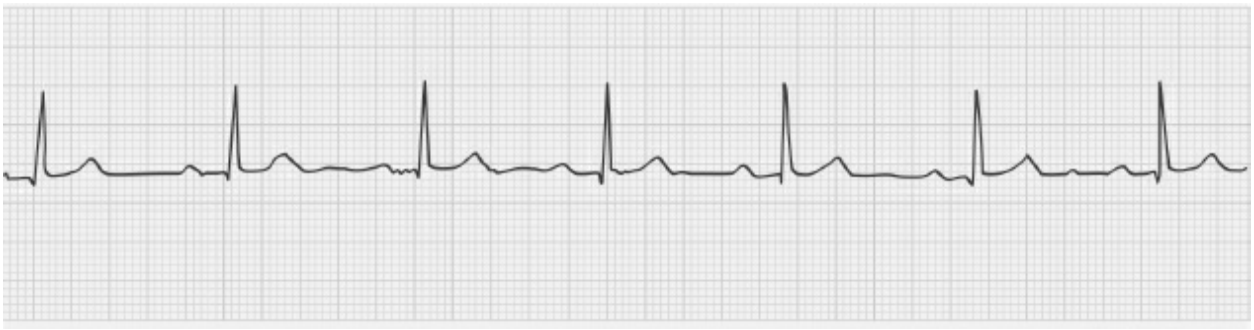


Figure 4.2: Normal sinus rhythm.

Diagnosis and Treatment

It must be remembered that several factors related to anaesthesia such as anaesthetic agents (especially inhalational agents), electrolyte and acid-base abnormalities, temperature and depth of anaesthesia may be responsible for some arrhythmias. Therefore, before any pharmacological treatment of arrhythmias is instituted, it must be ensured that these problems are ruled out or corrected.

Common arrhythmias during perioperative period

Supraventricular arrhythmias

Premature atrial contraction: An ectopic pacemaker site in the right or left atrium (LA) initiates the premature atrial contraction. The shape of the P wave is different and may be inverted. There is no compensatory pause between the premature atrial contraction and the next sinus beat that differentiates it from the premature ventricular contraction. The premature atrial contractions have little clinical significance and treatment is rarely necessary.

Sinus or junctional bradycardia: The normal sinus rate slowed down to less than 60 beats/min. is sinus bradycardia (Fig. 4.3). In junctional bradycardia, the sinus rate decreases below that of the atrioventricular junction so that the atrioventricular junction takes over (Fig. 4.4). Causes of this slowing include vagal stimulation or patients receiving beta-blockers [patients with coronary artery disease (CAD)] or digoxin toxicity (patients with valvular disease). It can also be frequently seen during hypothermia. Junctional bradycardia is more likely to cause haemodynamic compromise as the atrial contribution to the ventricular filling is lost. Treatment is required only if the bradyarrhythmia is accompanied by haemodynamic compromise (hypotension and low CO). Atropine in increments of 0.4 to 0.5 mg can be used, but if bradycardia persists, isoprenaline bolus (5 to 10 μg) followed by an infusion can be used.

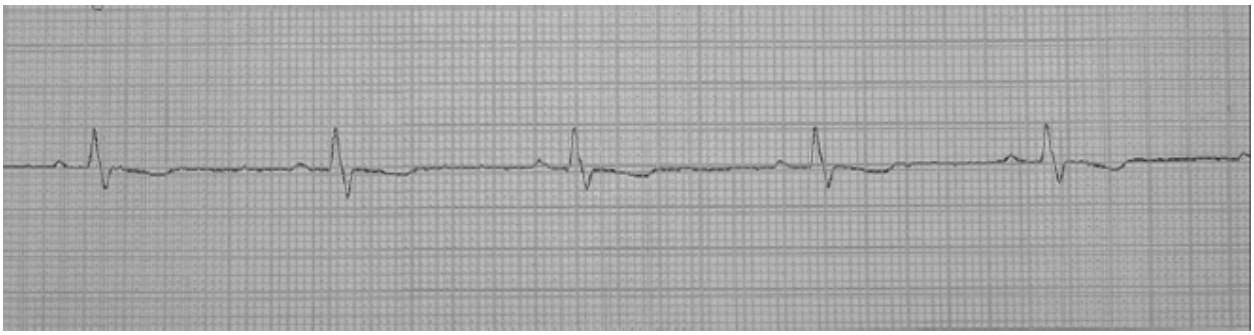


Figure 4.3: Sinus bradycardia; heart rate of 58/min.

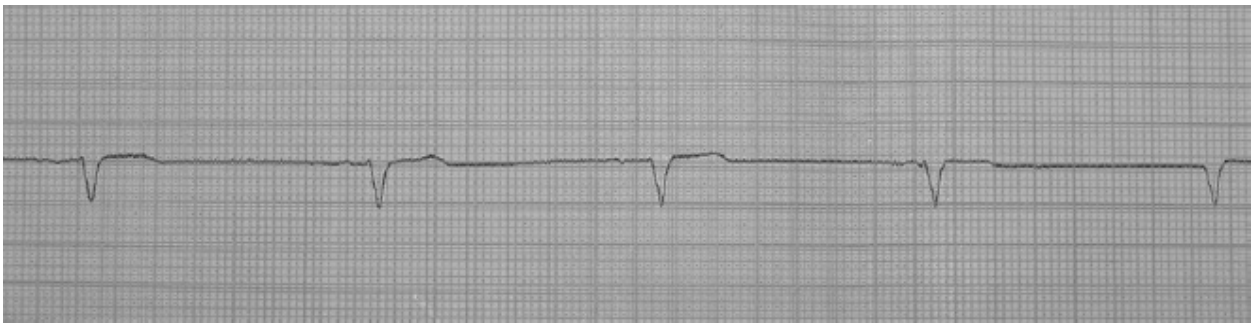


Figure 4.4: Junctional bradycardia.

Sinus tachycardia: It is defined as an increase in the sinus rate to more than 100 beats/min. (Fig. 4.5). It can be seen very commonly following stressful stimuli, such as endotracheal intubation, skin incision, and sternotomy. It is especially undesirable in patients undergoing coronary artery bypass grafting (CABG), as it increases the myocardial oxygen demand. It should therefore, be treated with beta-blockers (metoprolol, atenolol or esmolol) particularly when accompanied by hypertension. It should however, be ensured that the patient is adequately anaesthetised before the treatment of tachycardia is instituted. Hypovolaemia and terminal heart failure can also lead to tachycardia that should not be treated with beta-blockers.

Atrial flutter: It usually results due to a circus movement of excitation within the atrium. The atrial rate ranges between 250 and 350 beats/ min. Conduction into the ventricles is usually at a constant rate, thereby resulting into 2:1 or 3:1 block (Fig. 4.6). It can lead to haemodynamic compromise, if the ventricular rate becomes fast or atrial contribution is lost. However, this type of arrhythmia is relatively rare during cardiac surgery. The increasing incidence of postoperative atrial flutter following CABG that is reported, can occur on the postoperative day 2 or 3.[3,4] Although, medical therapy with digoxin, verapamil or beta-blocker can be used, synchronised direct current (DC) cardioversion may be used if the chest is open. However, facility of pacing also should be ready as cardioversion may sometimes result in an asystole. Overdrive atrial pacing using atrial pacing wires can also be used to convert atrial flutter to sinus rhythm. This involves pacing the atrium at rates more rapid than the tachycardia. This results in AV block of more atrial impulses that results in reduction of the ventricular rate.

Atrial fibrillation: It is caused by re-entry of the atrial impulse and is usually present as a chronic disorder in patients undergoing valve surgery. It can also be present in the elderly patients with or without CAD. It can occur acutely during RA handling or cannulation. There is a rapid atrial electrical activity (400-700 beats/min.) and the ventricular response is irregular (160-180 beats/min.-Fig. 4.7). Therapy is generally not required in the preby-pass stage, if blood pressure is maintained. However, cardioversion (5 to 10 joules, mono-phasic) can be used if the chest is open and there is an associated haemodynamic compromise. It is the most common form of arrhythmia seen in patients with rheumatic heart disease undergoing valve surgery. It is a usual practice in the author’s institution to cardiovert these

patients following cardiopulmonary bypass (CPB). However, it has a limited success rate in patients who have chronic AF with a large LA.

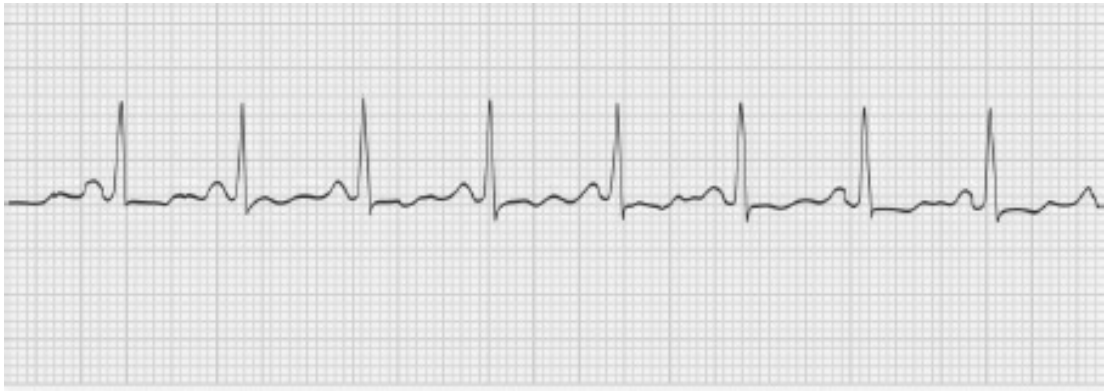


Figure 4.5: Sinus tachycardia.

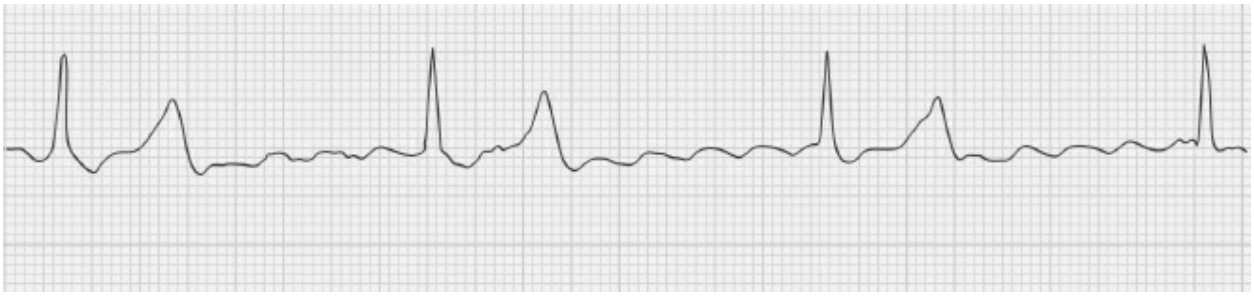


Figure 4.6: Atrial flutter.

Esmolol, an ultra-short acting beta adrenergic blocker is reported to be effective in the treatment of AF.[5] However, it may not be effective in the treatment of chronic AF that is present in valvular heart disease. Increasing incidence of AF following CABG is reported which is possibly related to age. This, however, commonly occurs on the second or third postoperative day.[3,4]

Paroxysmal supraventricular tachycardia: Re-entry mechanism is responsible for this arrhythmia that is characterised by a regular rhythm with rates of 160 to 200 beats/min. (Fig. 4.8). The re-entry circuit may be in the SA node, AV node, atrial muscle or an atrioventricular bypass pathway (Wolff-Parkinson-White syndrome) or within the bundle of His.[6] In addition, abnormal automaticity in the atrial tissues may also be responsible.

The arrhythmia is identified as supraventricular in origin because the QRS complexes are of normal duration (narrow complex tachycardia). Vagal stimulating manoeuvres such as carotid sinus massage or eyeball pressure and pharmacological treatment with verapamil, beta-blocker, etc. may be tried in the operating room, provided there is no alarming haemodynamic

compromise. In the event of haemodynamic instability, synchronised DC cardioversion that is nearly always effective must be used.

While using verapamil or beta-blockers, it must be remembered that their use can lead to hypotension. In the rare instance when both pharmacological cardioversion and electrical cardioversion have failed, rapid overdrive pacing can be used.

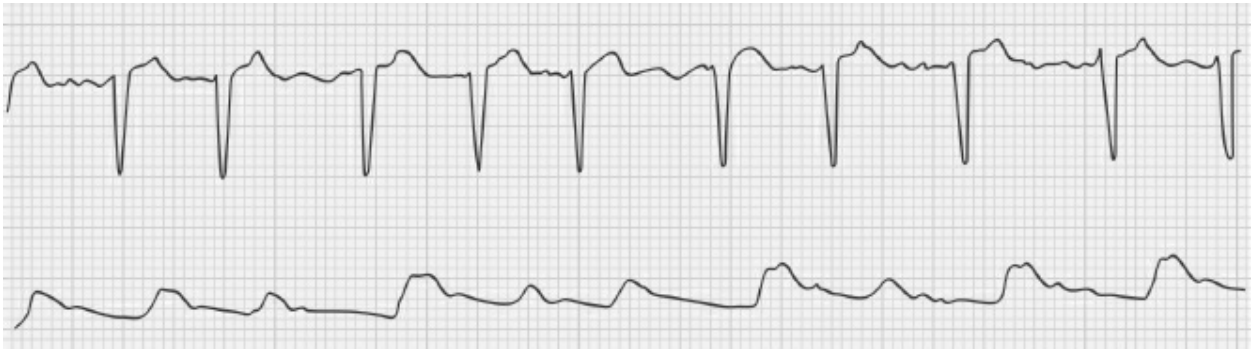


Figure 4.7: Atrial fibrillation. Lower waveform is the simultaneous recording of arterial pressure.

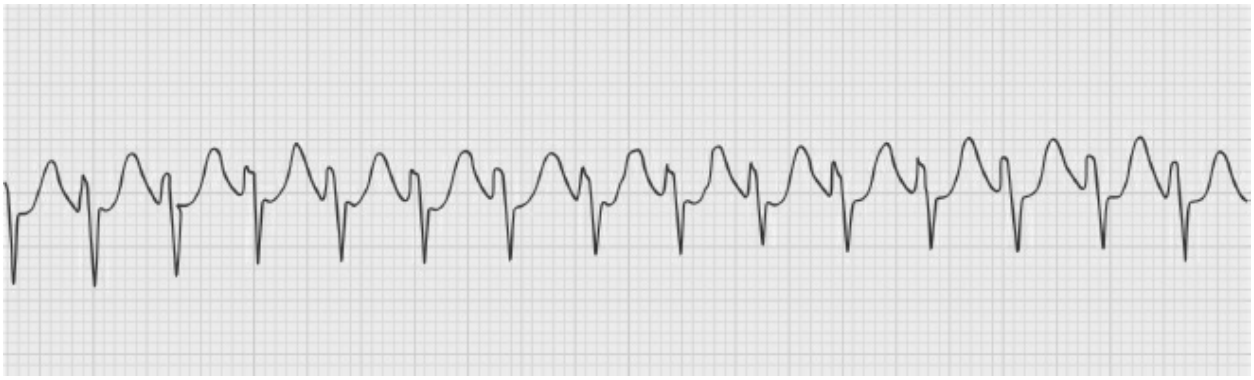


Figure 4.8: Paroxysmal supraventricular tachycardia.

Atrioventricular block

First degree AV block can be defined as a PR interval of 210 milliseconds or greater, without failure of atrial impulses to capture the ventricles[7] (Fig. 4.9). It usually reflects excessive vagal blockade or drug effects such as digitalis toxicity. The treatment is usually not necessary, however, the patient should be carefully observed for progression to a higher degree of block. It is also justified to place a temporary pacing wire before sternal closure so that pacing can be instituted quickly in the event of a further block.

Second degree atrioventricular block, Mobitz type I (Wenckebach's phenomenon): It is characterised by failure of some supraventricular impulses to cross the AV junction. In this type of second degree block, there

is a progressive prolongation of the PR interval leading finally to a dropped beat (Fig. 4.10). The cycle is then repeated. This type of block can be seen following acute infarction with ischaemia and oedema in the region of AV junction or with agents that depress AV nodal conduction (digitalis, beta-blockers, verapamil, etc.). Unless the ventricular rate is very slow, treatment is usually not necessary. Isoprenaline or atropine can be used.

Mobitz type II block: In this type of second degree block, there is no progressive lengthening of the PR interval prior to dropped beats (Fig. 4.11). QRS widening is usually present. It may progress suddenly and unpredictably to complete heart block. It is a clear indication for the placement of a temporary pacemaker.

Third degree (complete) atrioventricular block: There is a complete disruption of the conduction between atria and ventricles. The P waves and QRS complexes bear no constant relationship to each other (Fig. 4.12). In acquired complete heart block, the impulse generation is idioventricular in location and QRS complex is wide with a slow rate (35-40 beats/minute). It is not uncommon to notice it after the closure of ventricular septal defects (VSD) and aortic valve replacement (AVR). Pacing is indicated in this situation to maintain the normal haemodynamics.

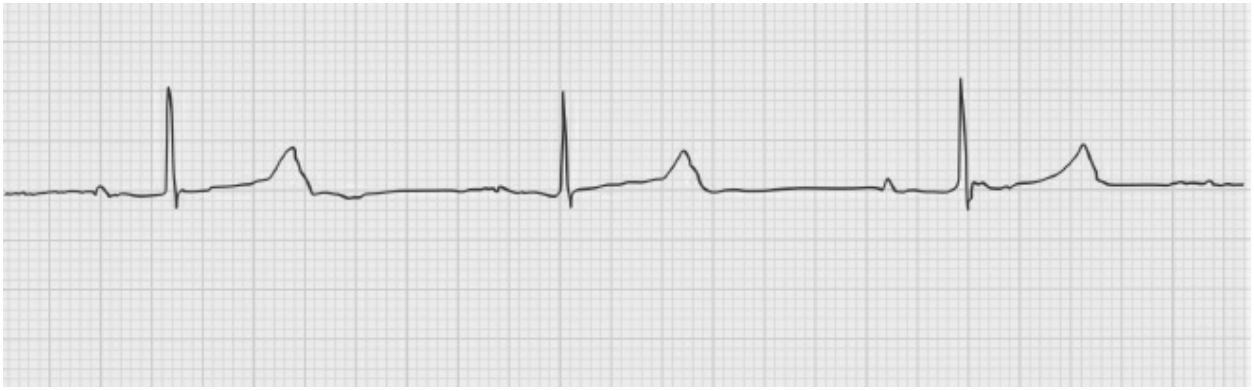


Figure 4.9: First degree heart block; note the increased PR interval.

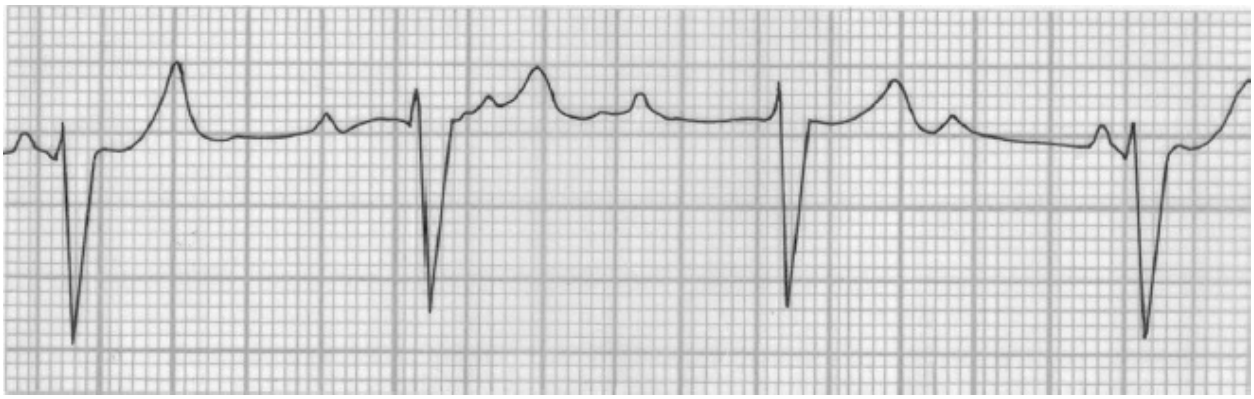


Figure 4.10: Mobitz type I Heart block (Wenckebach's phenomenon); note the progressive prolongation of PR interval leading finally to a dropped beat. The cycle then resumes.

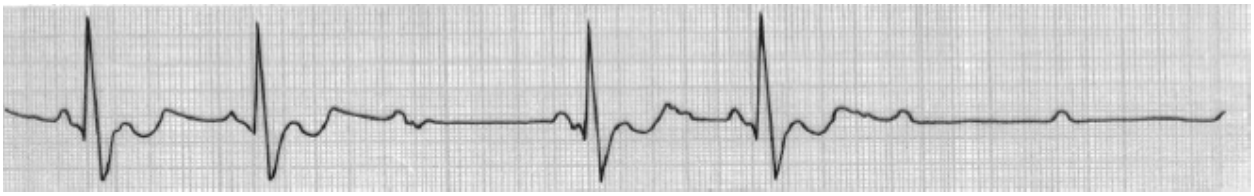


Figure 4.11: Second degree atrioventricular block. The PR interval of conducted beats is normal but some P waves are not conducted.

Ventricular arrhythmias

These arrhythmias are seen frequently in patients undergoing cardiac surgery.

Ventricular ectopic beats: They result from ectopic pacemaker activity arising from below the AV junction that results in a wide (0.12 sec) bizarre QRS complex (Fig. 4.13). Manipulation of the heart by the surgeon or insertion of a guidewire through internal jugular vein (IJV) during central venous cannulation often provokes ventricular ectopic beats. Hypokalaemia in patients with valvular heart disease receiving diuretic therapy is another common cause of ventricular ectopics. In patients with CAD, an acute imbalance between myocardial oxygen supply and demand can lead to ectopic activity. An ischaemic focus can discharge ventricular premature depolarisation necessitating treatment with antiarrhythmic drugs. Ventricular ectopic beats occurring frequently (> 5 beats/min.), multifocal in origin and occurring in succession should be actively treated as these can turn into more dangerous arrhythmias such as ventricular tachycardia or ventricular fibrillation (VF). Lidocaine is usually the treatment of choice with an initial bolus of 1.5 mg/Kg followed by an infusion (1 to 4 mg/min.), if ventricular ectopics are recurrent. In addition, esmolol, propranolol, atenolol, disopyramide, amiodarone etc. can be considered.

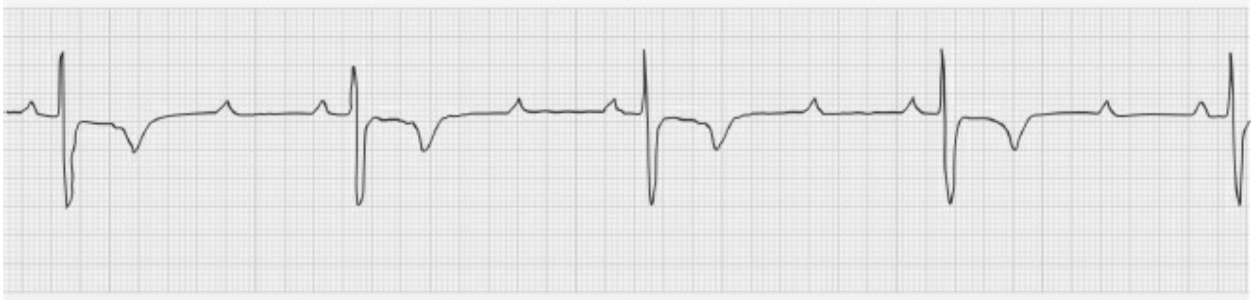


Figure 4.12: Complete or third degree heart block; note total dissociation between atrial and ventricular complexes with a very slow ventricular rate.

Ventricular tachycardia: It is a run of 3 or more consecutive ventricular ectopic beats that are potentially life threatening (Fig. 4.14). The heart rate (HR) varies from 100 to 200 beats/min. that is usually regular. The P waves have no fixed relation to the QRS complex that is wide (> 0.12 seconds). Immediate treatment is usually necessary. Lidocaine bolus followed by an infusion is useful, but cardioversion may also be needed.

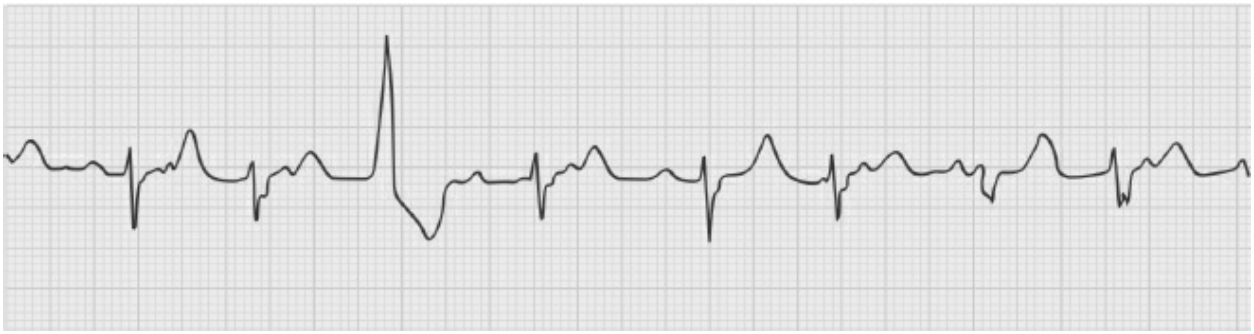


Figure 4.13: Ventricular ectopic beat.

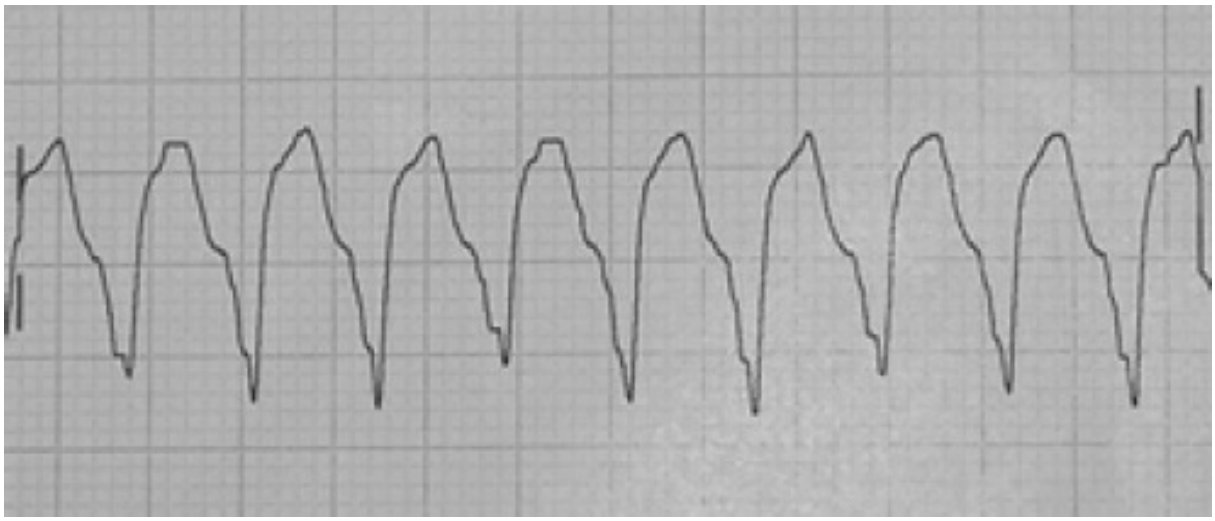


Figure 4.14: Ventricular tachycardia.

Ventricular fibrillation: It is an irregular rhythm that results from a rapid discharge of impulses from one or more foci in the ventricles. There are no defined QRS complexes and there is no CO (Fig. 4.15). It is frequently observed following release of the aortic cross clamp. Spontaneous reversion is sometimes observed but, DC cardioversion is generally necessary. Other important causes include myocardial ischaemia, hypoxia, hypothermia and electrolyte imbalance.

Diagnosis of ischaemia

Presence of CAD is an important prerequisite for the occurrence of preoperative ischaemia. CABG is a frequently performed cardiac surgery so that the cardiac anaesthesiologist must be familiar with the diagnosis of this important ECG abnormality. There is a high incidence of ECG evidence of ischaemia (20 to 80 percent) in patients with CAD undergoing cardiac or noncardiac surgery.[8,9] The criteria for diagnosis of ischaemia include: 1. horizontal or down-sloping ST segment depression of 0.1 mV; 2. ST segment elevation of 0.1 mV in a non-Q wave lead; 3. slowly upsloping ST segment depression of 0.2 mV (all measured from 60 to 80 milliseconds after the J point)[10] (Fig. 4.16).

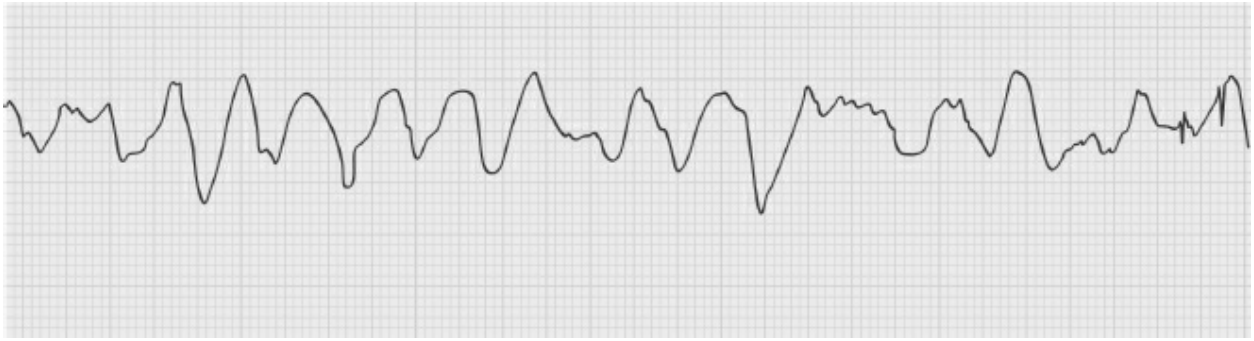


Figure 4.15: Ventricular fibrillation.

Computer assisted ECG interpretation

It is reasonable to believe that during prolonged visual observation of ECG on the monitor, certain abnormalities may go undetected. Computers have, therefore, been designed for the automatic detection of arrhythmias and ST segment abnormalities. One such system (Philips India) is shown in Figure 4.17 that analyses ST segment by analysing the first 16 beats in all the leads.

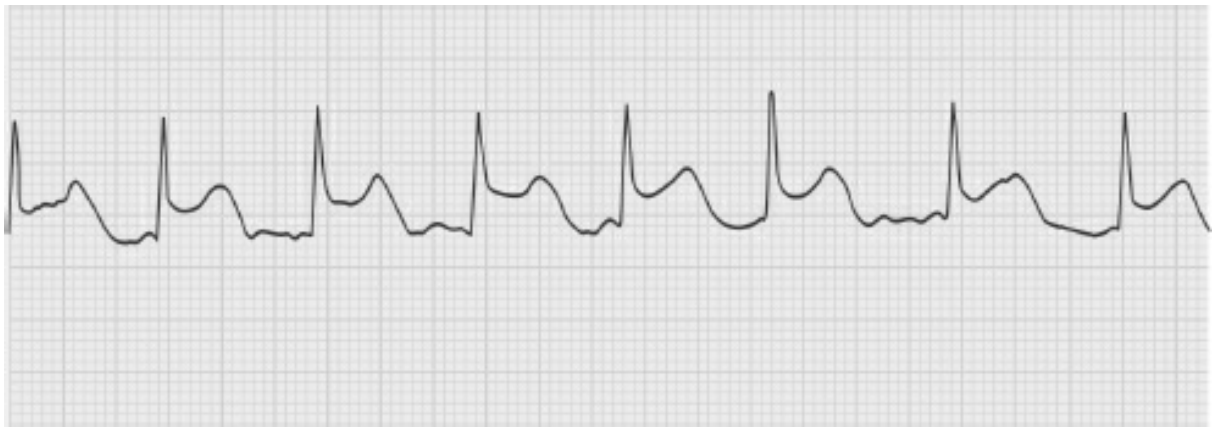


Figure 4.16A: ST elevation.

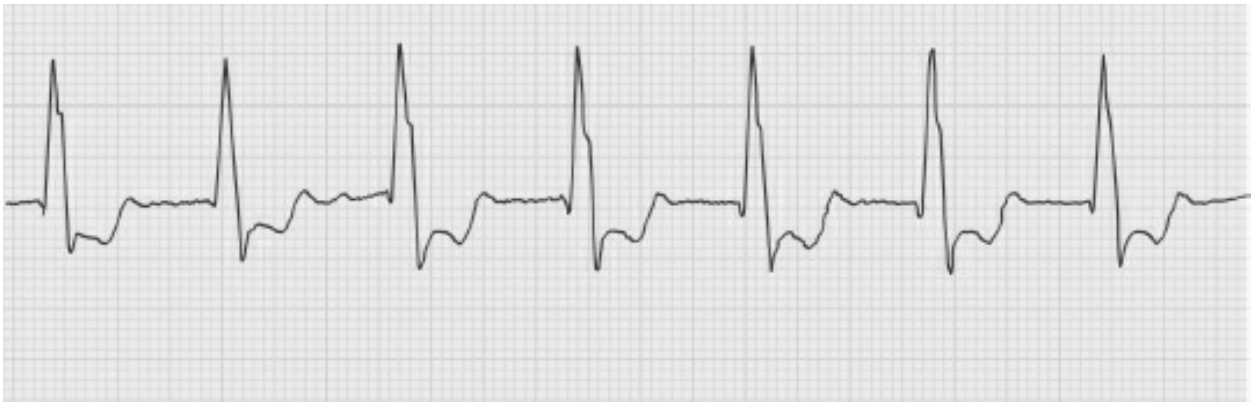


Figure 4.16B: ST depression.

Arterial Pressure

Cardiac surgery is frequently associated with wide swings in the arterial pressure. This may be due to surgical manipulation, effects of anaesthetic agents or deterioration in cardiovascular performance of the patient. In addition, there is a loss of pulsatile flow during CPB. Therefore, it is essential to measure arterial pressure directly and continuously in patients undergoing open-heart surgery. Although, several arterial cannulation sites are available, radial artery is the most preferred site because of accessibility, size, ease of cannulation and lack of complications. However, one or both radial artery conduits may be used for arterial vascularisation in patients undergoing CABG. Therefore, if one radial artery is being used by the surgeon (usually left), right radial artery should be cannulated and if both are being used, femoral arterial cannulation is performed. Allen's test is performed to check that the collateral circulation to the hand is adequate and that the circulation

will not be compromised in the event of radial artery occlusion. The test is performed by occluding both the radial and ulnar arteries by compressing them and exercising the hand until it is pale. The ulnar artery is then released and the time required to regain the normal colour of the hand is noted.[11] If the colour returns to normal within 5 seconds, the collateral circulation is normal. If it takes longer than 15 seconds cannulation of the radial artery on that side should be avoided. The fingers should be open loosely, should not be hyper-extended or widely spread apart. A Doppler probe or a pulse oximeter may be used to document the collateral flow.[12,13]

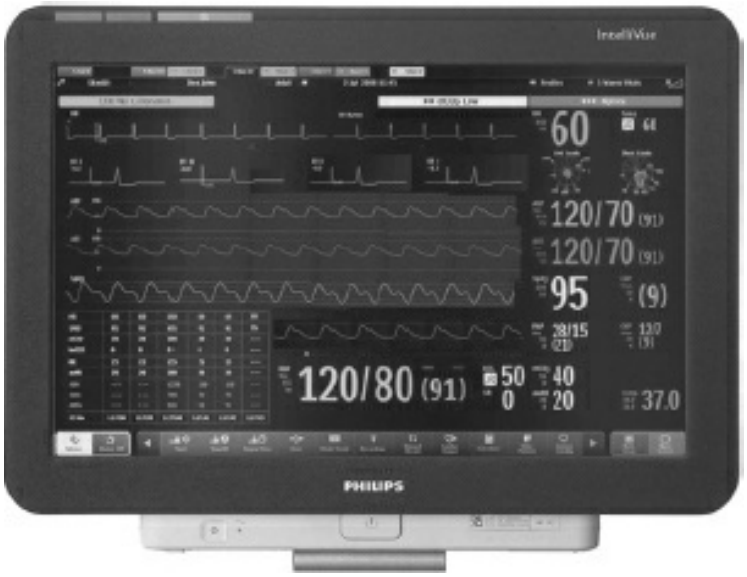


Figure 4.17: Philips intelliVue Mx 800 patient monitor.

The predictive value of Allen's test to identify patients at high risk of ischaemic complications from radial artery cannulation has remained questionable. This may be due to the fact that the test requires patient cooperation and the results can be subjective. It has been shown to have high false positive and false negative rates.[14] The use of a digital blood pressure monitor may prove to be an acceptable alternative to the Allen's test.[15]

The Favaloro retractor used for harvesting the internal mammary artery may impede radial arterial pressure. Therefore, some anaesthesiologists prefer to cannulate right radial artery when the left internal mammary artery is used for myocardial revascularisation.

Technique of cannulation

Direct cannulation

The hand is supinated and dorsiflexed sharply over a support (pack of sponges). The skin is prepared with an antiseptic solution and local anaesthetic is infiltrated if the patient is awake. The radial artery is palpated proximal to the wrist, where it is just below the subcutaneous tissue and anterior to the radius. A small skin nick may be made with a 20 G needle. The arterial cannula is inserted through this skin hole. By doing so, fraying of the tip of the catheter as it passes through the skin is avoided. A 22 G Teflon or polyurethane catheter is advanced through the skin hole towards the radial artery at an angle of approximately 30° (Fig. 4.18). No syringe should be attached to the cannula and the blocker at the hub of the cannula should be removed so that the blood flows back freely in the event of an arterial puncture. When the artery is punctured, bright red blood can be seen in the hub of the cannula. The blood will not be red in patients suffering from cyanotic heart disease. At this time the angle between the cannula and the skin is reduced and the outer catheter is advanced over the needle to enter the arterial lumen.

Transfixation

In this technique, the artery is transfixed by passing the cannula through and through the artery. The needle is then removed and the cannula is slowly withdrawn. When the cannula tip enters the lumen of the artery, blood flow emerges from the cannula. At this time the cannula is advanced into the artery.

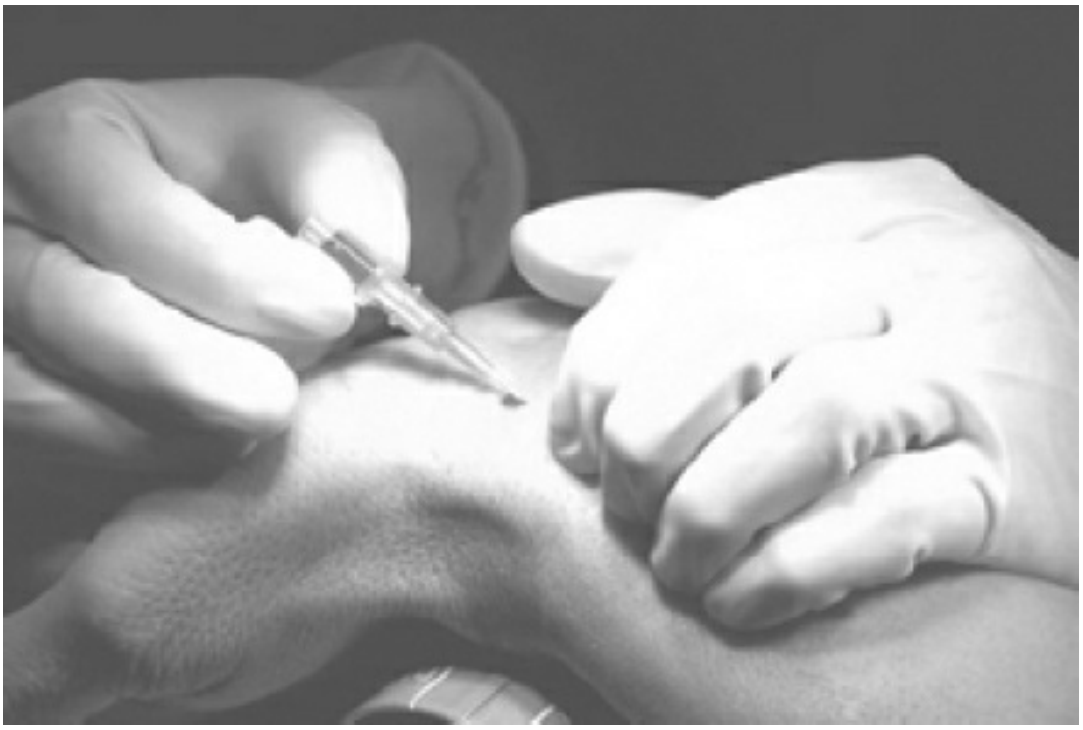


Figure 4.18A: Showing percutaneous radial artery cannulation; note the flashback of blood in the hub of the cannula after arterial puncture.

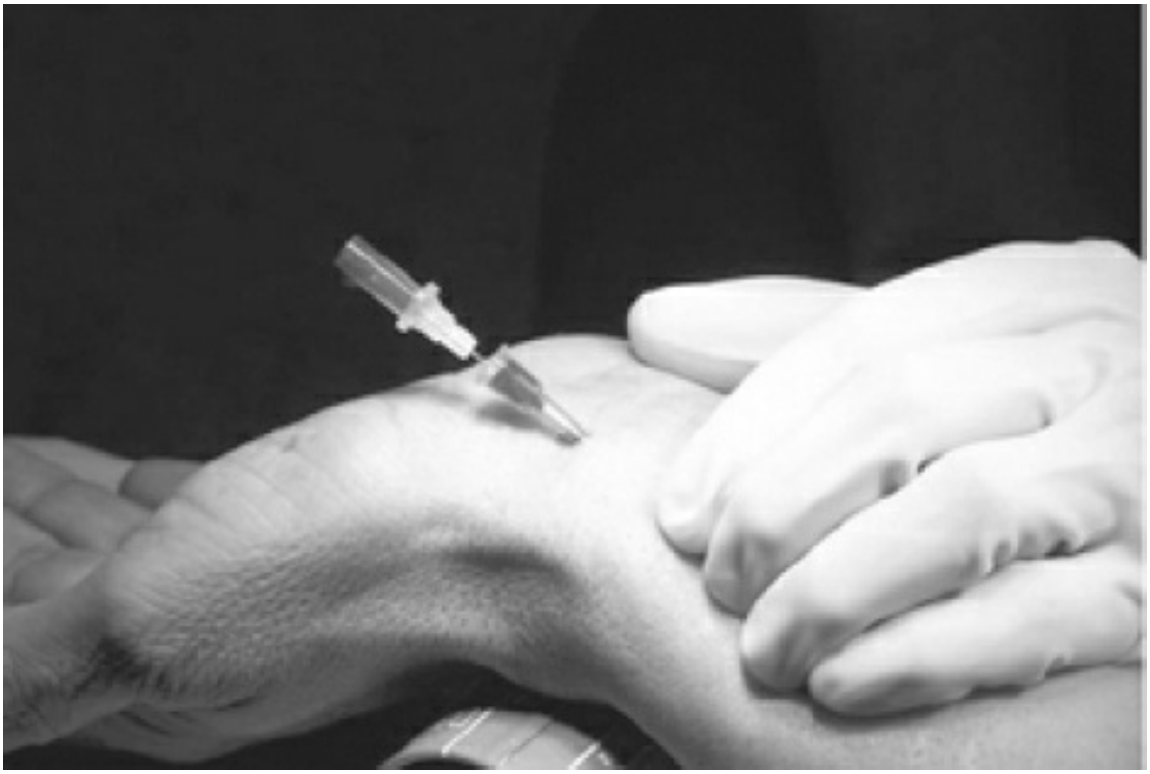


Figure 4.18B: The cannula has been threaded into the radial artery.

Seldinger Technique

In this technique, the artery is localised with a needle and a guide wire is passed through the needle into the artery. The needle is removed and an appropriate sized cannula is then passed over the wire into the artery. The catheter is secured by a sterile occlusive dressing and is connected to the monitor via a pressure transducer to obtain a continuous waveform of the blood pressure (Fig. 4.19). A normal arterial pressure waveform is shown in figure 4.20.

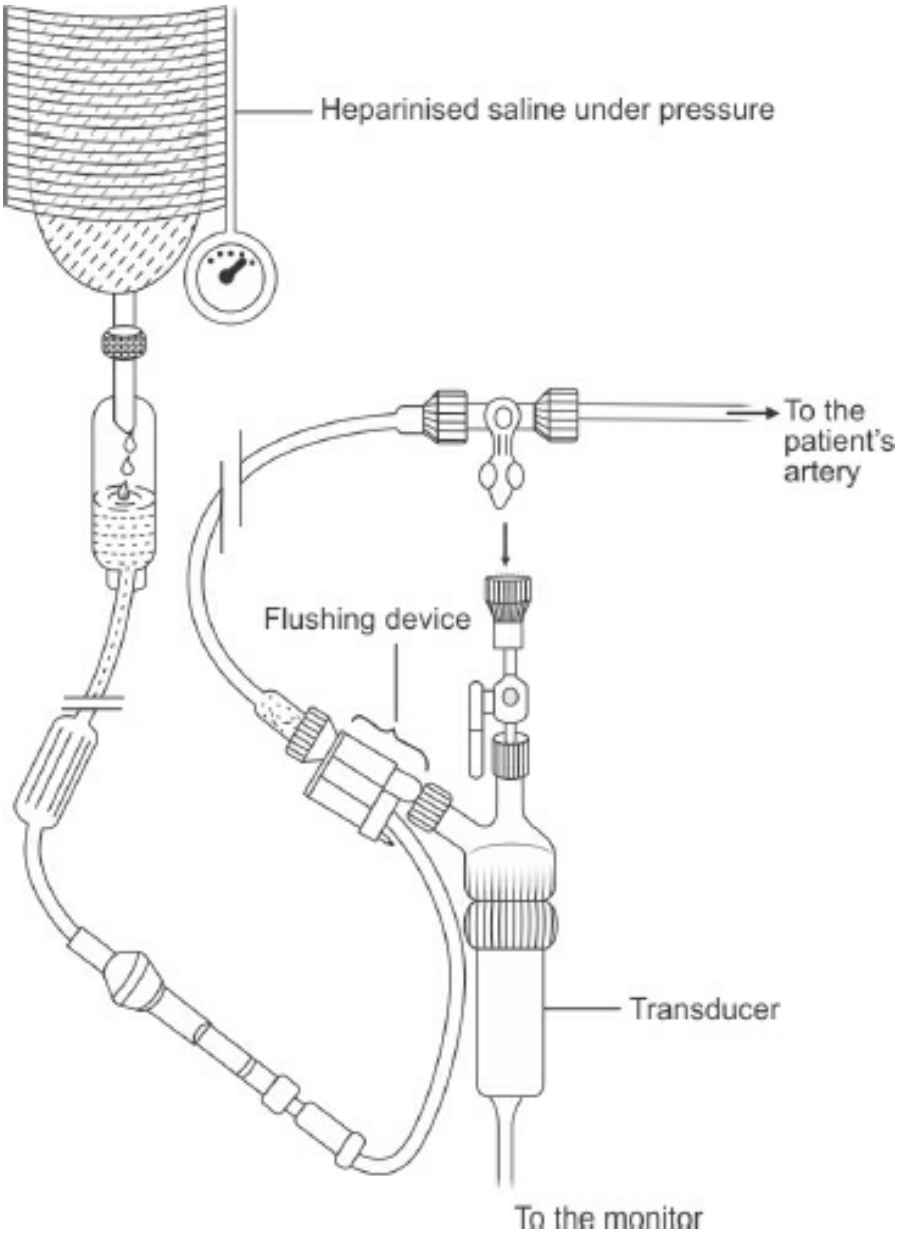


Figure 4.19: Transducer assembly: Heparinised saline for flushing is prepared by addition of 500 units of heparin to 500 mL of 0.9% saline. This is pressurised to 300 mm Hg for continuous flushing of the

transducer dome and pressure monitoring line via a flush device that regulates the flow at 3 mL/ hour.

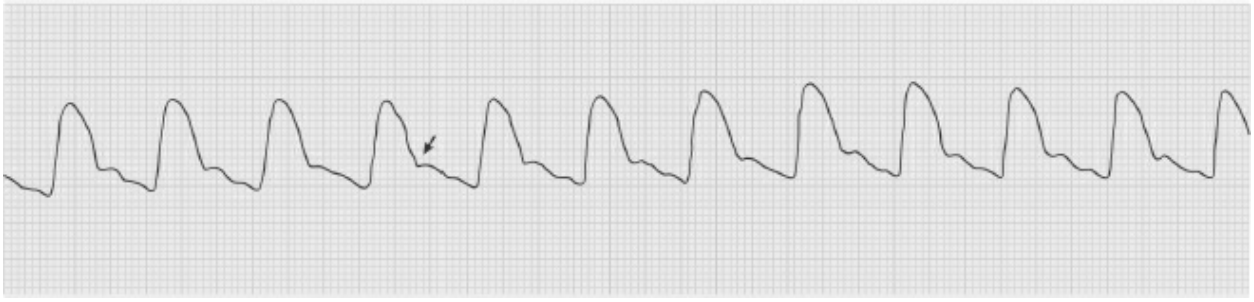


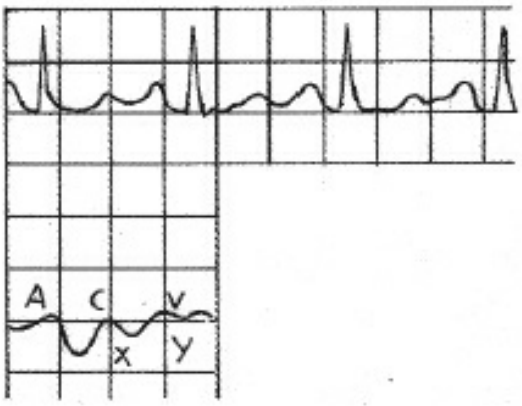
Figure 4.20: Normal arterial pressure waveform (radial artery); note the dicrotic notch (arrow) that signifies closure of the aortic valve.

Central Venous Pressure

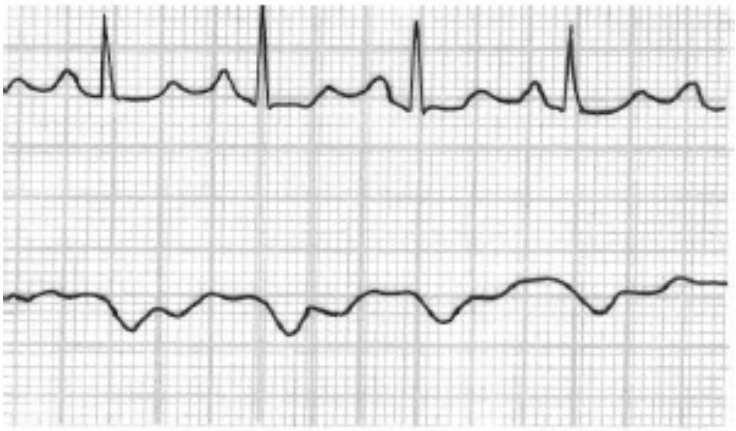
CVP monitoring is used to measure the filling pressure of the RV and to give an assessment of the intravascular volume. The central venous catheter is also useful for infusion of the inotropes. The catheter tip should lie within one of the large intrathoracic veins close to the RA. The catheter should not be inserted into the RA, to avoid the rare complication of perforation by the tip of catheter. The RA waveform has three upward deflections (A, C and V) and two downward deflections (x and y descents) (Fig. 4.21). The A wave is a result of atrial contraction, the C wave occurs due to closure and bulging of tricuspid valve into the RA and the V wave occurs during passive atrial filling during ventricular systole. The x descent is caused by pulling away of the tricuspid valve from the RA as the RV systole progresses and the y descent occurs as the tricuspid valve opens.

Technique

Cannulation of the internal jugular vein (IJV) is commonly preferred because of its reliability in obtaining the central venous access. The right IJV is preferred because of its short straight course to the RA, the right cupola of the lung is lower than the left, and the thoracic duct is on the left side. Figure 4.22 shows the anatomical landmarks that are useful for the cannulation of IJV. The IJV is located under the medial border of the lateral head of the sternocleidomastoid (SCM) muscle. The carotid artery is deep and medial to the IJV.



A



B

Figure 4.21: **(A)** Diagrammatic representation of the central venous pressure tracing and its relation to ECG in normal sinus rhythm. **(B)** Actual recording of the central venous pressure and simultaneous ECG. Refer to the text for description of A, C and V waves and x and y descent.

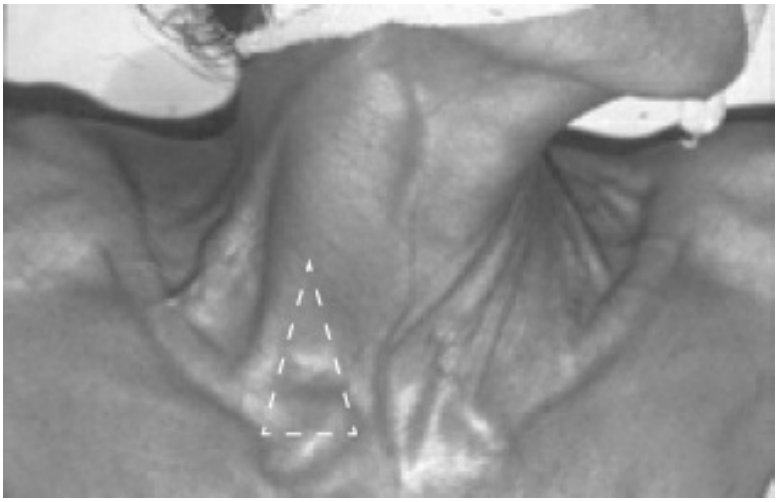


Figure 4.22A: Anatomical landmarks for the cannulation of internal jugular vein. Note the triangle (dotted line) formed by the sternal and clavicular heads of sternocleidomastoid muscle.

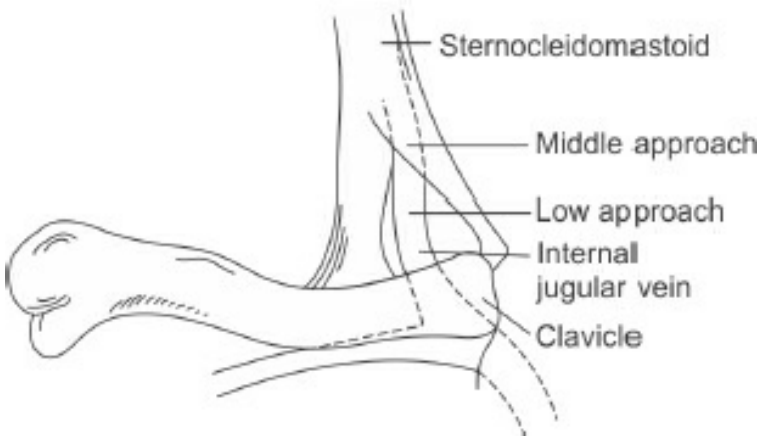


Figure 4.22B: Diagrammatic representation of the various anatomical landmarks in the cannulation of internal jugular vein.

Middle Approach

The IJV is punctured at the apex of the triangle formed by clavicle and the two heads of SCM. The patient is placed in a 10 to 20 degrees Trendelenburg position with head turned to the left side. The skin is prepared and draped in a sterile fashion. The Trendelenburg position may not be necessary in some patients with valvular heart disease who have a history of recurrent congestive heart failure (CHF) and in whom the IJV is dilated and full. It should also be used with caution in patients having poor LV function, as the increase in preload may not be well tolerated. The fingers of the left hand are used to palpate the two heads of the SCM and the carotid pulse. Although, these anatomical landmarks are helpful in locating the IJV, an experienced operator often relies on his ability to feel the vein by balloting it under his fingers. This is particularly useful when the IJV is abnormally placed, in obese patients or in patients with severe aortic regurgitation, in whom the dilated carotid artery may push the vein laterally.

A22 G ‘finder’ needle is placed at the apex of the triangle. This reduces the risk of inadvertent arterial puncture as well as tissue trauma, if localisation of the vein is difficult. The needle attached to a syringe is held at an angle of 45 degrees and directed towards the ipsilateral nipple before making the puncture. It is then advanced forward to puncture the vein. Venous blood is aspirated if the IJV is punctured. The ‘finder’ needle is then withdrawn and the puncture is repeated with an 18 G needle in a similar fashion. A successful venous puncture can be judged by aspiration of dark blood or measurement of venous oxygen saturation in the aspirated blood. However,

the absolute confirmatory method is to transduce the catheter and obtain venous waveform and pressure on the monitor. Therefore, some anaesthesiologists attach a three way tap to the needle with one end attached to a syringe and the side port connected to the transducer. The venous puncture is confirmed by aspirating venous blood and simultaneously observing venous waveform on the monitor. On successful puncture of the vein, the syringe is removed and a guidewire is inserted and a single or multilumen catheter is inserted by the Seldinger technique. Alternatively, one or two single lumen catheters (16 G) can also be inserted through a 14 G cannula (Fig. 4.23).

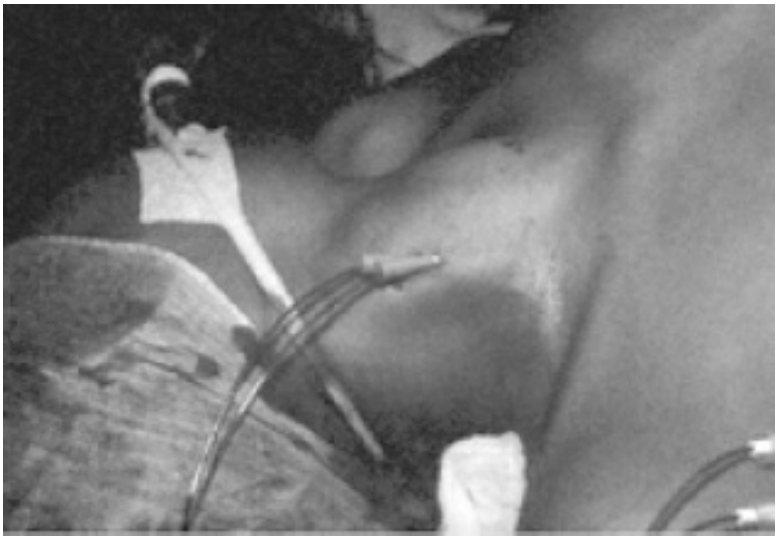


Figure 4.23: Showing insertion of two 16 gauge catheters into the internal jugular vein.

Although middle approach is the most commonly used approach, some other approaches have also been described. In the anterior (high) approach, the puncture is performed along the medial border of SCM but at the level of the laryngeal cartilage.[16] The posterior approach to IJV is performed at the intersection of external jugular vein (EJV) and the lateral border of SCM.[17] As the needle is aimed in the direction of the carotid artery, the incidence of arterial puncture may be higher. A lower approach describing the point of entry much closer to the clavicle with a high success rate has also been reported.[18] Cote and coworkers[19] however, discourage this approach because they encountered pneumothorax and intrapulmonary haemorrhage in two children. This method is contraindicated in patients with previous Blalock-Taussig shunt[20] and complete transposition of great arteries.[21]

Complications

Although a high success rate has been reported with IJV cannulation,[17,22,23] the technique is not without complications. There are reports of injury to almost every structure in the neck while performing the IJV puncture.[24-31] This may lead to pneumothorax, hydrothorax, chylothorax and pericardial effusion. The carotid artery puncture is by far the most common complication and if the artery has been punctured with a small bore needle, manual compression of the area for some time is usually sufficient to avoid any serious problem. However, if the artery is unintentionally punctured with a very large cannula (e.g. 8 F), surgical exploration and repair is recommended. Although complications are rare, the anaesthesiologist should be aware that they can occur and may be life threatening.[24] Malposition of the catheter can also occur. Figure 4.24 (A to C) depicts some of the manners in which the catheter can be malpositioned. Air can also be aspirated through the IJV catheter, if left open, especially, if the patient is breathing spontaneously. This is particularly important in patients having patent foramen ovale or atrial septal defect as it may lead to paradoxical air embolism.

External jugular vein

It can also be used for reaching the central circulation. However, the success rate with this approach is lower due to the tortuous path of the vein. The main advantage of this technique is that the puncture of deeper structures of the neck are avoided. A 'J' tipped wire should be used to negotiate the tortuous course of the vein. Although, one study has reported a success rate of 90 percent,[32] cannulation of EJV is not popular amongst cardiac anaesthesiologists.

Subclavian vein

It has also been used for central venous access. However, the success rate is lower than IJV cannulation, but higher than EJV cannulation. It is also associated with a higher incidence of complications than IJV approach.[33] Usually an infraclavicular approach is performed. The patient is placed in the Trendelenburg position with head turned to the contralateral side. A folded sheet is placed between the scapulae. The puncture is performed 1 cm below the midpoint of the clavicle and advanced towards the suprasternal notch under the posterior surface of the clavicle. Anew approach using

coracoclavicular line (from the lower border of the coracoid process to the upper border of the medial head of the clavicle) as a landmark has been described with a high success rate.[34] One of the most common misplacements of the subclavian catheter is into the ipsilateral IJV. Ambesh et al have described a simple manoeuvre (Ambesh manoeuvre) to prevent and diagnose the misplacement of the catheter into IJV.[35,36] They described that manual occlusion of the ipsilateral IJV in the supraclavicular fossa during and after insertion of subclavian vein catheter is successful in preventing and diagnosing the misplacement of the subclavian vein catheter into the IJV respectively. Due to the fear of higher complication rate, the cannulation of subclavian vein is generally not preferred except in situations such as carotid artery surgery or prolonged CVP access because the site is easily dressed and well tolerated by the patient.

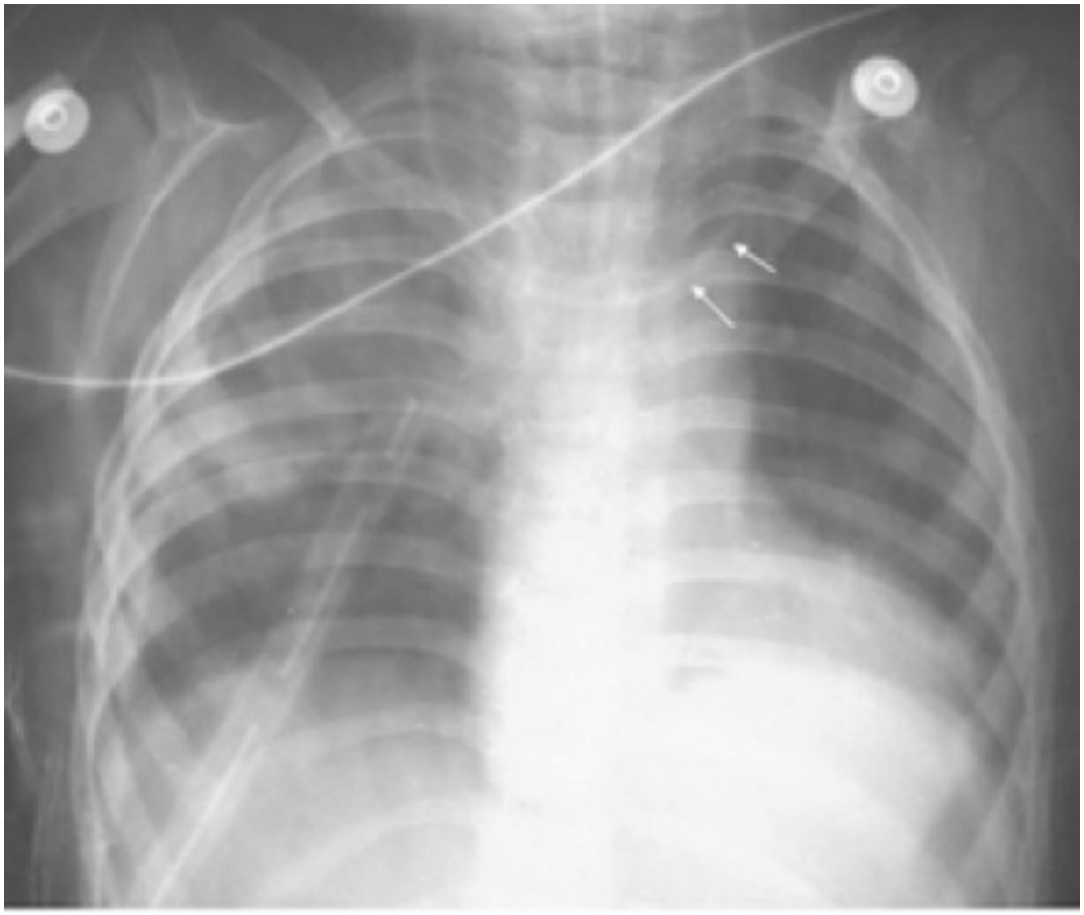


Figure 4.24A: X-ray chest showing malposition of the central venous catheter that was inserted in the right external jugular vein. Note that the catheter has gone to the left side via innominate vein (arrows).

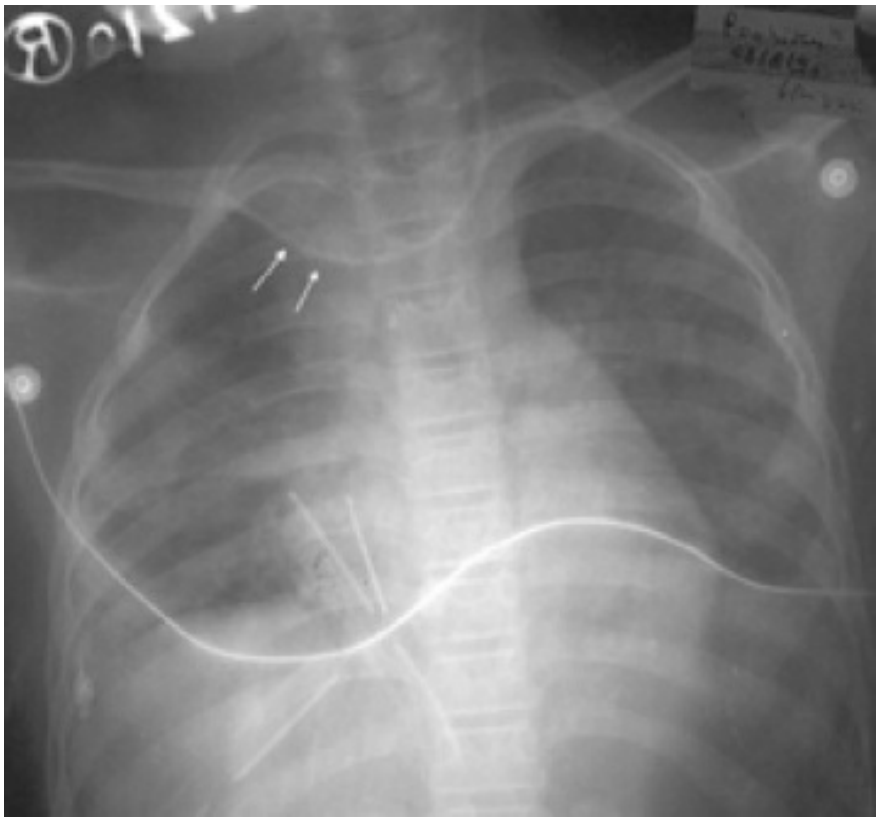


Figure 4.24B: Malposition of the central venous catheter that was inserted in the left internal jugular vein. Note that the catheter has gone to the right innominate vein (arrows).

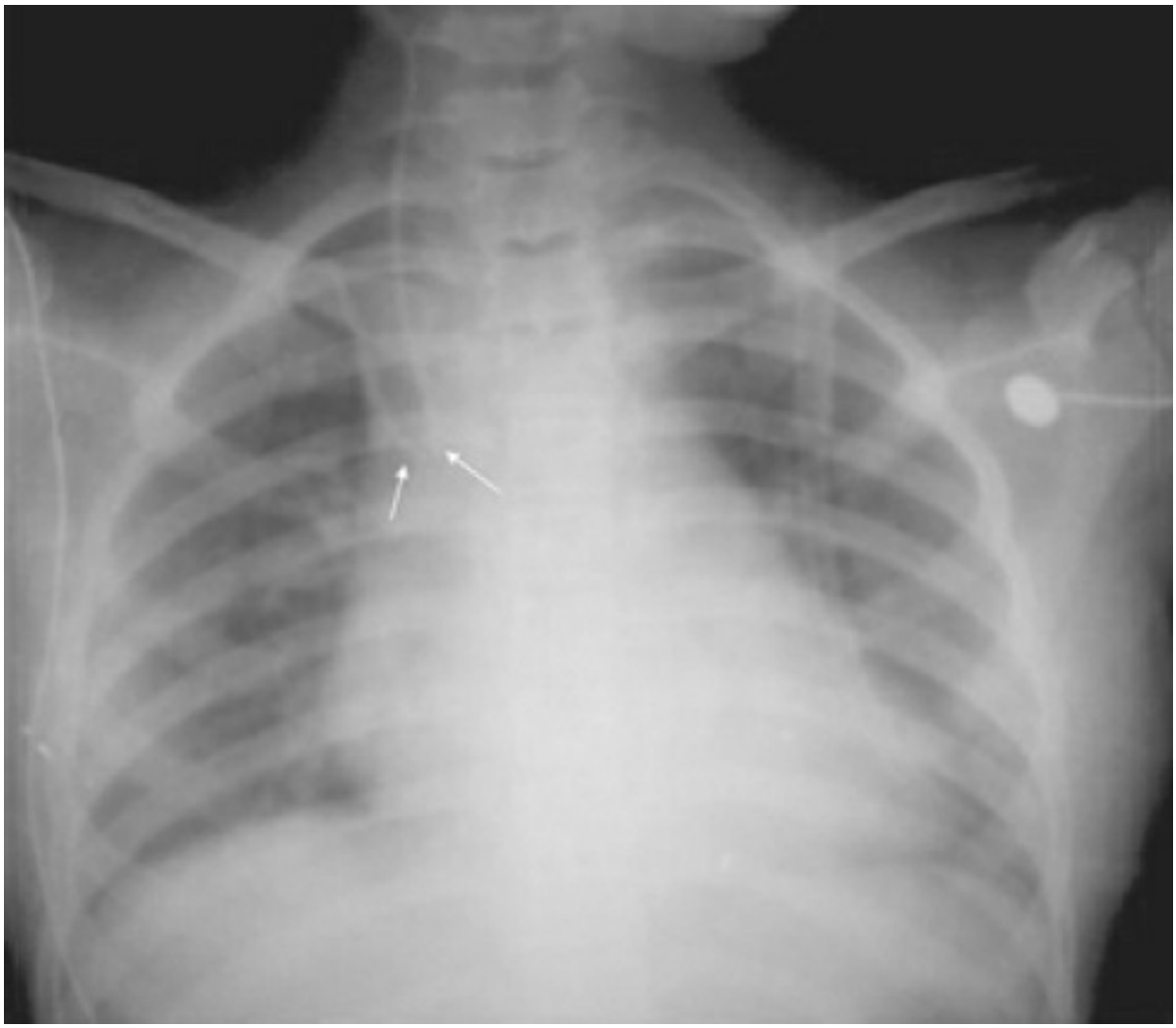


Figure 4.24C: Double backing of the central venous catheter that was inserted in the right internal jugular vein (arrows).

Antecubital Veins

Basilic and cephalic veins provide alternative routes for monitoring CVP. However, due to a low success rate in the placement of catheter in the central vein, these are rarely cannulated by cardiac anaesthesiologists.

Ultrasound Guided Central Venous Access

Traditionally, the central venous catheters are inserted blindly using the anatomical landmarks as described in the preceding paragraphs. However, ultrasound provides the operator the benefit of visualizing the target veins and the surrounding anatomical structures. This is expected to minimize the complications and increase the speed of placement. With the availability of

portable ultrasound machines in the operating room, it is being used at some centres for placement of the central venous catheters. The IJV can be visualized in the transverse as well as the longitudinal sections (Figs 4.25 A and B). It is seen as a lateral oval, nonpulsatile structure that can be easily compressed by pressing the transducer. The internal carotid artery is identified as a pulsatile structure medial and deeper to the IJV. Doppler interrogation can further help to identify the vein. Ultrasound guidance can be used in different ways during central venous catheterization. For instance, two dimensional (2-D) ultrasound can be used to confirm vessel location and mark it on the skin, and then the catheterization can be performed using the marks in the usual fashion. Alternatively, the ultrasound can be incorporated into the procedure itself to provide real-time visualization of vessel cannulation. Investigators have shown that ultrasound guidance reduces the time required for catheterization, increases overall success rates, and results in fewer complication.[37] The technique can be especially useful in infants and children in whom the percutaneous cannulation of the IJV may be technically difficult and can lead to complications. However, a recent meta-analysis has failed to show any benefit of ultrasound during IJV access in terms of increasing the success rate and in decreasing the complications.[38] Nevertheless, it may be beneficial in some difficult situations such as atypically placed or small sized veins.

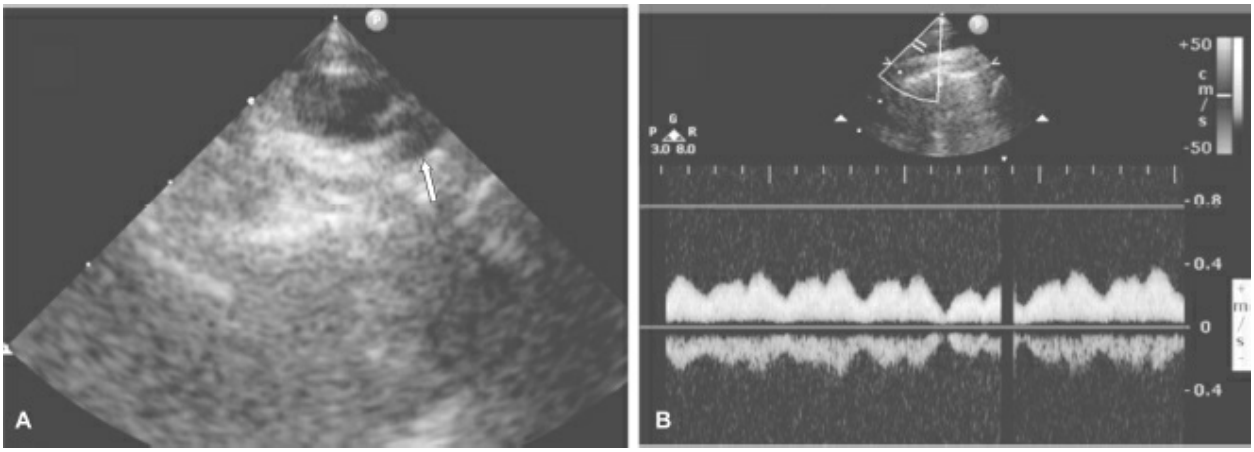


Figure 4.25: A: Ultrasound image showing transverse section of the right internal jugular vein seen as a central oval structure. The internal carotid artery (arrow) is seen medial and deeper to the vein. B: Pulsed wave Doppler profile obtained in the longitudinal section of the internal jugular vein. Note the continuous low velocity venous waveform

In clinical practice, the use of ultrasound for placement of central venous catheters continues to be low (less than 15 percent of the time).[39] One of the

questions that is raised is, whether increased dependence on this technique is desirable, as the traditional landmark technique will still be required in clinical settings where ultrasound is not available. This is especially so in the developing countries. Another view point is that, since the technology is available, it should be used and eventually will complement the conventional landmark technique. It is reasonable to conclude that routine use of ultrasound guidance during central venous cannulation is not required and that it should be reserved for difficult situations.

Pulmonary Arterial Pressure Monitoring

The flow directed PAC was introduced in the 1970s.[40] It has provided a means of obtaining invaluable diagnostic information at the bedside. The PACs are used with the intention of measuring pulmonary capillary wedge pressure (PCWP) and pulmonary artery diastolic pressure (PADP). However, other parameters such as pulmonary artery systolic pressure, mean pulmonary artery pressure (MPAP), mixed venous blood gases, and CO by thermodilution can also be measured. In addition, special purpose PACs for continuous CO and mixed venous oximetry, pacing and thermodilution right ventricular ejection fraction (RVEF) are also available. Despite providing these haemodynamic measurements that cannot be estimated clinically, it remains uncertain whether PAC monitoring leads to improved patient outcome.[41]

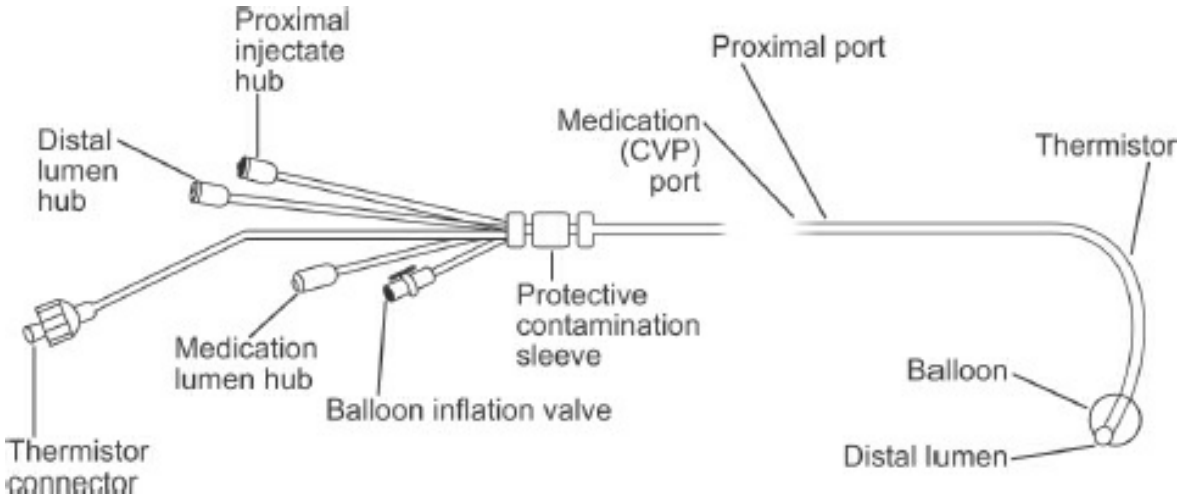


Figure 4.26: Diagram showing a five lumen pulmonary artery catheter.

PADP and PCWP are measured because they are indirect estimates of the LA pressure, which in turn is an estimate of the LV end-diastolic pressure (LVEDP). In the presence of pulmonary vascular or mitral valve disease, the PCWP and PADP do not accurately estimate the LVEDP. In addition, the distal port of the PAC should be placed in the dependent portion, i.e. zone III of the lung (pulmonary venous pressure exceeds the alveolar pressure in this zone) so that vascular channels distal to the port of PAC are patent. In this situation, the LA pressure has a close relationship to PCWP and PADP. The PAC is a flexible, flow directed, balloon tipped catheter (Fig. 4.26) that is available in various sizes (e.g. 5, 7 and 7.5 F) and number of lurnina (2 to 5). The standard catheter is 110 cm long and has marks every 10 cm to indicate how far it has been inserted. The distal lumen is placed in the pulmonary artery (PA) and is used to measure PCWP, and PA pressure (systolic, diastolic and mean). The second lumen connects to the 1.5 mL capacity balloon at the tip of the catheter. Inflation of this balloon with air allows the catheter to float in the blood stream (flow directed) and advance it to the point where the diameter of the PA equals that of the balloon. In this situation, the forward flow through the PA is obstructed and the distal lumen measures the pressure distal to it (PCWP). Since the pulmonary veins communicating with the LA are valveless, and have rruriimum resistance, PCWP reflects LA pressure in the absence of pulmonary vascular disease.

The third lumen transmits the electrical signal from the thermistor probe positioned approximately 2 cm proximal to the catheter tip. This is utilised for the CO measurements by thermodilution technique.

The fourth lumen terminates 30 cm proximal to the catheter's tip and is positioned in the RA in most adults, when the catheter tip is in a wedged position. It is used for the measurement of RA pressure and injection of the injectate necessary for the computation of CO. An additional fifth lumen is provided that can be used for infusion of the medicines. A fibreoptic lumen for measuring continuous oxygen saturation at the distal end of the catheter (mixed venous oxygen saturation) is also provided in some catheters.

Technique

The catheter is inserted percutaneously under sterile conditions and requires the aid of a skilled assistant. The assistant flushes all the lumens with heparinized saline to de-air them and attaches the distal port hub to the

transducer. The balloon is tested by filling it completely with 1.5 mL of air from a volume-limited syringe. Like CVP catheter, IJV is the most preferred site of cannulation of PAC. EJV, subclavian, cubital or femoral veins can also be used. After puncturing the IJV with an 18 G needle, a flexible guide wire is passed into the vein and the needle is removed. The skin puncture site is then enlarged with a knife and an 8 F sheath with the vein dilator is passed over the guide wire. The guide wire and the dilator are then withdrawn leaving the sheath in the IJV. The progress of PAC via its sheath to the PA is followed by continuously monitoring the pressure waveform from the distal port of the catheter that is connected to the transducer. After the catheter tip has been advanced 15 to 20 cm (approximate distance of the RA from the IJV puncture site), the balloon is inflated. The further course of catheter is guided by the pressure waveform and measurements.

The pressure waveforms seen during advancement of the catheter are shown in Figure 4.27. The RA pressure waveform with a mean pressure of 5 mm Hg (range 1 to 10) confirms that the catheter has reached the RA. As the catheter negotiates the tricuspid valve and enters the RV, there is a sudden increase in the systolic pressure but little change in the diastolic pressure (systolic, 15 to 30 mm Hg and diastolic, 0 to 8 mm Hg). Premature ventricular contractions can usually be observed at this time. The right ventricular tracing is generally obtained at 25 to 35 cm of catheter insertion. The catheter is advanced further towards the PA. As it enters the PA, an increase in the diastolic pressure is observed that is accompanied by a dicrotic notch on the pressure waveform. The PA waveform is generally obtained at 40 to 50 cm of catheter insertion. The PCWP tracing is obtained by passing the catheter 3 to 5 cm further until there is a change in the waveform to that of the LA waveform with associated decrease in the mean pressure. Deflation of the balloon results in reappearance of the PA waveform. If the catheter does not enter the RV by 40 cm and PA by 50 cm, it should be withdrawn up to 20 cm (if there is a failure to enter the RV from the RA) and up to 30 cm (if there is a failure to enter the PA from the RV) and another pass made. According to one study, the RV is reached at 24.6 ± 3 cm, PA at 36 ± 4 cm, and wedge position at 42.8 ± 5.7 cm.[42] The study further showed that the length of catheter to reach the RV, PA and wedge position was significantly more in patients undergoing valve surgery as compared with those undergoing CABG. These landmarks form a useful guideline for accurate placement of the catheter and minimizing the complications related to coiling

of the catheter.

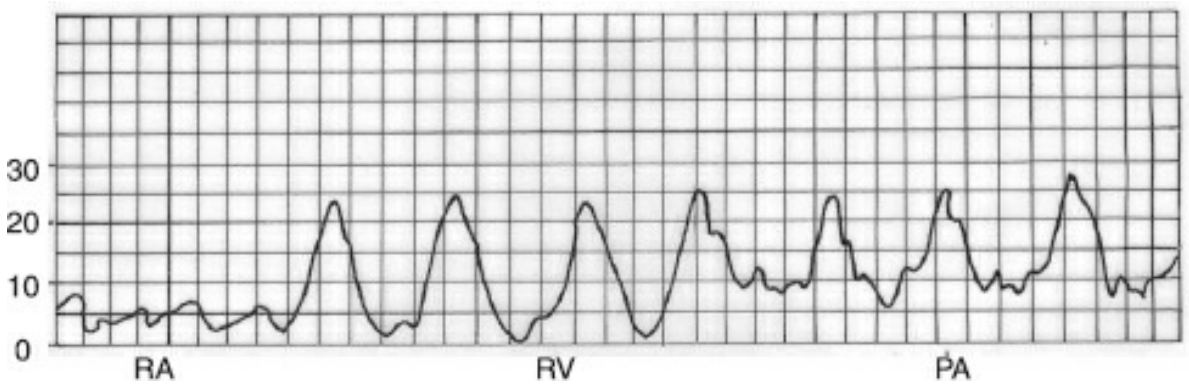


Figure 4.27A: Standard pressure waveforms obtained during insertion of the pulmonary artery catheter; note right atrium (RA), right ventricle (RV) and pulmonary artery (PA) progression.

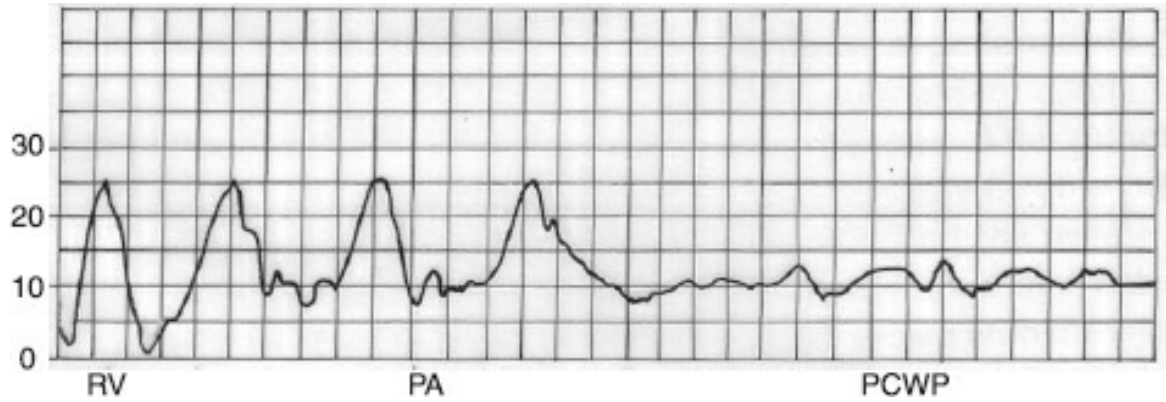


Figure 4.27B: Pulmonary artery pressure waveform and wedge pressure after balloon inflation. (RV: right ventricle, PA: pulmonary artery, PCWP: pulmonary capillary wedge pressure).

Difficulty in negotiating the tricuspid valve may be encountered in patients with tricuspid regurgitation. Excessive coiling of the catheter in the right atrium should be avoided to prevent knotting of the catheter. The PA waveform should be continuously monitored to ensure that the catheter does not migrate to a constant wedge position. Similarly balloon should be inflated only for short periods of time to measure the PCWP. In some patients, PAC may migrate distally, especially during CPB because of the repeated cardiac manipulations. Therefore, proper catheter position must be ensured throughout by frequent observation of the pressure waveform. If PCWP trace appears without balloon inflation, the catheter should be withdrawn a few centimeters to reduce the risk of pulmonary vascular injury. A few useful tips may help successful positioning of the PAC. The air-filled balloon floats to non-dependent regions, hence, positioning a patient head-down will aid flotation past the tricuspid valve, and right-sided tilt with head-up position

will aid flotation out of the RV.[43]

Indications

The effective use of PACs requires a great deal of expertise and clinical experience. Unfortunately, a wide-spread knowledge deficit exists among the practitioners who use PACs.[44,45] Furthermore, misinterpretation of the PAC derived data by the clinicians is also not unknown.[46,47] The controversial outcome related data regarding PAC use should be viewed in this background.

Since the time, a strongly worded editorial calling for a moratorium on PAC use has been published[48], a great deal of work has been performed to know whether patients are being helped or harmed by the use of PACs. Two meta-analysis of 11 and 13 published randomized controlled trials involving PAC use have reported a higher incidence of adverse events, but no effect on mortality or on hospital or ICU length of stay.[49,50] Conversely, some investigators have reported a treatment benefit from PAC use, especially in high-risk group of patients.[51,52]

In 2007, the American Society of Anesthesiologists published an updated practice guideline for pulmonary artery catheterisation.[53] According to this, use of a PAC may be reasonable in patients at risk for major haemodynamic disturbances that are easily detected by a PAC. However, the decision must be based on patient disease, surgical procedure (i.e. intraoperative and postoperative fluid shifts), and practice setting (experience in PAC use and interpretation of results). Indications of using PAC vary from place to place and although, their routine use is controversial, there is no denying that it provides valuable information in very sick patients such as patients with recent myocardial infarction (MI) or unstable angina, patients with poor LV function (CHF), and patients in hypovolemic or cardiogenic shock. Its use is therefore, recommended in such situations.

Contraindications

Absolute

PAC should not be used in patients with tricuspid or pulmonary stenosis, patients with RA, RV or PA masses (tumour, thrombus) and tetralogy of

Fallot.

Relative

Arrhythmia, coagulopathy and bundle branch block are relative contraindications for the use of PAC.

Complications

Arrhythmias (usually premature ventricular contractions) are the most common complications associated with the PAC insertion.[54] They are usually benign and disappear as the catheter enters the PA. However, fatal arrhythmias have also rarely been reported.[55] Complete heart block, endobronchial haemorrhage, pulmonary infarction, catheter knotting and entrapment, valvular damage, thrombocytopaenia, thrombus formation, incorrect placement and balloon rupture are some other rare complications of the PAC placement. Amongst these, endobronchial haemorrhage due to PA rupture is the most dangerous complication. It is more likely to occur if the patient has pulmonary artery hypertension (PAH) or coagulopathy. Correction of the coagulopathy, if present, and protection of the uninvolved lung by tilting the patient to the affected side or placement of a double lumen endobronchial tube may be necessary.[56] Sometimes pulmonary resection may be needed.[57]

Catheter knotting and entrapment in the surgical suture are well known.[58] Rarely knotting and entrapment can occur in the same patient.[59] Several nonsurgical measures including untying a knot[60-63] or tightening a knot[58] have been described to solve this problem. Frequent manipulations of the catheter should be avoided to prevent the knotting.

Right Ventricular Ejection Fraction

The standard PAC has been modified to incorporate a rapid response thermistor and ECG electrodes. The catheter is placed so that the injectate port is positioned in the RA. With each injection, the thermodilution curve is plotted. The RVEF is calculated from the exponential decay of the thermodilution curve. The R wave signal is used to identify the end-diastolic temperature points in the thermodilution curve. The computer is able to measure the HR, RVEF, right ventricular end-diastolic (RVEDV) and end-

systolic (RVESV) volumes. The volumetric measurements along with RVEF can be useful in the management of patients who have RV dysfunction or PAH (patients with right coronary artery disease, mitral valve disease). However, these catheters are rarely used during cardiac surgery. They have been found to be useful in critically ill patients, especially those with respiratory failure[64,65], but the benefit in terms of patient outcome remains unproven.[66]

Mixed Venous Oxygen Saturation

Continuous monitoring of mixed venous oxygen saturation (SVO_2) has become possible due to the addition of fibreoptic bundles to the PACs. Changes in SVO_2 reflect changes in the CO, if oxygen consumption and arterial oxygen content remain constant. Thus, SVO_2 has been shown to provide a valuable measure of CO.[67] It indicates the balance between oxygen delivery and consumption and has been found to have a prognostic value.[68] In general, SVO_2 of < 50 percent has a bad prognosis. It is also useful for knowing the efficacy of the therapy that has been instituted for the treatment of low CO state.

Pacing Pulmonary Artery Catheters

Temporary endocardial pacing can be performed with specialized PACs that may have combinations of electrodes permanently implanted along its length to allow bipolar ventricular, atrial, or atrioventricular pacing.[69] Some other catheters have a special lumen that opens in the RV, or have separate atrial and ventricular lumens through which pacing wires can be inserted for endocardial ventricular pacing and bichamber sequential pacing, respectively.[70]

Left Atrial Pressure Monitoring

During operation, a catheter can be placed by the surgeon into the LA directly or through the right superior pulmonary vein. The catheter is brought out through the skin in the epigastric area before sternal closure. The LA pressure

monitoring is very informative and provides an accurate estimation of the left-sided filling pressures. However, it requires extreme caution in its use. There is a possibility of air embolism (coronary/cerebral) or clot formation and embolisation. Continuous heparinised flushing system is required for its use in the postoperative period. There is also a risk of bleeding leading to cardiac tamponade when the catheter is removed. It is therefore, advisable to remove it when the chest tubes are still in place.

Due to these problems, as well as a wider application of the PAC, LA lines are rarely inserted, e.g. in children, and in situations where PAC insertion has failed or PCWP does not accurately estimate the LA pressure (pulmonary vascular disease). In today's practice, direct LA pressure monitoring has largely been replaced by PAC monitoring.

Cardiac Output

The CO is the amount of blood pumped by the heart each minute and reflects the overall performance of the cardiovascular system. Therefore, its measurement is of vital importance in patients with cardiac disease. Amongst the several methods that are available (dye dilution, Fick method, thermodilution, Doppler, and pulse contour analysis), thermodilution technique is considered the clinical standard and is most widely used.

Thermodilution Technique

Presently, CO measurement using thermodilution PAC is the method of choice. Frequent CO measurements are possible with this method. A bolus of iced or room temperature fluid (usually 10 mL of normal saline) is injected into the RA and the resulting temperature change is detected by the thermistor in the PA. A temperature time curve is plotted, and the CO that is inversely proportional to the area under the curve is calculated by the computer.

In clinical practice, a series of 3 to 5 measurements of CO are obtained and a mean is calculated to improve the precision. For additional accuracy, the rate and duration of each injection should be kept as constant as possible. In addition, the timing of the injection in respiratory cycle should also be the same. Patients with tricuspid or pulmonary regurgitation pose additional problems due to recirculation of the indicator across the incompetent valve.

The measurements obtained in the presence of severe tricuspid or pulmonary regurgitation are not reliable.

The present day computers have the ability to calculate all the haemodynamic parameters such as systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), left ventricular stroke work (LSW), right ventricular stroke work (RSW), etc. based on the CO and pressure measurements.

Continuous thermodilution cardiac output

PAC and monitors that are able to perform continuous CO measurements are available. The PAC has a 10 cm heating element incorporated into the RV portion of the PAC. The thermal energy is delivered to this heating element from the outside source and the thermodilution temperature curve is plotted to obtain continuous CO measurements. The heating filament is cycled on and off in a random sequence and the displayed value of CO is updated every 30 to 60 seconds and represents the average value for the CO measured over the previous 3 to 6 min. It has been shown that changes in continuous CO are markedly slower than changes detected by other methods such as ultrasonic flow probe, blood pressure or SVO_2.[71] These catheters are more expensive, but have some practical advantages. Since, bolus injections are not required, nursing workload and potential risk of fluid overload or infection are reduced. However, as already emphasized, acute changes in CO are detected more slowly by continuous CO monitoring.

Interpretation of haemodynamic data

The current monitors are capable of calculating the various derived haemodynamic parameters. These monitors have an inbuilt online facility to calculate these parameters with the help of standard formulae. The formulae and the normal values of the various haemodynamic parameters are shown in Table 4.1.

Table 4.1: Standard formulae and normal values of haemodynamic parameters

Formula	*Normal values*
$CI = \frac{CO}{BSA}$	2.8–4.2 L/min/m^2
$SV = \frac{CO \times 1000}{HR}$	50–110 mL/beat
$SI = \frac{SV}{BSA}$	30–65 mL/beat/m^2
$LVSWI = \frac{1.36 \times (MAP - PCWP) \times SI}{100}$	40–60 g.m/m^2
$RVSWI = \frac{1.36 \times (MPAP - CVP) \times SI}{100}$	5–10 g.m/m^2
$SVR = \frac{(MAP - CVP) \times 80}{CO}$	900–1400 dyne.sec.cm^{-5}
$SVRI = \frac{(MAP - CVP) \times 80}{CI}$	1500–2400 dyne.sec.cm^{-5}.m^2
$PVR = \frac{(MPAP - PCWP) \times 80}{CO}$	150–250 dyne. sec.cm^{-5}
$PVRI = \frac{(MPAP - PCWP) \times 80}{CI}$	250–400 dyne. sec.cm^{-5}.m^2

(CI: cardiac index, CO: cardiac output, BSA: body surface area, SV: stroke volume, SI: stroke index, LVSWI: left ventricular stroke work index, RVSWI: right ventricular stroke work index, MAP: mean arterial pressure, PCWP: pulmonary capillary wedge pressure, MPAP: mean pulmonary artery pressure, CVP: central venous pressure, SVR: systemic vascular resistance, SVRI: systemic vascular resistance index, PVR: pulmonary vascular resistance, PVRI: pulmonary vascular resistance index).

These values can be used to interpret the ventricular function. Determining an ideal CVP or PCWP in often a clinical challenge as the pressure-volume relationship of the LV is not linear. At the extremes of high and low values, the interpretation is more obvious, but things are rarely so clear-cut in a sick patient. Hence optimal CVP or PCWP is often chosen empirically. A fluid challenge (250 to 500 mL of crystalloid or colloid given over 15 min.) can be useful in determining the optimal filling pressure. Small increases in PCWP suggest that the ventricle is operating on the flat portion of the diastolic filling curve (can take more volume), and large increases in PCWP suggest that the steep portion of the curve has been reached (no more volume required). The Starling curve can be used to interpret the data and institute

therapy. Figure 4.28 merely illustrates the relationship between systolic blood pressure, CVP or PCWP and the normal or failing heart. The curve can be utilized by choosing empirical values as follows:

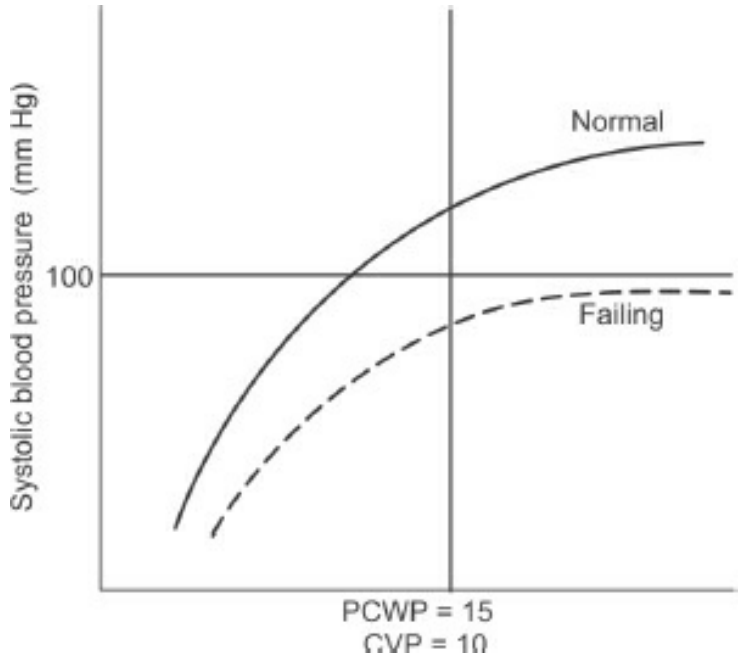


Figure 4.28: Diagram illustrating the relationship between systolic blood pressure (presuming it is directly related to the cardiac output) and pulmonary capillary wedge pressure (PCWP) or central venous pressure (CVP) in normal and failing heart. For details refer to the text.

The patient needs transfusion, if the systolic pressure is less than 100 mm Hg when the CVP is less than 10 mm Hg or PCWP is less than 15 mm Hg. Inotropic support is required, if the systolic pressure is less than 100 mm Hg when the CVP is more than 10 mm Hg or PCWP is more than 15 mm Hg. Cardiac tamponade, however, should be ruled out in this situation. In addition, diuretics may be required. Vasodilators may be used, if there is an associated increase in the SVR. The SVR is used to assess the response to inotropes, vasodilators and vasoconstrictive agents. A patient who is hypotensive in the presence of a normal CO has a low SVR. Thus, depending upon the various haemodynamic parameters, appropriate therapy can be instituted.

Other methods for monitoring cardiac output

Over the years, some other less invasive methods of monitoring CO have been described. These include ultrasound based methods, (oesophageal Doppler and suparsternal Doppler), bioimpedence, pulse contour analysis,

partial CO_2 rebreathing, and lithium dilution. Amongst these, oesophageal Doppler and pulse contour analysis that provide continuous CO measurements have been used in cardiac surgery.

The oesophageal Doppler measures the Doppler shift frequency, which is directly related to the velocity of blood in the descending thoracic aorta. The SV is calculated by the formula

SV = VTI × CSA where SV is stroke volume (mL), VTI = velocity time integral and CSA = cross-sectional area of the aorta. Since the method interogates blood flow in the descending thoracic aorta, it measures only a fraction of total CO. Therefore, in order to calculate the CO, some assumptions are made such as blood flow in the descending thoracic aorta is 70 percent of total CO and cross-sectional area of the aorta remains constant throughout systole. The device is easy to use, minimally invasive and can be useful in a tracheally intubated patient, if PAC cannot be inserted or is contraindicated. The technique has been validated in comparison with thermodilution by several studies.[72-74] The limitations are that it provides only an estimate of total CO, is inaccurate in patients with aortic valve disease or thoracic aortic disease, and is not easy in awake patients. Furthermore, the assumption that aortic blood flow is 70 percent of total CO is not valid in patients with redistribution of blood flow, e.g. pregnancy and post-cardiopulmonary bypass.

The pulse contour analysis techniques for the measurement of CO are attractive because they provide beat-to-beat CO. However, these techniques usually require frequent calibration to remain accurate over time. The calibration can be obtained by using transpulmonary thermodilution (PiCCO™, Pulsion, Germany) or lithium chloride dilution (Pulse CO™, LIDCO, UK). This increases the invasiveness, the cost, and the complexity of the procedure. A new self calibrating arterial pulse contour CO monitoring system (Flo Track/Vigileo™) is now available. It is less invasive than the PAC and needs a flow sensor that is connected to the standard arterial line. Controversies exist among studies regarding the ability of this technique to provide reliable stroke volume estimation.[75] Three different versions of the Vigileo software have been used, and the exact algorithm remains undisclosed by the manufacturer. A reasonable quality of arterial pressure waveform is needed for accurate identification of systole and diastole. This might not exist in patients with severe tachycardia or dysrhythmia.

Transoesophageal Echocardiography

The use of TOE during intraoperative as well as postoperative period has advanced greatly during the last decade. The echocardiographic imaging system along with simultaneous representation of intracardiac blood flow in real time (Doppler colour flow imaging) has transformed the field of noninvasive diagnostic cardiology. It has been found to be very useful particularly during cardiac surgery and numerous applications have been developed including its ability to alter surgical management and to predict the outcome.[76] In addition, it can also be used in cardiac patients undergoing non-cardiac surgery as well as in the intensive care units.

In echocardiography, the heart and great vessels are probed with ultrasound (sound with frequency above 20,000 Hz) which is the sound above the human audible range. The ultrasound is partially reflected by the cardiac structures. From these reflections, information on distance, velocity and density of objects within the chest is derived. Perioperative TOE was introduced in cardiac anaesthesia in the late 1980s in the USA, and it extended to the UK and European cardiothoracic centres in the mid-1990s.[77] In India, it was introduced in the cardiac operating room in the late 1990s (in 1998 in the author's unit). Since then, its use has expanded enormously and is now a recognized perioperative diagnostic tool rather than just a monitoring device providing new and important information guiding through both the surgery and anaesthesia.[78]

Imaging techniques

The most simple form of ultrasound imaging is M-mode echocardiography. The density and position of all the tissues in the path of a narrow ultrasound beam are displayed as a scroll on a video screen. As only a limited part of the heart is being observed at any one time, and because the image requires considerable interpretation, M-mode is not used as a primary imaging technique. The mode is, however, useful for the precise timing of events with the cardiac cycle. Quantitative measurements of size, distance and velocity are also easily performed in M-mode.

Two-dimensional mode

In this mode, rapid repetitive scanning along many different radii within an

area in the shape of a fan (sector), generates a 2-D image of a section of the heart. The image thus formed resembles an anatomical section and is more easily interpreted. Images are displayed in “realtime” on a monitor screen and by altering the position or angle of the ultrasound beam, the operator can produce several cross-sectional images of the heart and great vessels.

Doppler Technique

Most modern machines combine Doppler capabilities with 2-D imaging. After the desired image of the heart has been obtained by 2-D echocardiography, the Doppler beam represented by a cursor is superimposed on the 2-D image. The cursor is positioned as parallel as possible to the assumed direction of blood flow to optimise the audio and visual representations of the reflected signal.

The blood flow velocities are quantified by measuring the Doppler shift, which is a shift in the frequency of a wave when the source of wave (moving red cell) is moving. This is achieved either by the use of pulsed-wave (PWD) or continuous-wave Doppler (CWD) techniques. Pulses of sound are emitted and received by a single crystal in the PWD, and two separate crystals; one to emit ultrasound and another to receive it continuously are used in the CWD.

Colour Doppler

Colour Doppler imaging permits sampling of the Doppler shift simultaneously in a wide area of the sector scan. A colour code is used to denote flow towards (red) and away (blue) from the transducer. Relatively faster and slower velocities are depicted by lighter and darker shades of red and blue respectively. When the ultrasonograph detects two different velocities within the same sample volume (as in the turbulent flow produced in mitral regurgitation), a mixture of colours (mosaic) is displayed, which is commonly termed as “colour jet”. Colour Doppler is useful in the recognition of valvular abnormalities and intracardiac shunts.

Equipment

Because fat, bone and air containing lung interfere with sound wave penetration, clear transthoracic echocardiogram views are difficult to obtain in patients with obesity, emphysema or abnormal chest wall anatomy. TOE transducers were developed to avoid these problems. Sound waves emitted from an oesophageal transducer only have to pass through the oesophageal

wall and pericardium to reach the heart, thus there is less likelihood of image distortion. In addition, there are potentially new echocardiographic windows. The other advantages of TOE include a steady transducer position and a possibility of obtaining continuous recordings of the cardiac activity for prolonged periods of time. 2-D TOE was first performed with a mechanical system in 1977.[79] Subsequently, phased array transducers were mounted on the gastroscope[80,81] allowing greater flexibility and control. These probes allowed 2-D scanning of the heart through many planes and became the prototypes of the currently used models. The simplest TOE probe has one phased array transducer. The ultrasound beam is oriented at right angles to the gastroscope to create transverse imaging planes of the heart. Biplane transducers integrate a second transducer mounted proximal and at right angles to the first one. This offers longitudinal imaging plane. The currently available TOE probes employ a multiplane 3.7 to 7.5 MHz transducer that is mounted on the tip of a gastroscope housing. The tip can be manipulated by the adjustment of rotary knobs (wheels) placed at the proximal handle. One of the wheels anteflexes and retroflexes the transducer and the other flexes the transducer rightward or leftward. In addition, the multiplane transducer can be made to spin on its axis within the transducer housing from 0 to 180 degrees with the help of buttons on the handle. This helps to provide many echocardiacgraphic windows. The TOE console and the probe are shown in figure 4.29, and the movement of the transducer beam at various levels is show in figures 4.30A to E.

The American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists established the task force to develop evidence based guidelines on the proper indications for performing TOE in the operating setting in 1996[82], these were updated in the year 2010.[83]

Procedure

In the operating room, the TOE machine is positioned behind the patient's head placed on the left side. The probe should be inserted smoothly without application of undue force. The biting block should be used in all patients except in the edentulous so that injury to the probe by the teeth is prevented during its movement. It is a good practice to aspirate the stomach (air and gastric secretions) in order to improve the acoustic window and the picture quality. The operator gently introduces the lubricated (with lignocaine jelly)

transducer tip into the oropharynx. Once in the oropharynx, the probe is anteflexed (by the control wheel on the handle) and advanced into the oesophagus. This blind technique of probe insertion is almost always successful, however, in some patients, direct laryngoscopy may be required. It is preferable to use a laryngoscope rather than applying undue force to insert the probe so that unnecessary injury to the structures is avoided. Once into the oesophagus, the probe is advanced approximately 30 cm from the teeth and is connected to the console. Ahyperinflated cuff of the endotracheal tube may offer resistance high in the oesophagus, while stenosis or stricture of the hiatus may do so lower down in the oesophagus. It must be remembered that undue force should never be applied to overcome any resistance at any stage of insertion of the probe.

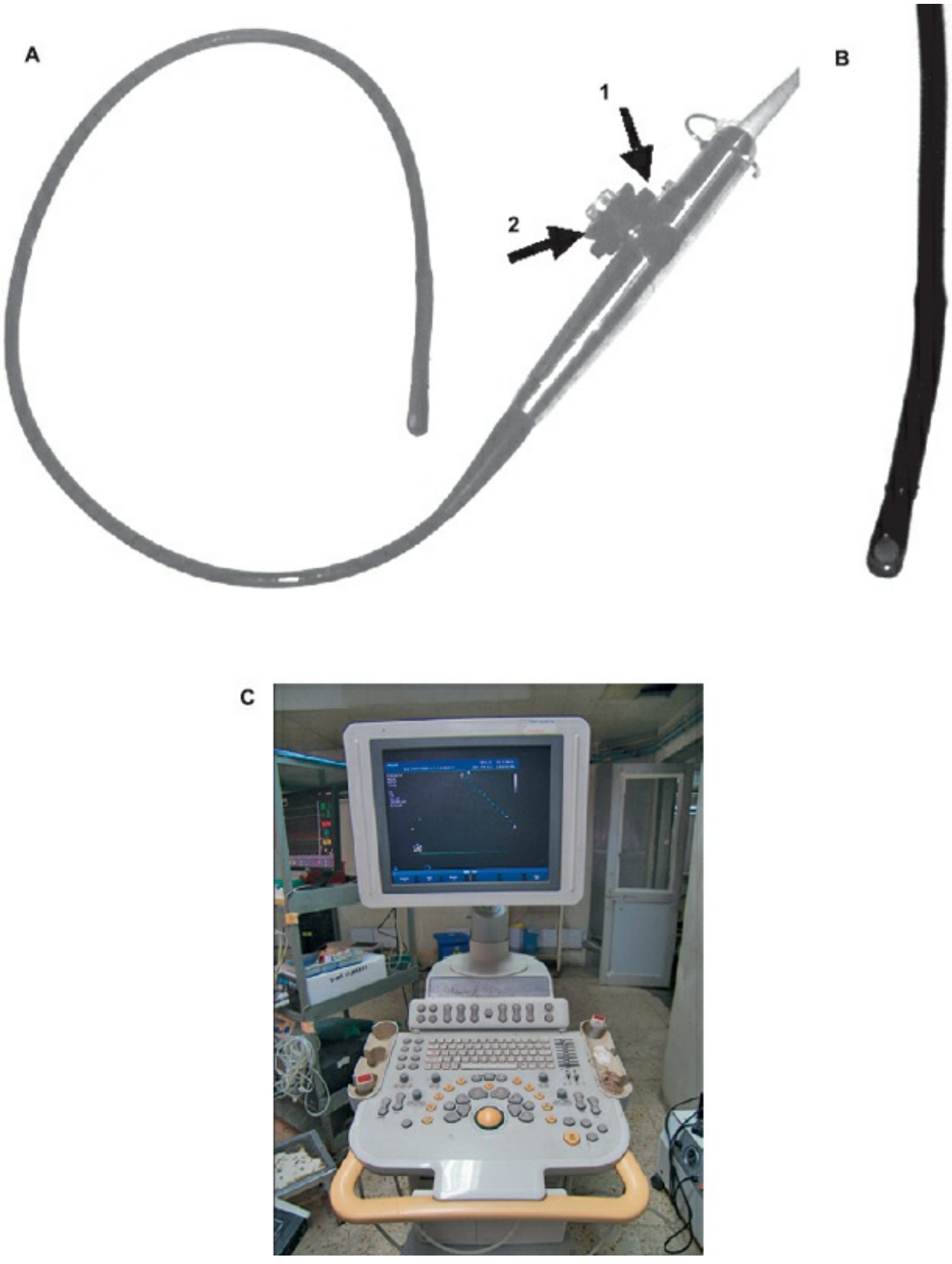


Figure 4.29: **A:** Adult TOE Probe. The probe is a 100-cm modified gastroscope. There are two control knobs present on the handle of the probe. The larger inner knob (arrow 1) controls anterior and

posterior flexion and the smaller outer knob (arrow 2) controls leftward and rightward angulation. **B:** Close up of the tip of the probe. **C:** The TOE console.

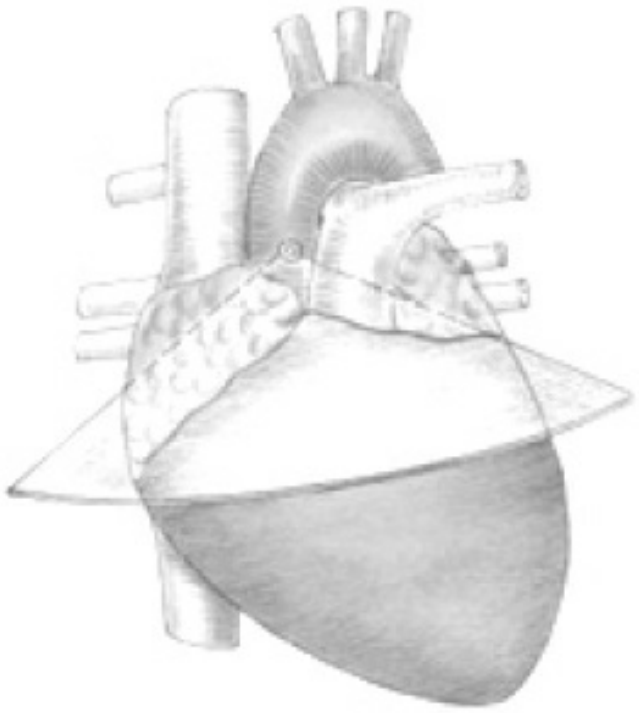


Figure 4.30A: Diagrammatic representation of the transverse ultrasound beam in the mid-oesophageal view directed through the aortic valve.

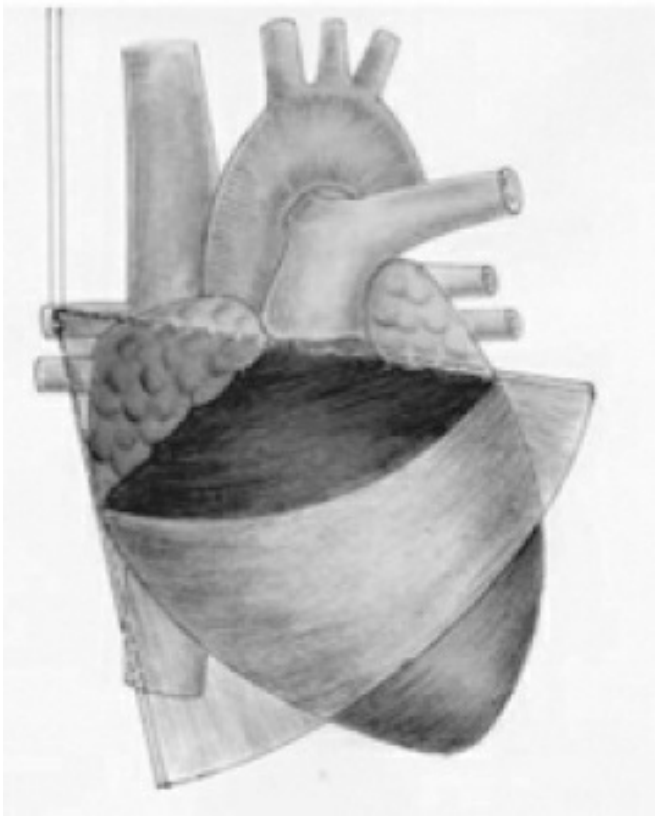


Figure 4.30B: Diagrammatic representation of the longitudinal ultrasound beam in the mid-oesophageal view.

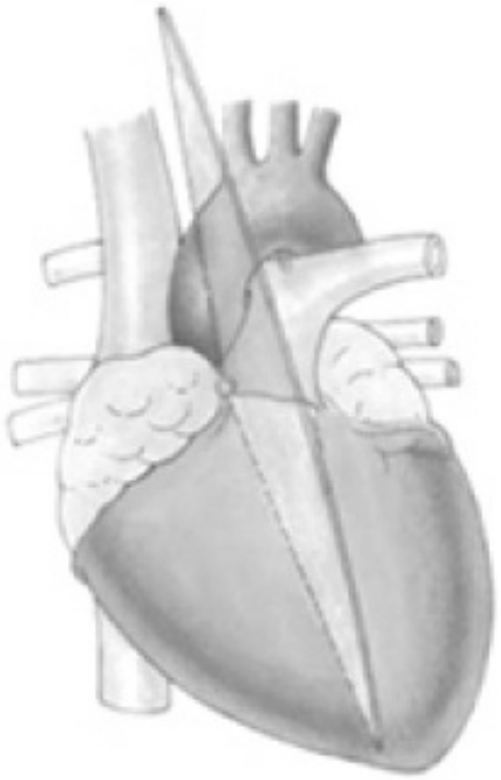


Figure 4.30C: Diagrammatic representation of the longitudinal ultrasound beam through the ascending aorta, aortic valve and left ventricular outflow tract.

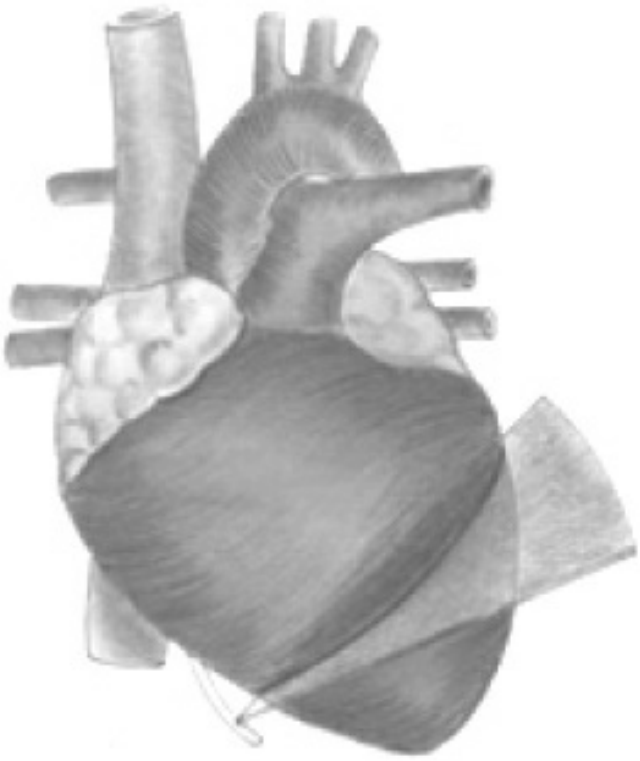


Figure 4.30D: Diagrammatic representation of the transverse ultrasound beam through the left ventricle at the level of papillary muscle (transgastric view).

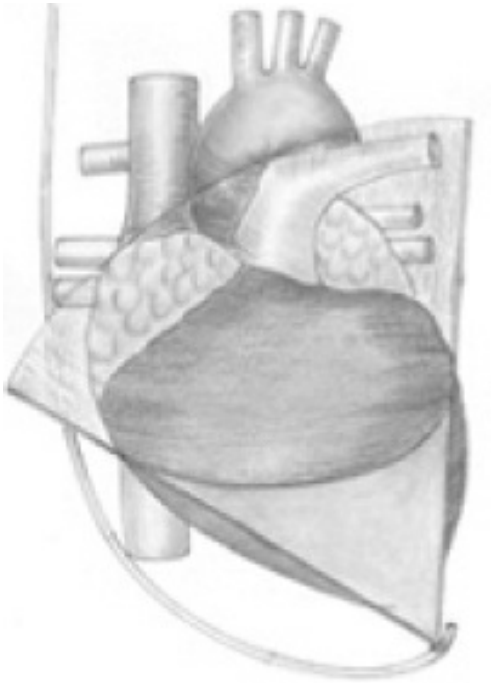


Figure 4.30E: Diagrammatic representation of the ultrasound beam in the deep transgastric view.

Table 4.2: Showing the 20 standard cross-sectional views and their abbreviated names

Upper-oesophageal	***Mid-oesophageal***	***Transgastric***
UE aortic arch LAX	ME four-chamber	TG mid SAX
UE aortic arch SAX	ME Two-chamber	TG two chamber
	ME LAX	TG basal SAX
	ME mitral commissural	TG LAX
	ME AV SAX	Deep TG LAX
	ME AV LAX	TG RV inflow
	ME bicaval	
	ME RV inflow-outflow	
	ME asc aortic SAX	
	ME asc aortic LAX	
	desc aortic SAX	
	desc aortic LAX	

(UE: upper-esophageal, ME: mid-esophageal, TG: trans-gastric, LAX: long-axis, SAX: short-axis, AV: aortic valve, RV: right ventricle)

TOE views

The practice guidelines of the American Society of Echocardiography (ASE) Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography recommend 20 standard views for comprehensive TOE examination (Table 4.2).[84]

In clinical practice, most practitioners believe that unless urgency precludes, all patients should have full and comprehensive examination of the heart and as much of the great vessels as can be seen. This should include the pulmonary veins, and the vena-cava and hepatic veins.

The order in which the examination proceeds may vary from examiner to examiner. In general, the mid-oesophageal views are obtained first. With the TOE imaging plane at 0°, a four-chamber view demonstrating the basal and mid segments of the inf ero-septum and anterolateral LV wall is obtained (Fig. 4.31) at 30–35 cm depth at upper incisors. This view demonstrates the mitral valve (MV), tricuspid valve (TV), LA, right atrium (RA), RV, inter-atrial septum (IAS), and the inter-ventricular septum (IVS). Colour Doppler is applied to assess the valvular regurgitation ensuring that the colour sector includes the LA portion of any mitral regurgitation (MR) jet as well as the ventricular aspect to detect any flow convergence caused by the MR. The transmitral flow velocity profile can be examined using the spectral PWD. The fourchamber view also demonstrates the septal leaflet of the TV, and if the probe is retroflexed, the posterior leaflet of the TV. By advancing the probe little further by 1 to 2 cm, coronary sinus opening into the RA can be seen (Fig. 4.32). The mid-oesophageal two-chamber view (Fig. 4.33) is obtained by rotating the multiplane angle to between 80° and 100° until the LA and LV appear. This cross-section shows the basal, mid, and apical segments of the LV in each of the anterior and inferior walls. It also shows the LA appendage. The mitral commissural view (Fig. 4.34) is obtained at 60° to 80° and shows the P_3-A_2 and A_2-P_1 coaptation points. The mid-oesophageal long-axis view (Fig. 4.35) is obtained by rotating the transducer to 135°. It shows the antero-septal and infero-lateral wall segments of the LV.

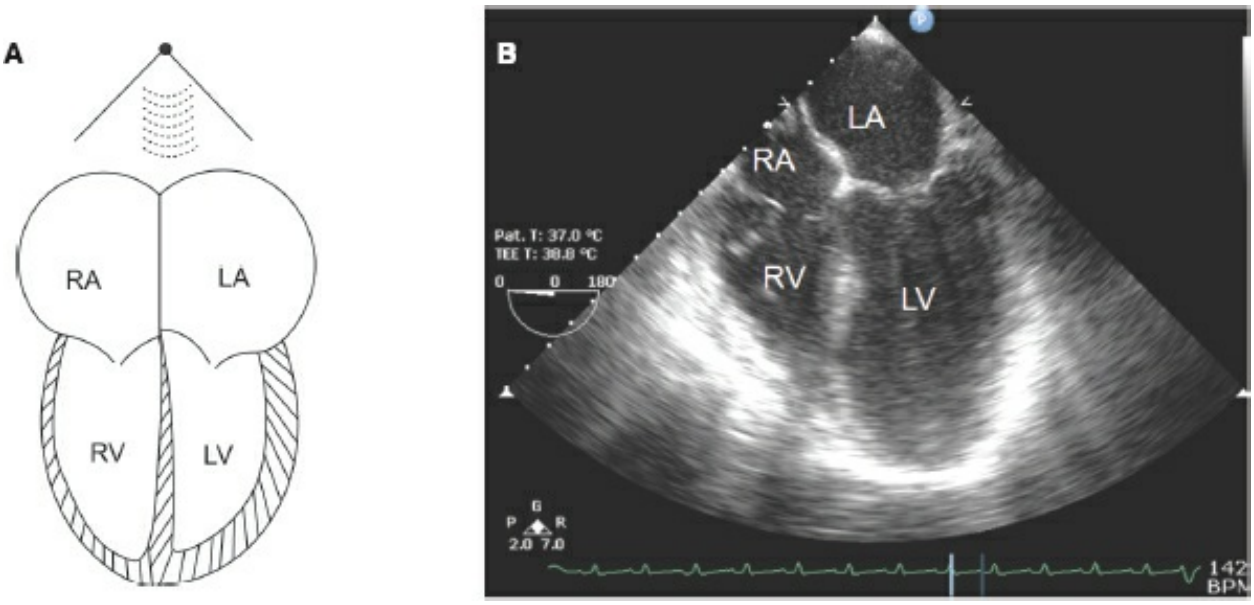


Figure 4.31: Mid-oesophageal four-chamber view (0°). A: Diagrammatic representation. B: This is the standard four-chamber view with both atria and both ventricles. The lateral free walls of both ventricles and the infero-septal portion of the inter-ventricular septum are seen. The mitral valve is close to the transducer and can be examined in detail. (RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle).

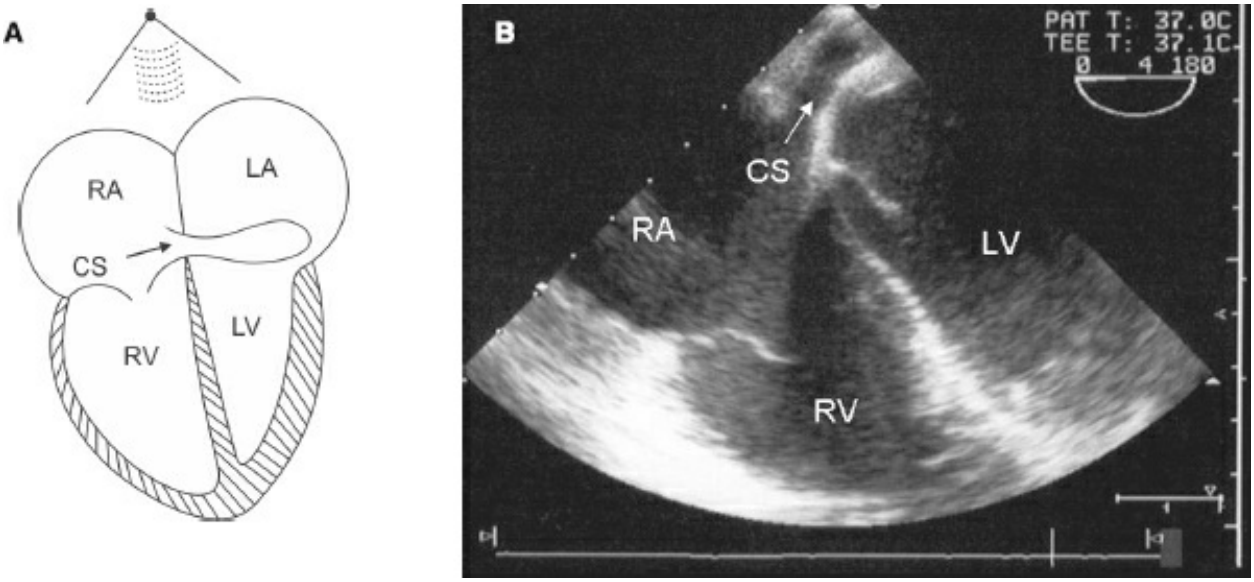


Figure 4.32: Coronary sinus. A: Diagrammatic representation. B: By advancing the probe a little further (1 to 2 cm) after obtaining the four-chamber view, the coronary sinus can be profiled opening into the right atrium (LA: left atrium, RA: right atrium, RV: right ventricle, LV: left ventricle, CS: coronary sinus).

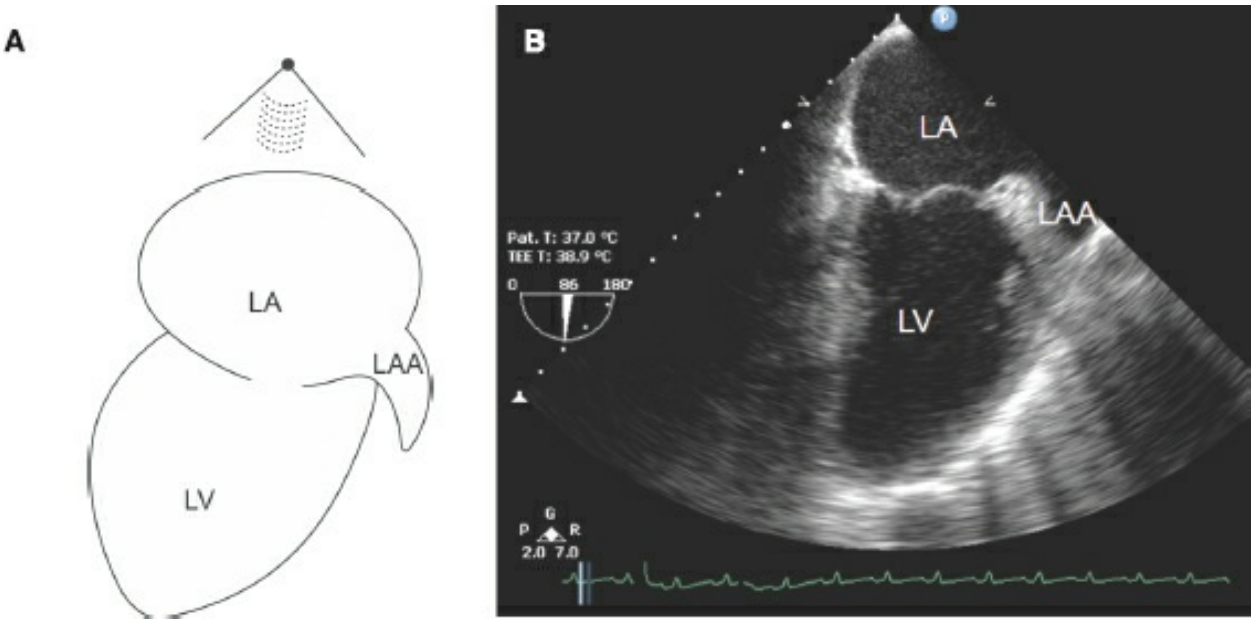


Figure 4.33: Mid-oesophageal two-chamber view. A: Diagrammatic representation. B: By rotating the plane to 90°, the two-chamber view with the left atrium at the top and the left ventricle below is obtained. The view helps to examine the mitral valve and the left ventricular wall motion abnormality of the inferior wall (left of the sector) and anterior wall (right of the sector). The left atrial appendage can also be seen (LA: left atrium, LV: left ventricle, LAA: left atrial appendage).

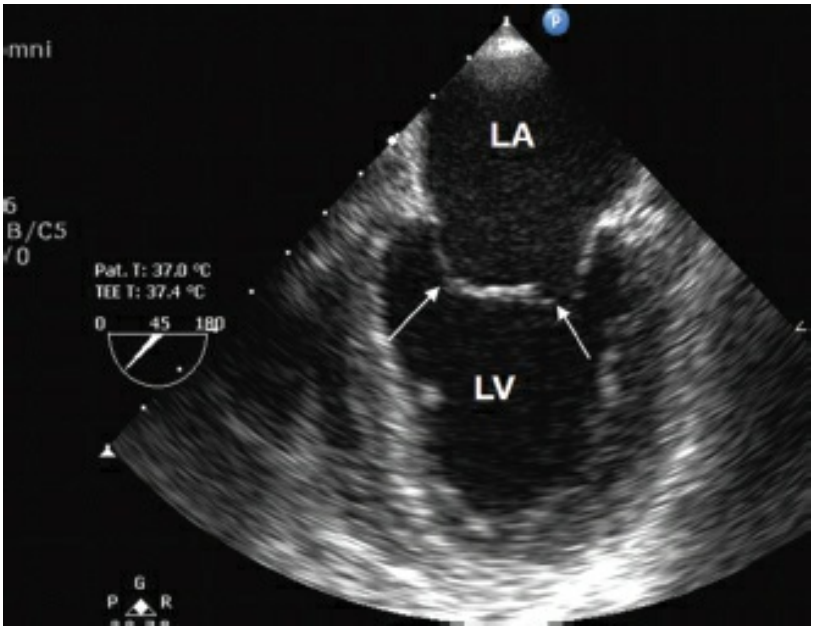


Figure 4.34: Mid-oesophageal mitral commissural view showing 2 coaptation points (arrows). Please refer to the text for details (LA: left atrium, LV: left ventricle).

The mid-oesophageal five-chamber view is obtained by gently withdrawing the probe from the four-chamber view till the appearance of the left ventricular outflow tract (LVOT) and the aortic valve (AV) (Fig. 4.36).

The A_1 segment of the anterior mitral leaflet is to the left and the P_1 scallop of the posterior mitral leaflet is to the right of the imaging sector.

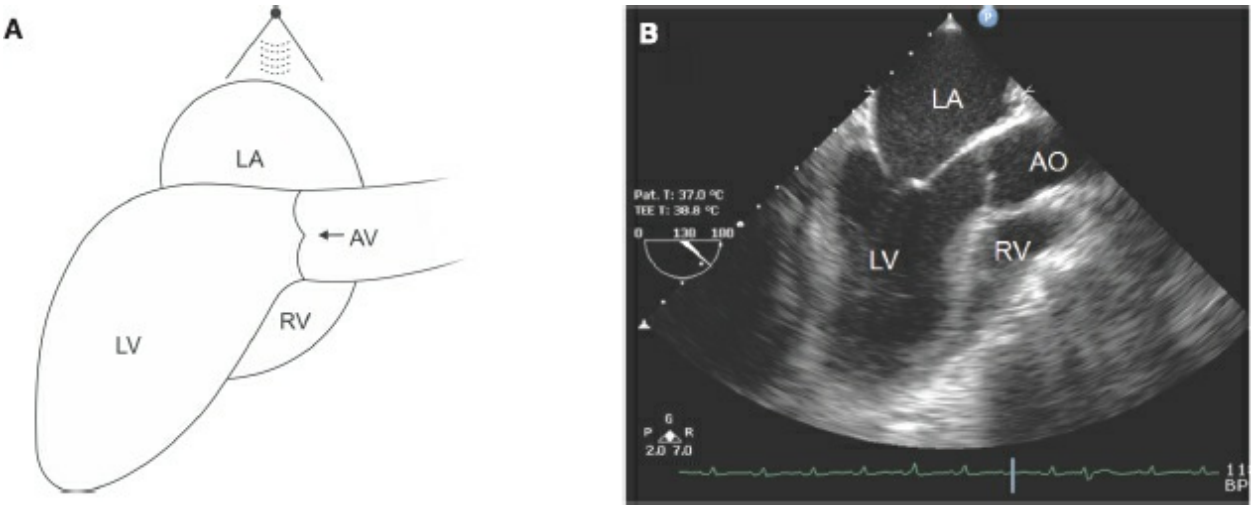


Figure 4.35: Mid-oesophageal long-axis view (130–150°). A: Diagrammatic representation. B: Rotation of the plane to 130–150° shows the long axis view of the left atrium, left ventricular outflow, aortic valve and a part of the ascending aorta (LA: left atrium, LV: left ventricle, RV: right ventricle, AO: aorta, AV: aortic valve).

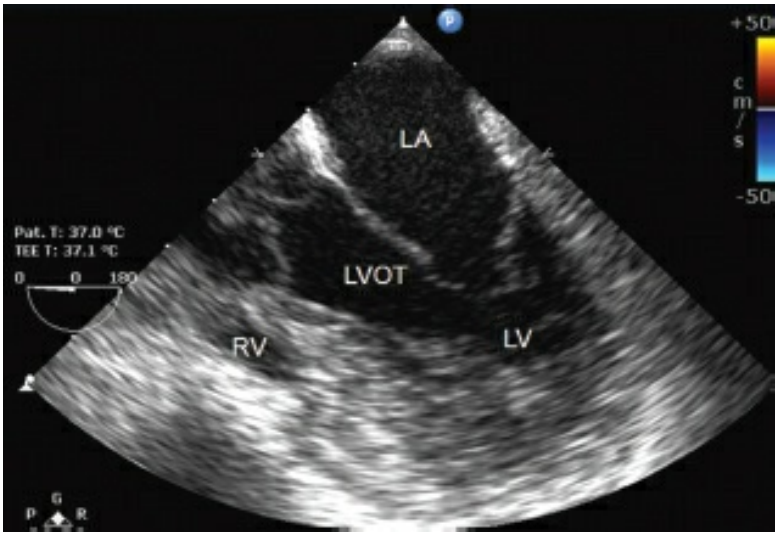


Figure 4.36: The mid-oesophageal five-chamber view showing the left ventricular outflow tract (LVOT). (LA: left atrium, LV: left ventricle, RV: right ventricle).

Next, the mid-oesophageal AV short-axis view (Fig. 4.37) is obtained by withdrawing the probe by 3–5 cm and adjusting the multiplane angle to 20° to 30°. The probe may have to be rotated clockwise in order to display the AV. The image depth is adjusted to 10–12 cm as required to position the AV in the centre of the display screen. By increasing the angle to 60°-80°, the RV inflowoutflow view is obtained (Fig. 4.38). This is an excellent view to

examine the RV outflow as well as the RV free wall contractility. Finally, the mid-oesophageal AV long-axis view (Fig. 4.39) is obtained by rotating the multiplane angle to between 120° and 160°, until the LVOT, AV, and the proximal ascending aorta come into view. The mid-oesophageal bicaval view (Fig. 4.40) is obtained from the mid-oesophageal AV long-axis view by turning the probe clockwise until both SVC and the IVC come into view. This view provides an excellent image of the IAS as well as the body and appendage of the RA and the vena-cavae. It is particularly useful for diagnosing the superior sinus-venous type of atrial septal defect (ASD). By withdrawing the probe upwards, the SVC-RA junction and the cross-section of the right pulmonary artery can be seen. Colour Doppler examination at this point reveals the right upper pulmonary vein draining into the LA (Fig. 4.41).

Trans-gastric views

Next, the multiplane angle is set at zero and the probe is advanced into the stomach to obtain the trans-gastric views. By anteflexing the tip and clockwise rotation of the probe, the transverse section of the LV comes into view. The mid-papillary view shows the two papillary muscles clearly (Fig. 4.42). This cross-section shows the six mid-level segments of the LV and is the most popular view for monitoring the LV function, as it simultaneously shows portions of the LV supplied by the right, the circumflex, and the left anterior descending coronary arteries. The view is also used for assessing the LV chamber size and the wall thickness at end-diastole. Normal LV short-axis diameter is less than 55 mm, and the LV wall thickness is less than 1.2 cm. By withdrawing the probe upwards, the basal trans-gastric view of the LV (showing cross-section of the MV) is obtained (Fig. 4.43). Next, the multiplane angle is rotated to 90° to show the trans-gastric two-chamber view showing LV in long-axis with the apex to the left and mitral annulus to the right of the display (Fig. 4.44). This view shows the basal and mid segments of the inferior and anterior walls, but usually not the apex. The subvalvular apparatus of the MV also can be examined in this view. The trans-gastric long-axis view is obtained by increasing the angle to 120° and withdrawing the probe a little bit (Fig. 4.45). The LVOT and the AV can be seen. This view can be utilized to measure the gradients across the AV, as the Doppler beam can be aligned with the aortic flow.

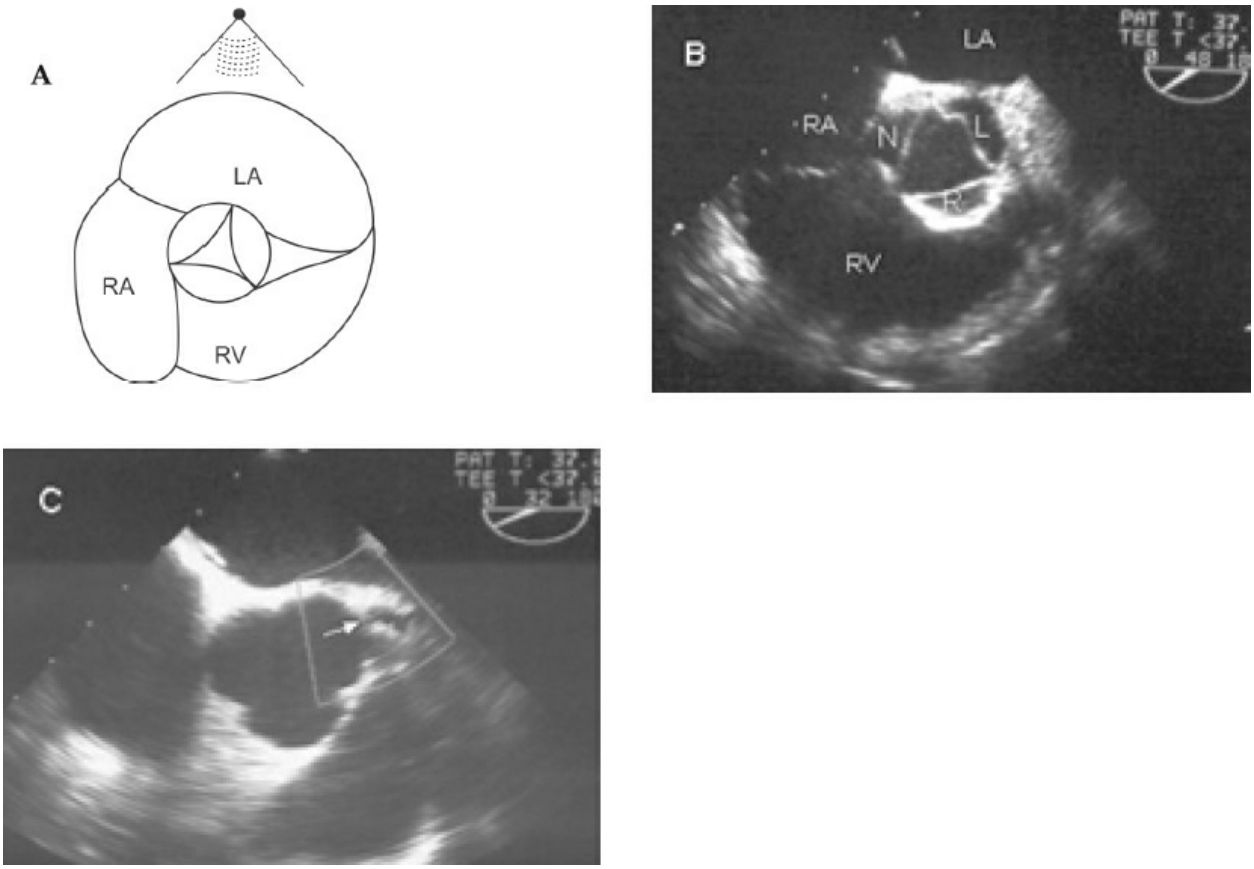


Figure 4.37: Mid-oesophageal aortic valve short axis view: 40–60°. A: Diagrammatic representation. B: This is an important view that images the aortic valve in short axis. The left coronary cusp (L) is on the right side, the right coronary cusp (R) is at the bottom and the non-coronary cusp (N) lies on the left. C: The left main coronary artery can be seen originating at this level (arrow) and can be followed further till its bifurcation (LA: left atrium, RA: right atrium, RV: right ventricle).

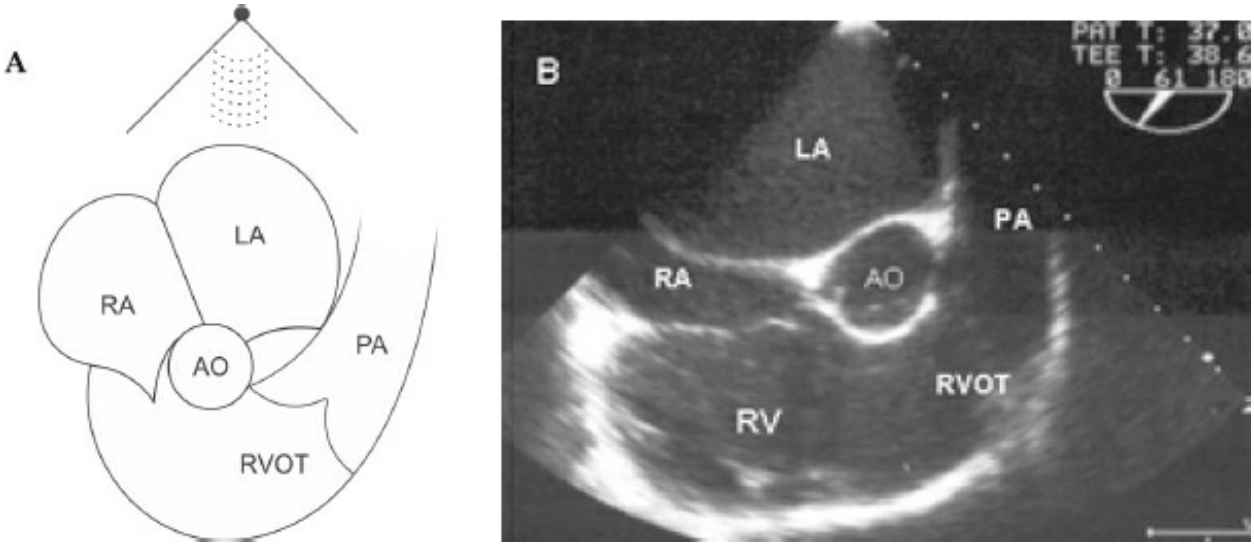


Figure 4.38: Mid-oesophageal right ventricular inflow-outflow view (60–100°). A: Diagrammatic representation. B: The transverse section of the aorta remains in the centre and left atrium lies at the top

of the screen, while from left to right, the right atrium, tricuspid valve, right ventricle, pulmonary valve, and the main pulmonary artery are visualised as they circle around the aorta. The view is useful for the evaluation of the right ventricular outflow tract, especially in the congenital lesions involving the right ventricle and pulmonary artery. (LA: left atrium, RA: right atrium, AO: aorta, RVOT: right ventricular outflow tract, PA: pulmonary artery).

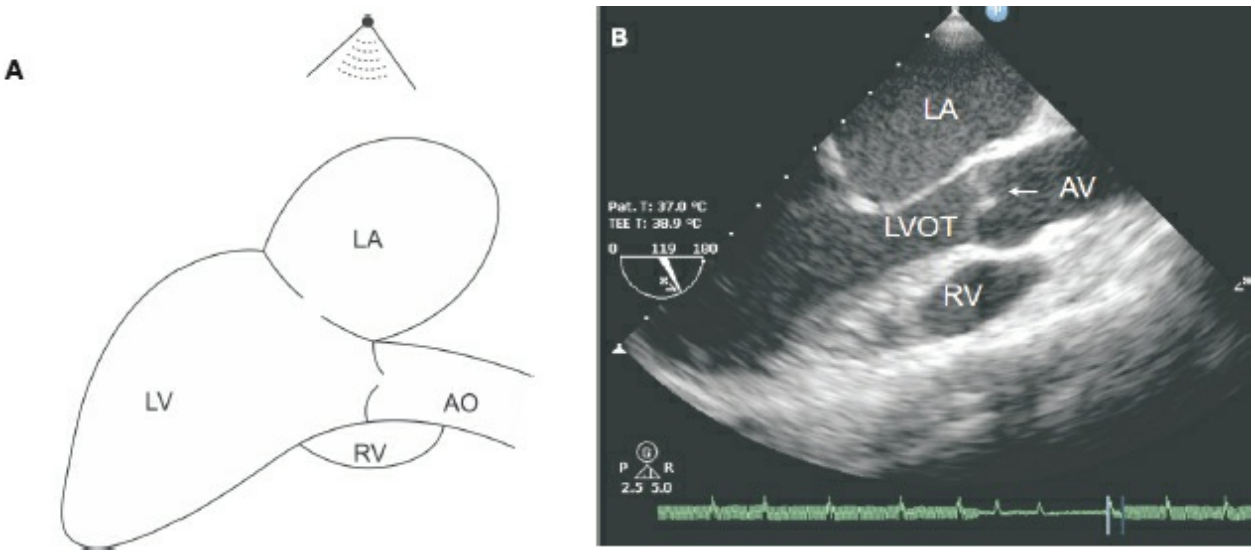


Figure 4.39: Mid-oesophageal aortic valve long-axis view (110–130°). A: Diagrammatic representation. B: The imaging plane beyond 110° displays the distal part of the left ventricular outflow tract, the aortic valve and the ascending aorta in the longitudinal axis. (LA: left atrium, LVOT: left ventricular outflow tract, AV: aortic valve, RV: right ventricle, AO: aorta).

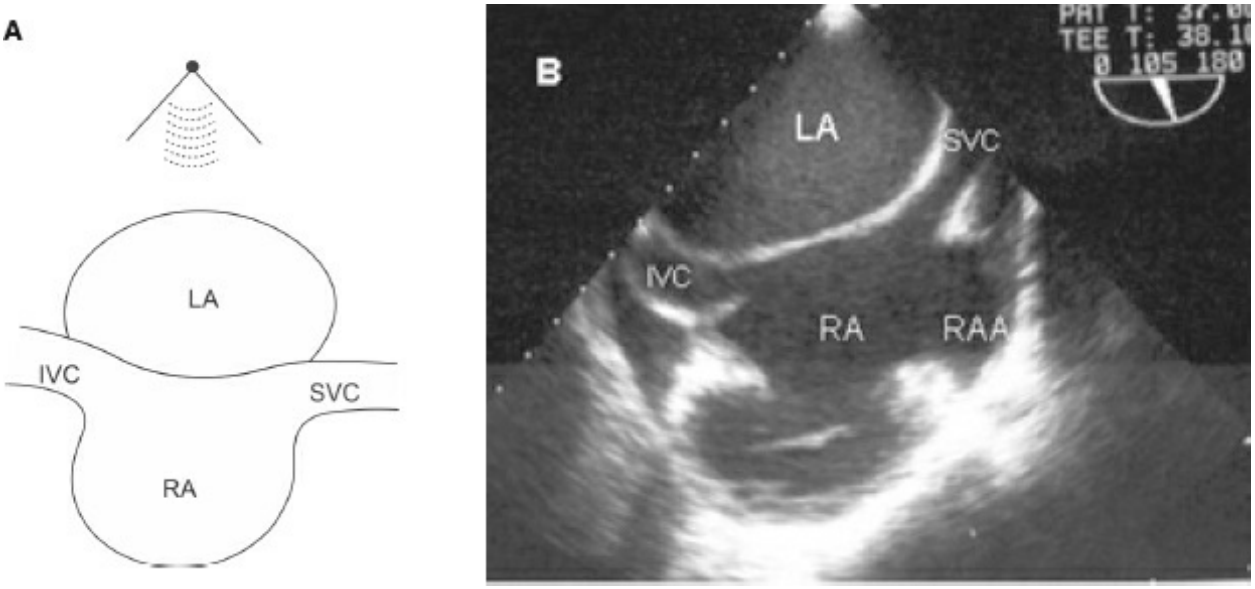


Figure 4.40: Mid-oesophageal bicaval view (120-130°). A: Diagrammatic representation. B: This is an extremely important view for evaluating the anatomy of the inter-atrial septum. Inferior vena-cava is seen on the left, superior vena-cava on the right connected by the inter-atrial septum. Left atrium lies at the top. The TOE probe needs to be rotated clockwise to obtain this view (LA: left atrium, IVC: inferior vena-cava, SVC: superior vena-cava, RA: right atrium, RAA: right atrial appendage).

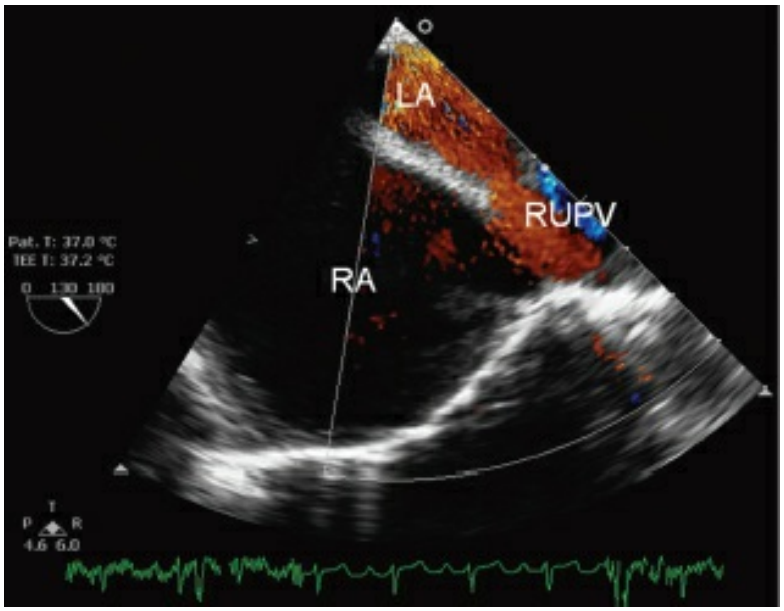


Figure 4.41: Modified bicaval view (colour flow) showing the right upper pulmonary vein (RUPV) opening in the left atrium (LA) (RA: right atrium).

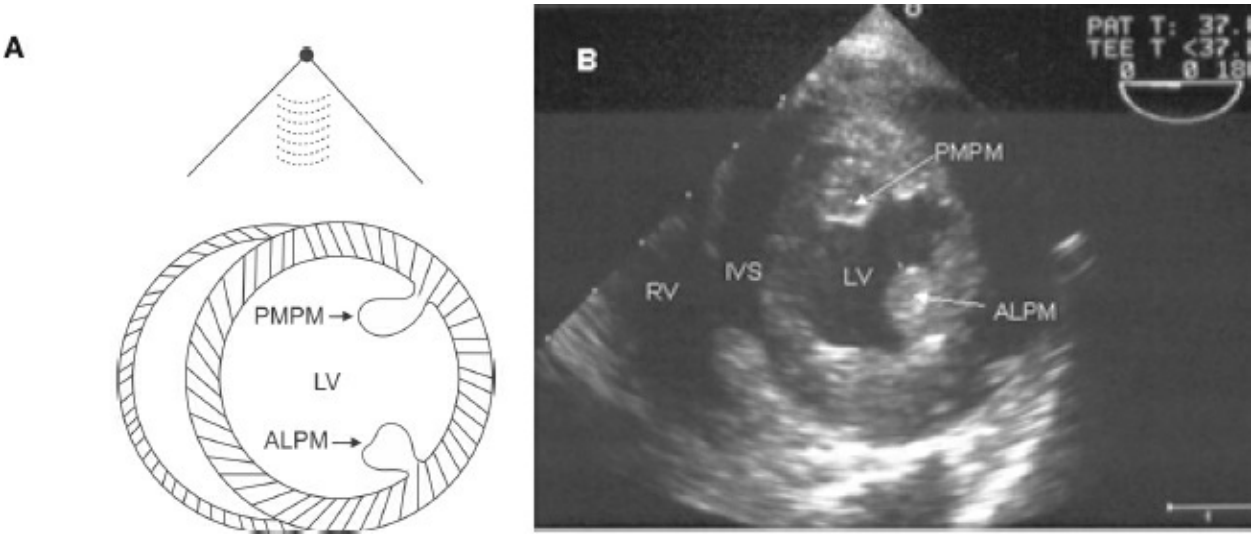


Figure 4.42: Trans-gastric mid-papillary short-axis view. A: Diagrammatic representation. B: The standard short-axis view of the left ventricle at mid-papillary muscle level. The inferior left ventricular wall lies at the top of the section, close to the transducer, and the anterior wall at the bottom. The inter-ventricular septum is located on the left of the image and the lateral wall is seen on the right side. (PMPM: postero-medial papillary muscle, ALPM: antero-lateral papillary muscle, IVS: interventricular septum, LV: left ventricle, RV: right ventricle).

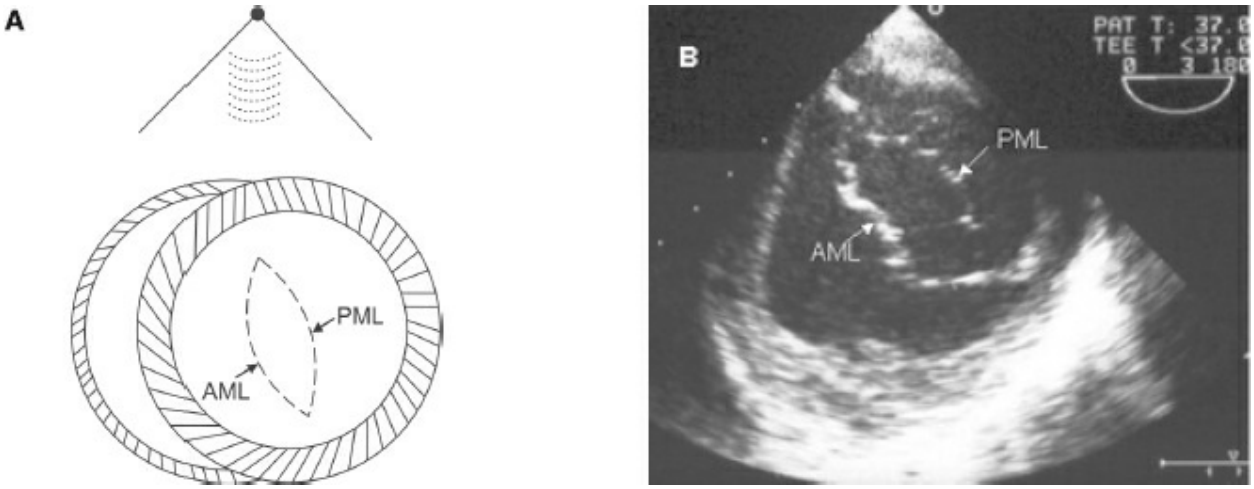


Figure 4.43: Trans-gastric basal short-axis view. A: Diagrammatic representation. B: Actual image. (AML: anterior mitral leaflet, PML: posterior mitral leaflet).

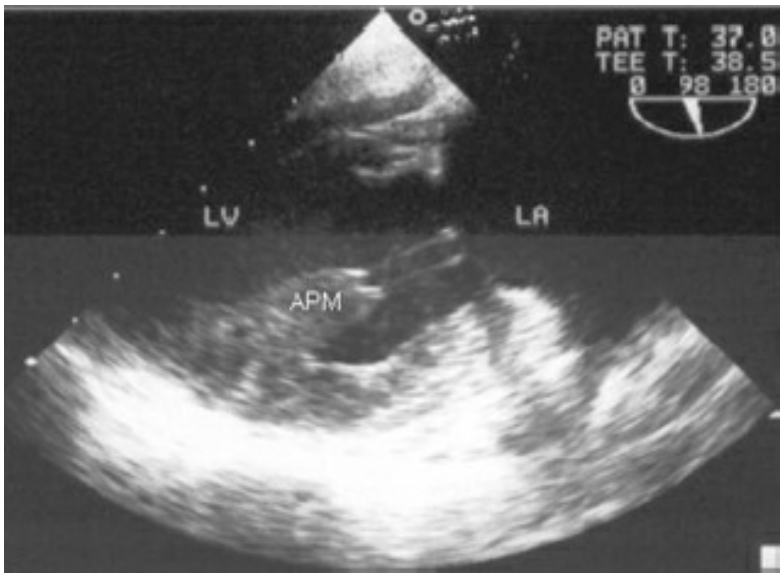


Figure 4.44: Trans-gastric two-chamber view. This view is derived from the mid-papillary short-axis view of the left ventricle by rotating the imaging plane from 0 to 90° and beyond. At 90 degrees, the long-axis view of the left atrium, mitral valve, two papillary muscles and the left ventricle are obtained. The anterior wall of the left ventricle is at the bottom, while the inferior wall is at the top (LA: left atrium, LV: left ventricle, APM: anterior papillary muscle).

The deep transgastric view is obtained by advancing the probe deep into the stomach and positioning it adjacent to the LV apex. The probe is anteflexed to direct the imaging plane superiorly towards the base of the heart. The probe is then withdrawn gradually until the longitudinal section of the heart appears (Fig. 4.46). The image depth should be decreased as required to position the image at the centre of the display screen. The tip of the probe may have to be moved sideways (by the knob on the handle or by

rotating the probe) to centre the image. This is a difficult view to obtain, but with a little practice, it can be obtained in most patients. Since, the LVOT, AV and the ascending aorta can be nicely aligned with the Doppler beam, it is an important view for measuring the AV gradients and the CO.

Aorta

The aorta can be examined almost completely barring the part of the ascending aorta where the trachea is interposed between the oesophagus and the aorta. The AV short-axis view is achieved and the probe is slowly withdrawn 1 to 3 cm while keeping the aorta in the centre of the screen (Fig. 4.47). As the probe is withdrawn, the sections of the ascending aorta are seen until the image is lost due to interposed trachea. The probe is reinserted and the multiplane angle is increased to 100 to 120 degrees to view the ascending aorta in long-axis (Fig. 4.48). These views are useful for the diagnosis of aortic dissection and aortic atheromas. Next, the transducer is returned to zero degree and the probe turned anti-clockwise to reveal the descending thoracic aorta in short-axis (Fig. 4.49A). The probe is advanced while maintaining the aorta at the centre of the screen until the entire descending aorta is examined. The manoeuvre is repeated with the transducer at 90° to examine the descending aorta in longitudinal section (Fig. 4.49B). Next, the transducer is returned to zero degree and the probe withdrawn until the distal aortic arch is reached when the circular aortic image changes to oval (Fig. 4.50). Rotating the transducer to 90° reveals the distal arch in short-axis with the pulmonary artery in long-axis (Fig. 4.51). The probe is turned anti-clockwise until the aorta just disappears from view and then slowly turned clockwise to visualize the take-off of the left subclavian artery. All these aortic views are useful for the diagnosis of aortic dissection and atheromas.

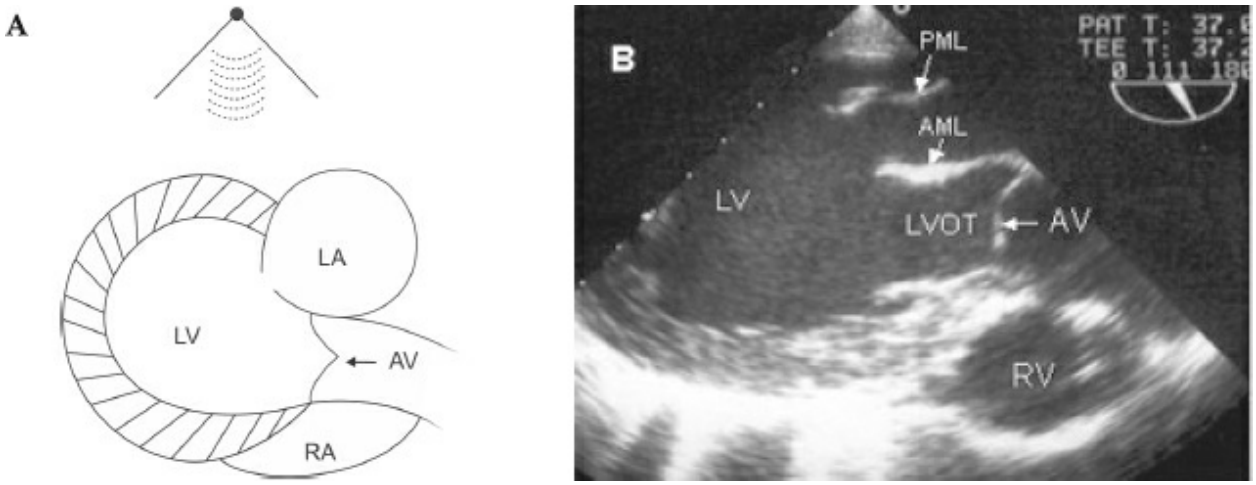


Figure 4.45: Trans-gastric long-axis view. A: Diagrammatic representation. B: At 110 to 120 degrees, the left ventricular outflow tract is seen to open into the aorta in its longitudinal course. This view can be used to evaluate the subvalvular apparatus of the mitral valve and the anterior and inferior wall of the left ventricle (LA: left atrium, LV: left ventricle, AML: anterior mitral leaflet, PML: posterior mitral leaflet, LVOT: left ventricular outflow tract, AV: aortic valve, RV: right ventricle).

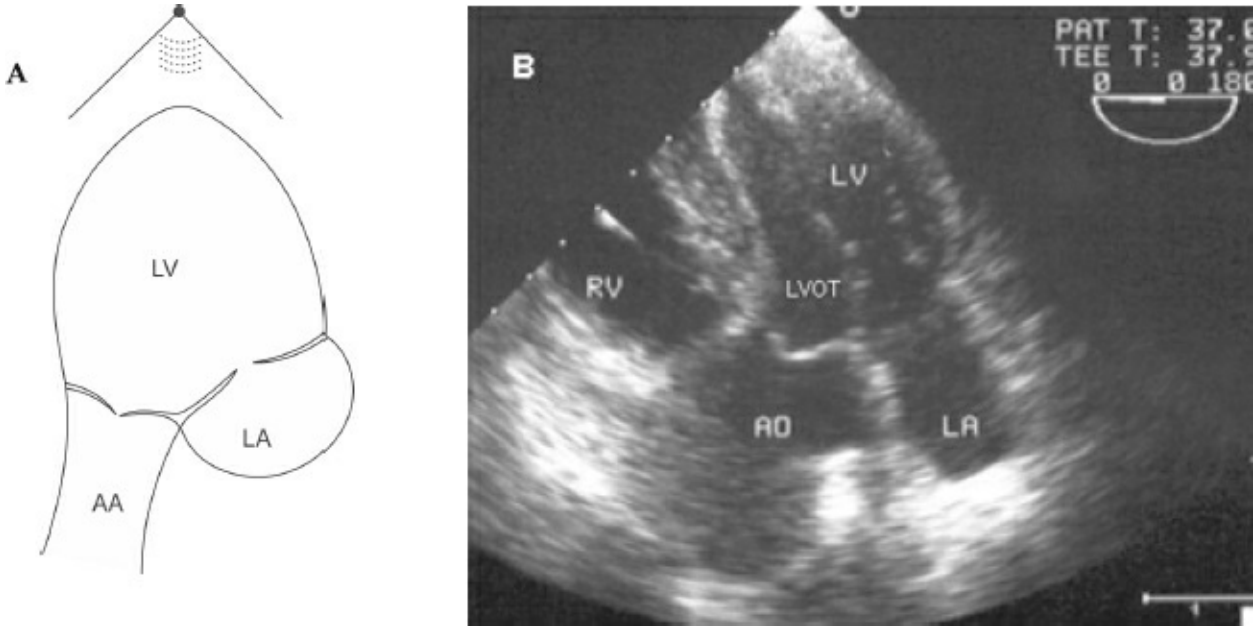


Figure 4.46: Deep trans-gastric view. A: Diagrammatic representation. B: With the imaging plane at 0°, a three chamber view with the left ventricular outflow tract, aortic valve and a proximal portion of the ascending aorta in the centre (left of the left atrium) is obtained. As this view allows an excellent alignment of the ultrasound beam and the blood flow out of the left ventricle, it remains the best view for Doppler measurement of cardiac output and the Doppler quantification of aortic stenosis (LV: left ventricle, LVOT: left ventricular outflow tract, AO: aorta, LA: left atrium, RV: right ventricle).

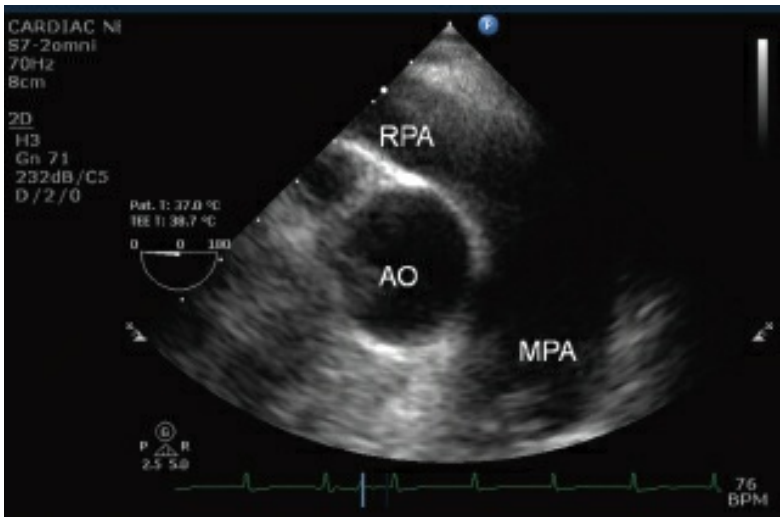


Figure 4.47: Mid-oesophageal ascending aortic short-axis view (AO: aorta MPA: main pulmonary artery, RPA: right pulmonary artery).

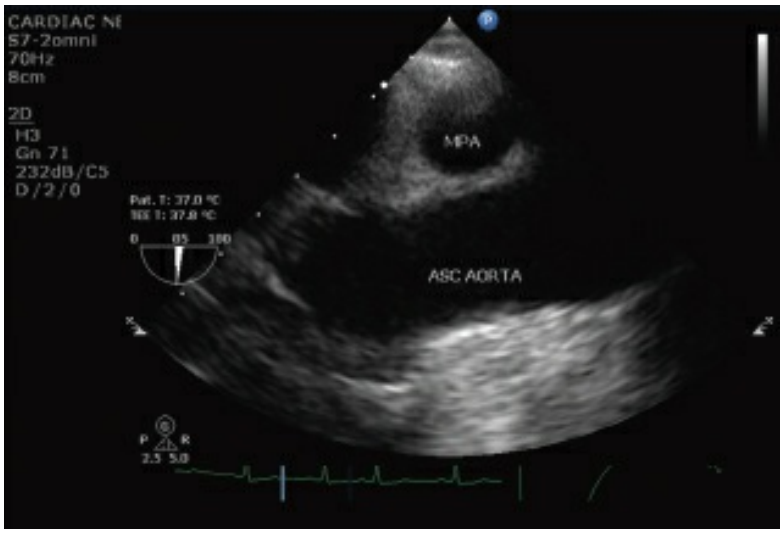
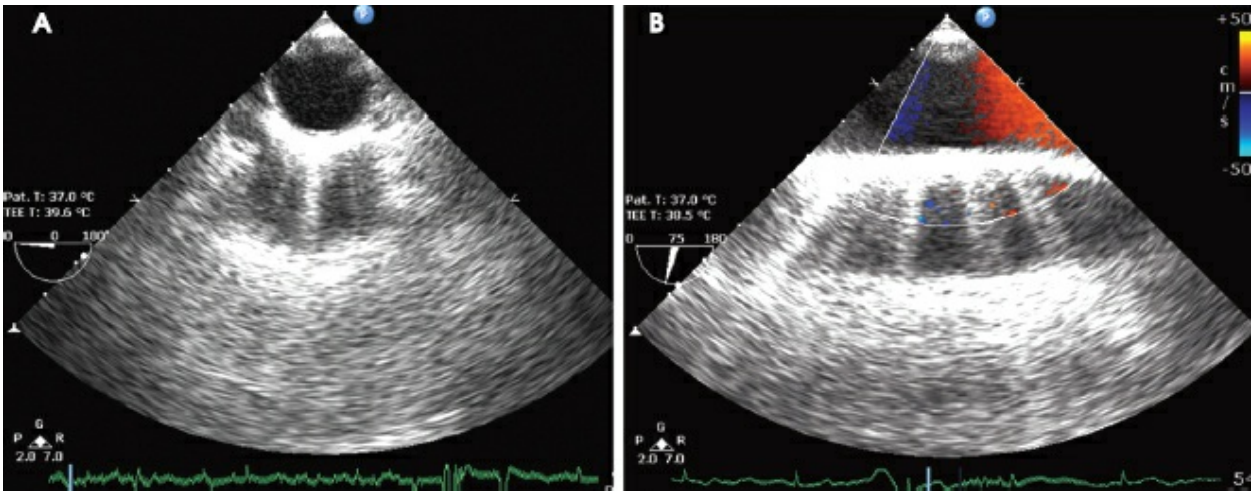


Figure 4.48: Mid-oesophageal ascending aortic long-axis view (MPA: main pulmonary artery).



Figures 4.49: Descending aortic short-axis view (A) and long-axis view with colour flow (B).

Pulmonary veins

The left upper pulmonary vein (LUPV) is the easiest pulmonary vein to image. From the AV short-axis view at 20 to 30 degrees, the probe is turned counter-clockwise and pulled up slightly, the LUPV lies above the LA appendage. (Fig. 4.52) The left lower pulmonary vein (LLPV) is the most difficult pulmonary vein to image. One technique is to image the LUPV, keeping it in view, the transducer angle is increased to 90°, the left-sided veins can be visualized as an inverted 'V' (Fig. 4.53). The right pulmonary veins can be visualized by turning the probe clockwise from the AV short-axis view at 20° to 30°. The right lower pulmonary vein (RLPV) is imaged above and perpendicular to the LA and the right upper pulmonary vein (RUPV) is imaged below to the RLPV (Fig. 4.54). The RUPV can also be visualized in the bicaval view at 120° by withdrawing the probe to see the SVC-RA junction. The application of colour Doppler shows the RUPV blood flow draining into the LA (Fig. 4.41).

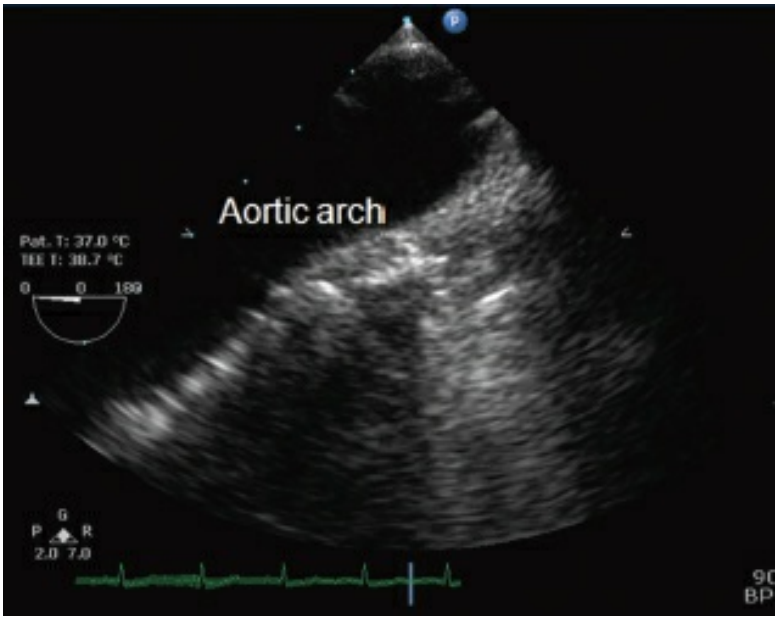


Figure 4.50: Upper-oesophageal aortic arch long-axis view at zero degree.

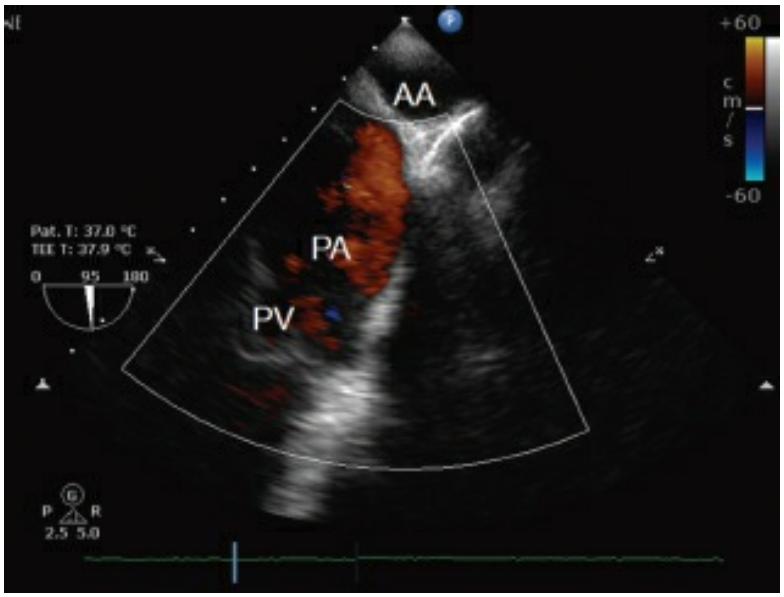


Figure 4.51: Upper-oesophageal aortic arch short-axis view with colour flow at 95 degrees: It shows the transverse section of the aortic arch and longitudinal section of the pulmonary artery (AA: aortic arch, PA: pulmonary artery, PV: pulmonary valve).

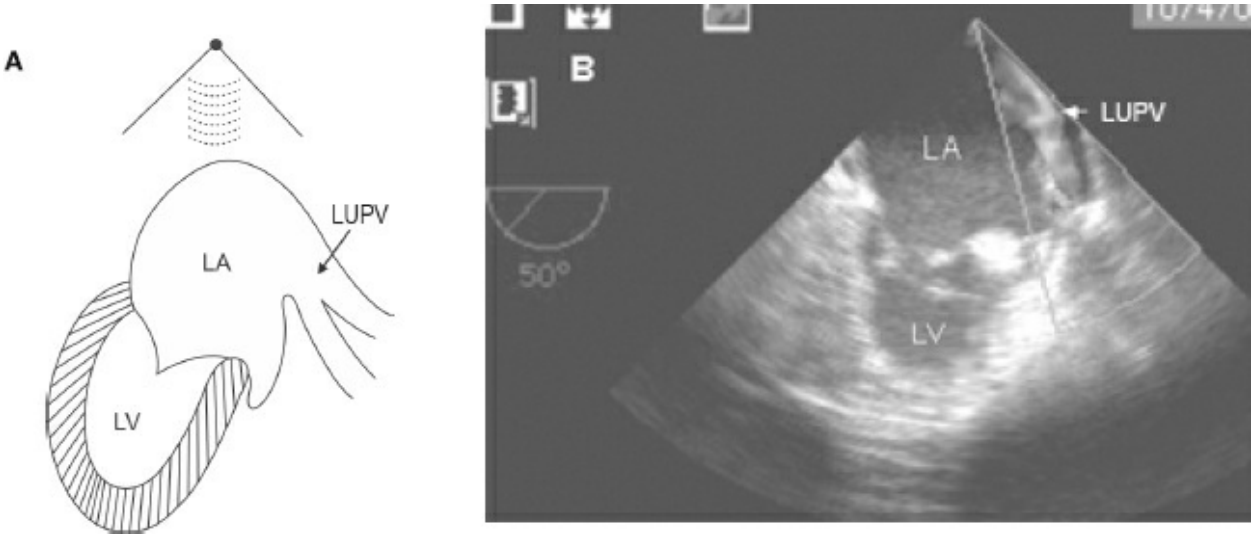


Figure 4.52: Left pulmonary vein view (20 to 40°). A: Diagrammatic representation. B: At 0-30° imaging plane, the left pulmonary vein can be visualised above the left atrial appendage. The left upper pulmonary vein has a more vertical and the lower one has a more horizontal course. This view can be used for Doppler interrogation of the pulmonary veins (LA: left atrium, LV: left ventricle, LUPV: left-upper pulmonary vein).

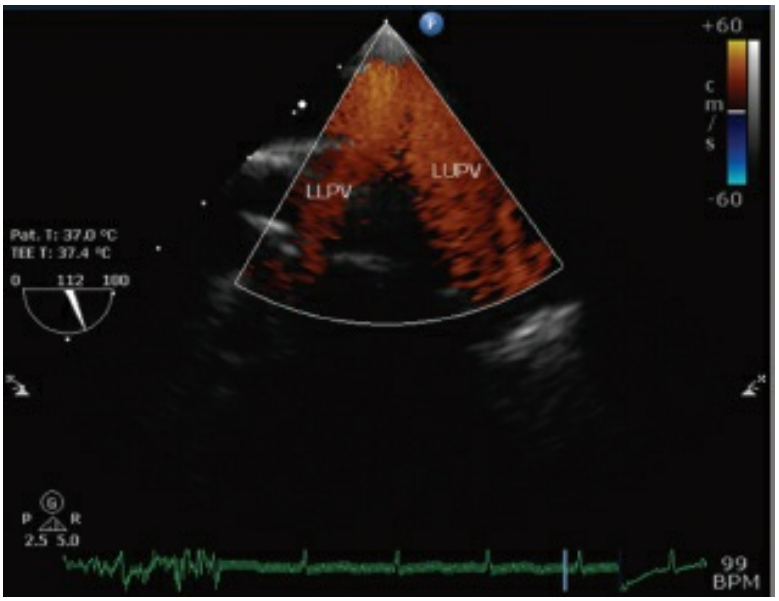


Figure 4.53: Colour flow mapping showing the left upper pulmonary vein (LUPV) and left lower pulmonary vein (LLPV) at 112° appearing as an inverted 'V'

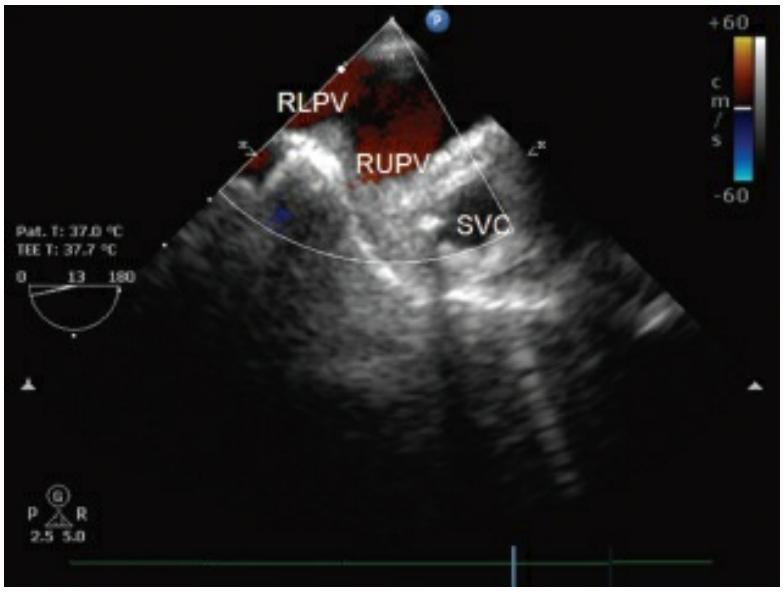


Figure 4.54: Upper oesophageal view with colour flow at 11° showing the right upper pulmonary vein (RUPV) and right lower pulmonary vein (RLPV). (SVC: superior vena-cava)

Clinical Applications

The TOE has become an important diagnostic as well as monitoring tool inside the cardiac operation theatre (OT) over a period of time. As proper imaging is essential to draw clearcut conclusions, the operator must be experienced in the technique. The cardiac anaesthesiologists are gradually taking over this job (after obtaining adequate training).[85]

TOE Evaluation of the Heart

A comprehensive TOE examination during cardiac surgery is an accepted practice nowadays and an increasing number of cardiac centres follow it. In general, the following can be evaluated.

- Evaluation of the ventricular function
- Evaluation of the valvular anatomy and function
- Evaluation of the aorta
- De-airing and separation from the CPB
- *Other uses:* Evaluation of congenital heart defects, prosthetic valves for valvular malfunction and/or vegetations, intracardiac masses, pericardial thickening, effusion, or tamponade.

A detailed description of each of these is beyond the scope of this book and the reader is referred to the standard books on the subject. A brief overview of the subject in presented.

Evaluation of the ventricular function

Regional wall motion abnormalities

The 17 segment LV model was created by the American Heart Association in the year 2002 that is used to describe the LV regional wall motion.[86] This model divides the LV into three levels from the base to the apex: basal (six segments), mid (six segments), and apical (4 segments). The 17th segment in the true apical segment devoid of cavity (Fig. 4.55). The trans-gastric basal and mid-papillary views are commonly employed to examine these segments. The individual myocardial segments are observed for systolic thickening and for endomyocardial movement. Areas, which do not thicken in systole or which do not move towards the centre of the ventricle in systole are described as regional wall motion abnormalities (RWMA). The recommended qualitative grading scale for wall motion is : 1 = normal (> 30 percent thickening), 2 = mildly hypokinetic (10 to 30 percent thickening), 3 : severely hypokinetic (< 10 percent thickening), 4 = akinetic (does not thicken), 5 : dyskinetic (moves paradoxically during systole).[84]TOE can detect LV RWMA before other modalities such as ECG[87] with the potential to resolve such problems in the OT itself. The RWMAs have been shown to take place within seconds of insufficient blood flow or oxygen supply.[88] Immediate

improvement of regional myocardial function of a previously dysfunctional segment has been demonstrated after CABG.[89,90] In addition, prebypass compensatory hypercontracting segments have been reported to revert towards normal immediately following successful CABG.[91] Persistence of RWMAs following CABG is related to adverse clinical outcome and absence of RWMAs following CABG has been shown to be associated with postoperative course without cardiac morbidity.[92]

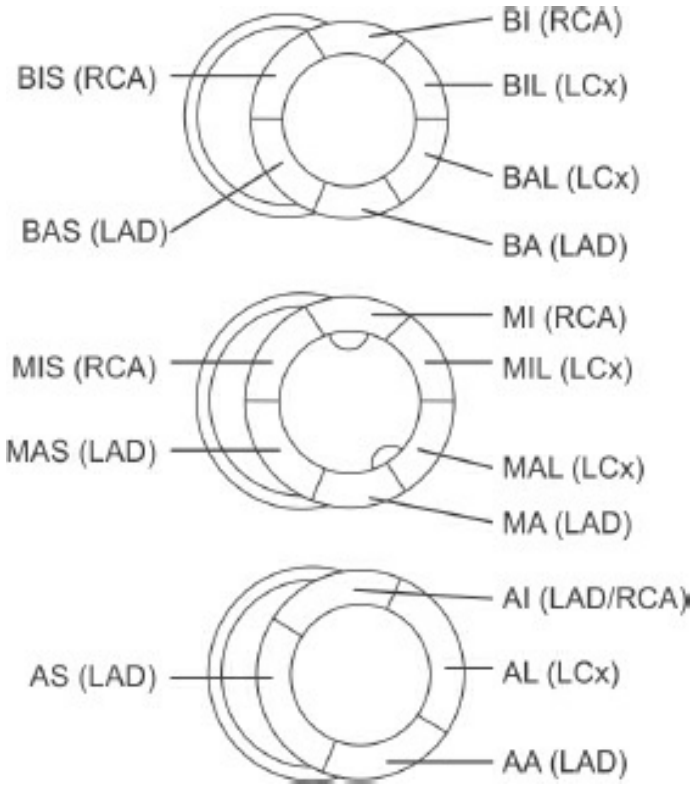


Figure 4.55: Diagrammatic representation of the left ventricular segments with blood supply (Bl: basal inferior, BIL: basal infero-lateral, BAL: basal antero-lateral, BA: basal anterior, BAS: basal antero-septal, BIS: basal infero-septal. Ml: mid-inferior, MIL: mid infero-lateral, MAL: mid anterolateral, MA: mid anterior, MAS: mid antero-septal, MIS: mid infero-septal, Al: apical inferior, AL: apical lateral, AA: apical anterior, AS: apical septal, LAD: left anterior descending artery, LCx: left circumflex artery, RCA: right coronary artery)

Systolic Function

Quantitative assessment of the LV systolic function can be made by measuring different systolic indices. The most commonly used parameter of systolic function is ejection fraction (EF), which is calculated using the formula: EF = EDV - ESV/EDV, where EDV is end-diastolic volume, and ESV is end-systolic volume. The mid-oesophageal 4-chamber and 2-chamber views are utilised for the volume measurements. An echocardiographer may

become efficient in visually estimating the EF, however, accuracy depends upon the individual's skill and inter-observer measurements may vary considerably. The ASE recommends that even experienced echocardiographers should regularly cross check quantitative evaluations against calibrated measurements.[93] Fractional shortening (FS) is calculated using the formula, FS = LV end-diastolic diameter - LV end-systolic diameter/LV end-diastolic diameter. The transgastric view (2-D or M-mode) is used for the measurements. FS only assesses mid or basal segments and is a poor reflection of the overall LV function. The fractional area change (FAC) in calculated from the formula: LVEDA-LVESA/LVEDA, where LVEDA is left ventricular end-diastolic area, and LVESA is left ventricular end-systolic area. The area is measured in the trans-gastric mid-papillary short-axis view using eye ball technique for largest end-diastolic and smallest end-systolic size. Normal global function with no RWMA is assumed. Some other quantitative measurements of the LV systolic function are, LV wall thickness, LV mass, and rate of ventricular pressure rise (dP/dT).

Diastolic Function

The diastolic function of the LV is determined by the PWD recording of the trans-mitral diastolic flow velocity and the pulmonary venous flow velocity. In addition, the isovolumetric relaxation time is also used. The trans-mitral diastolic flow velocity is obtained by placing the sample volume at the tip of the mitral valve leaflet. A typical velocity pattern is biphasic, an initial peak flow velocity (E wave) occurs during early diastolic filling and a later peak flow velocity (A wave) occurs during the atrial systole. The interposed period of diastasis usually has rninirnal or no flow (Fig. 4.56). The pulmonary venous flow velocity is obtained by placing the sample volume within one cm of the opening of the pulmonary vein into the LA (Fig. 4.57). The diastolic dysfunction progresses from impaired relaxation to restrictive pathophysiology. During this transition, the transmitral flow profile may assume a pseudonormal pattern with normal E/A ratio. This can be differentiated from the normal by pulmonary venous flow velocity that shows obtunded systolic wave. Table 4.3 shows the phases of diastolic dysfunction as determined by the echocardiography.

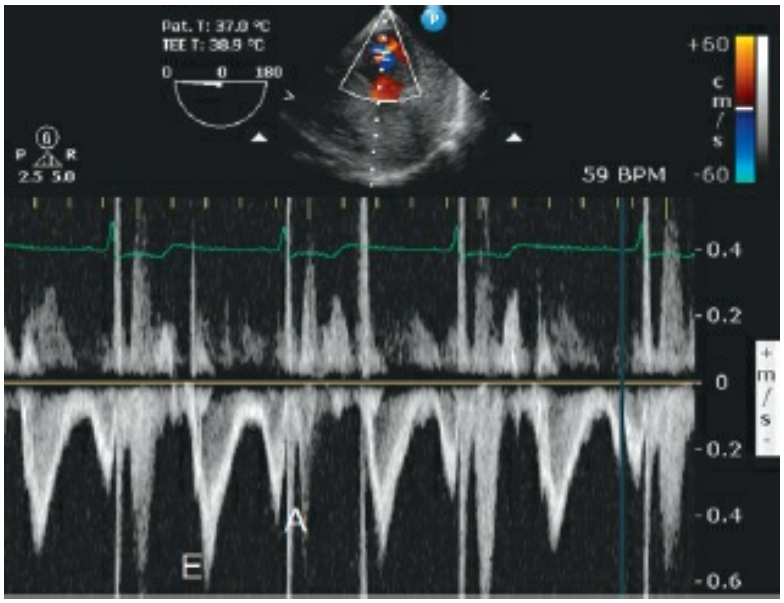


Figure 4.56: Trans-mitral flow on pulsed wave Doppler in a patient with normal left ventricular function. Note the early diastolic filling (E) and late diastolic filling (A) waves, with a normal E/A ratio (> 1)

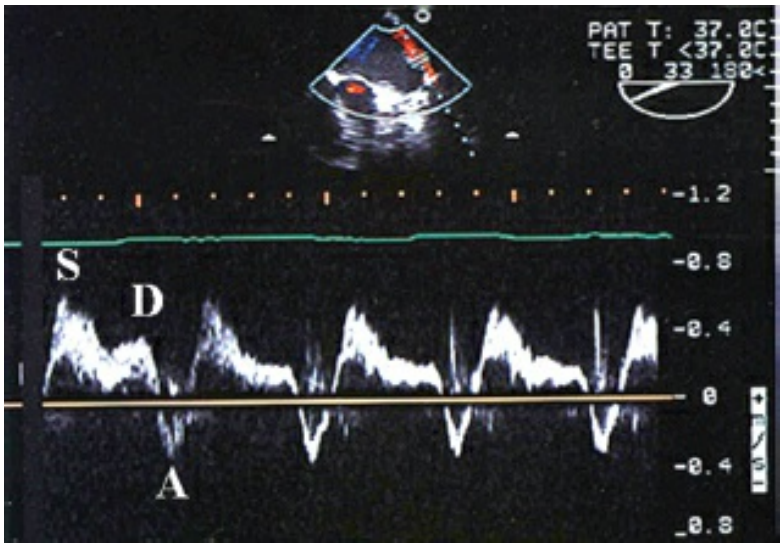


Figure 4.57: Pulsed wave Doppler from left upper pulmonary vein. Note the normal waveform (antegrade systolic S, diastolic D, and retrograde A waves).

Evaluation of ventricular filling and cardiac output

TOE reveals changes in LV preload very reliably. The trans-gastric mid-papillary view can be used to measure the end-diastolic area (EDA), an area of < 12 cm^2 indicates hypovolemia. Such quantitative measurement of LV volume is well validated,[94] but it is tedious to perform intraoperatively. Clinicians, therefore, assess the LV filling by 'eyeballing' the image. TOE

can precisely measure the CO by measuring both velocity and cross-sectional area of the blood flow at the LVOT or aorta. The product of these measurements gives the stroke volume. It has been shown to have a good agreement with the thermodilution method. A deep trans-gastric view is used for the measurements that are performed by the built-in software of the TOE machine.

Evaluation of valvular anatomy and function

TOE has profoundly influenced valvular heart surgery by providing intraoperative evaluation of the native valves as well as replaced or repaired valves so that revisions if any, can be performed immediately. This has been especially so in patients undergoing mitral valve repair.[95] TOE can identify the mechanism of failure as well as complication such as systolic anterior motion (SAM) and guide therapy.[96] During valve replacement surgery, TOE is useful in detecting the paravalular leaks, immobilized leaflets and any other abnormality.[97]

The mitral valve can be evaluated easily with TOE on mid-oesophageal four-chamber, two-chamber, commissural, long-axis or basal trans-gastric short-axis views. In mitral stenosis, the 2-D imaging reveals thickened and doming leaflets with poor opening. Colour Doppler reveals flow acceleration into the stenotic orifice (Fig. 4.58). PWD and CWD show characteristic flow pattern (Fig. 4.59). The software for performing the calculation of the mitral valve area by pressure half-time is built in the machine. In addition, LA enlargement and spontaneous echo contrast in the LA can be seen (Fig. 4.60). Thrombus in the LA and LA appendage should be carefully evaluated in all patients with mitral stenosis.

Table 4.3: Phases of diastolic dysfunction as determined by the echocardiography

Parameter	*Normal*	*Impaired relaxation*	*Pseudo normal filling*	*Restrictive filling*
E wave DT (ms)	160–240	> 240	160–200	< 160
IVRT (ms)	70–90	> 90	< 90	< 70
E : A	1–2	< 1	1–1.5	> 1.5
Am : Ap duration	Am ≥ AP	Am > Ap	Am < Ap	Am << Ap
$PV_S : PV_D$	$PV_S > PV_D$	$PV_S > PV_D$	$PV_S < PV_D$	$PV_S << PV_D$

DT: deceleration time, ms: milli second, IVRT; isovolumetric relaxation time, Am : Ap ratio : ratio of mitral (Am) and pulmonary venous inflow (Ap) "A" wave duration, PV_S: Pulmonary venous systolic flow, PV_D: Pulmonary venous diastolic flow.

The presence and degree of MR are evaluated in the same views as

described for the evaluation of mitral stenosis. Typically, the reguigitant jet width at the origin (vena-contracta), jet area and the jet depth into the LA are evaluated. Severe regurgitation is diagnosed on the basis of wide vena-contracta (more than 6 mm), jet area more than 8 cm^2 and extending deep into the LA into the pulmonary veins (Fig. 4.61). Eccentrically directed jet should be generally considered severe necessitating closer evaluation before labeling otherwise. Systolic reversal of pulmonary venous flow can be present in severe MR (Fig. 4.62).

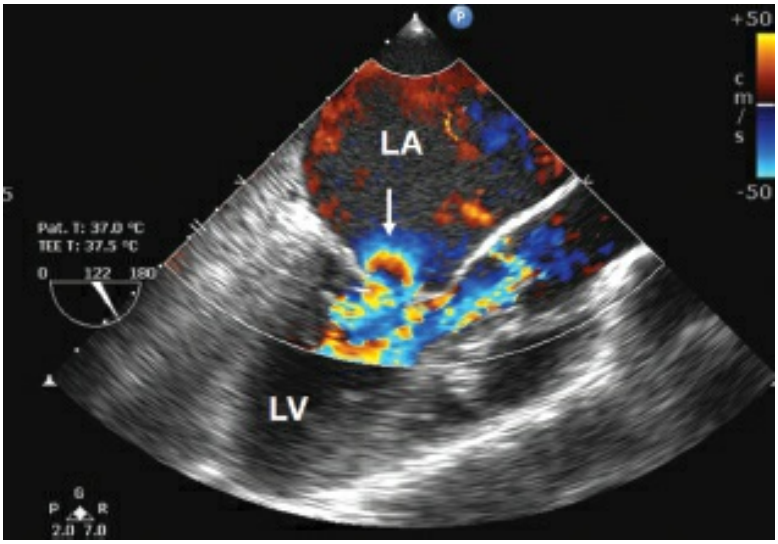


Figure 4.58: Mid-oesophageal view at 120° in a patient with mitral stenosis showing turbulent diastolic flow with flow acceleration across the mitral valve (arrow). (LA: left atrium, LV: left ventricle).

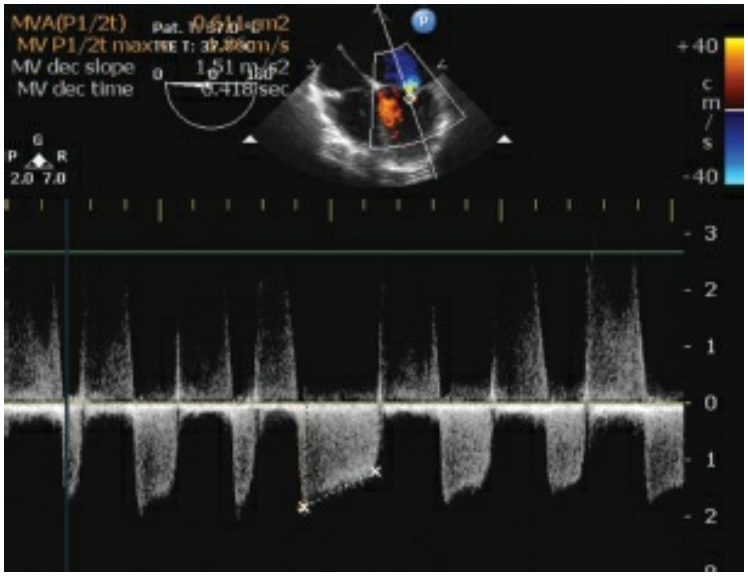


Figure 4.59: Continuous wave Doppler across the stenosed mitral valve showng increased velocity and the decceleration time. The pressure half-time method to calculate the mitral valve area can be used with this trace.

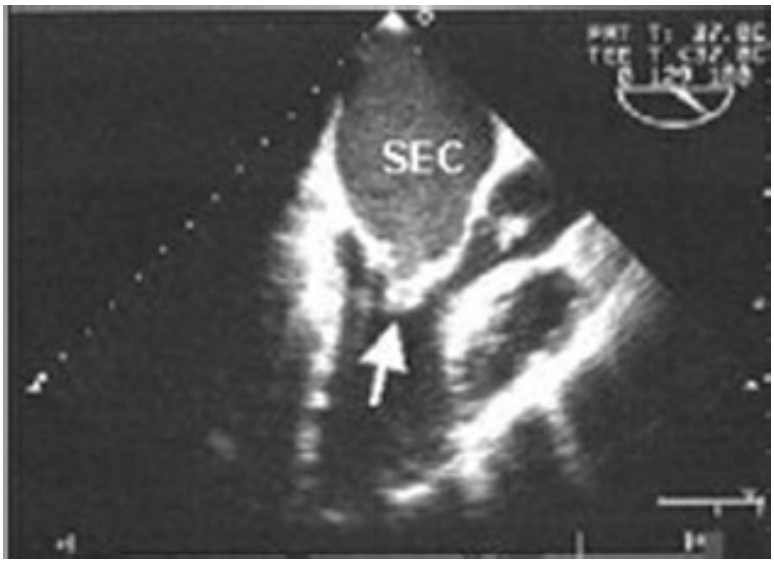


Figure 4.60: A patient with severe mitral stenosis. Note the doming of the mitral leaflets (arrow) and the dense left atrial spontaneous echo contrast (SEC).

Mild regurgitation is characterized by a narrow vena-contracta (< 3 mm), jet area of < 4 cm^2 and occupying < 20 percent of LA cross-sectional area. Moderate regurgitation has a vena-contracta of 4 to 6 cm, jet area of 4 to 8 cm^2, and occupying 20 to 40 percent of LA cross-sectional area.

There are several other criteria described for evaluating the MR. Amongst these, the quantitative measures such as the reguigitant orifice area based on proximal isovelocity surface area are less frequently used in the OT because of time constraints.

The degree of aortic stenosis can be evaluated easily in mid-oesophageal AV short-axis view where the extent of leaflet opening can be estimated visually or the orifice area can be measured by planimetry. Marked leaflet thickening and calcification leading to severely restricted valve opening (< 1 cm^2) is present in severe stenosis (Fig. 4.63). The gradient across the valve can be reliably measured by CWD in deep trans-gastric view (Fig. 4.64). A peak gradient of > 60 mm Hg signifies severe stenosis. Other valuable information that can be obtained includes dimensions of the annulus, sinotubular junction and ascending aorta (mid-oesophageal AV long-axis view). The same view is useful for evaluating the aortic regurgitation. The regurgitation jet can be visualized in the LVOT during diastole. The vena contracta (> 6 mm) and the ratio of jet width to the LVOT diameter (70 percent) are utilized for estimating the severity of regurgitation (Fig. 4.65).

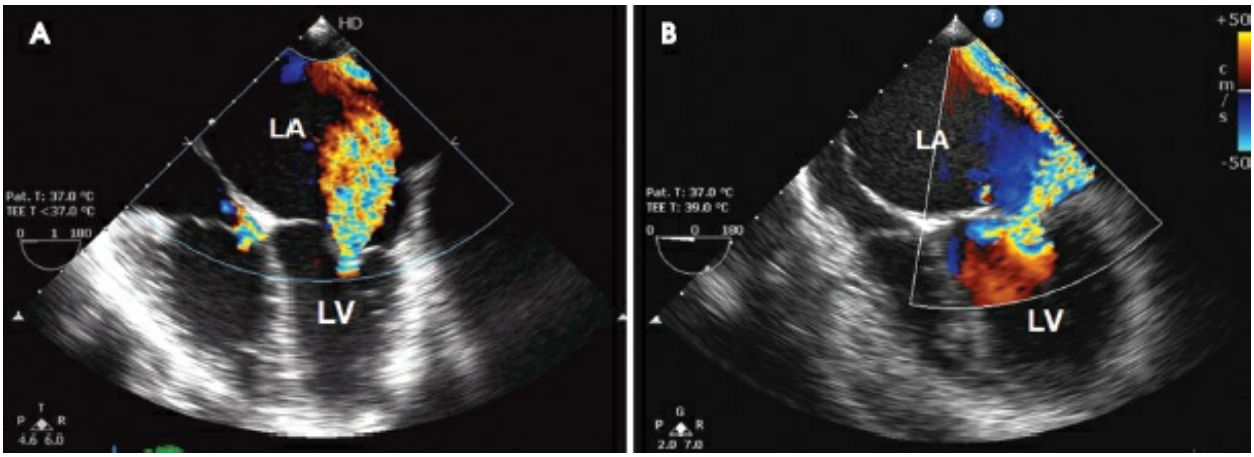


Figure 4.61: Mid-oesophageal 4-chamber view showing severe mitral regurgitation, central jet (A) and eccentric jet (B) Note the vena contracta at the level of the mitral valve and the flow convergence (B) (LA: left atrium, LV: left ventricle).

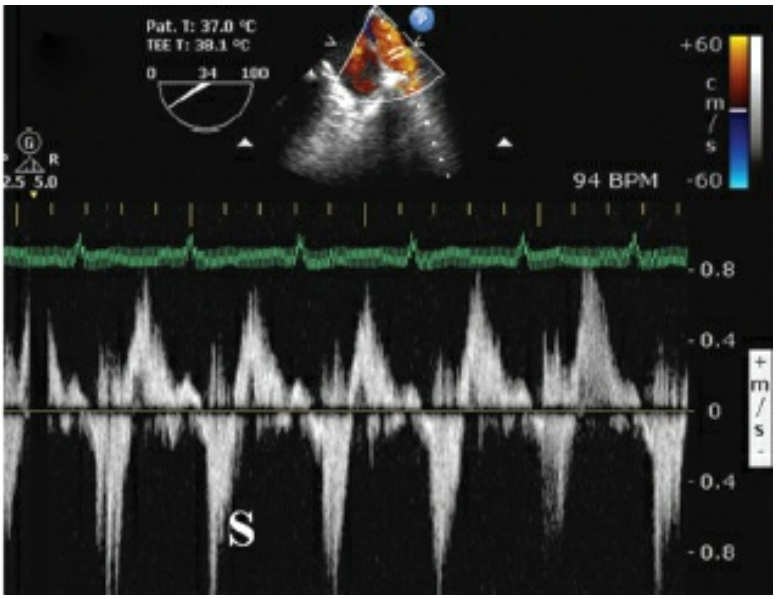


Figure 4.62: Pulsed wave Doppler from left pulmonary vein in a patient with severe mitral regurgitation. Note the systolic reversal (S).

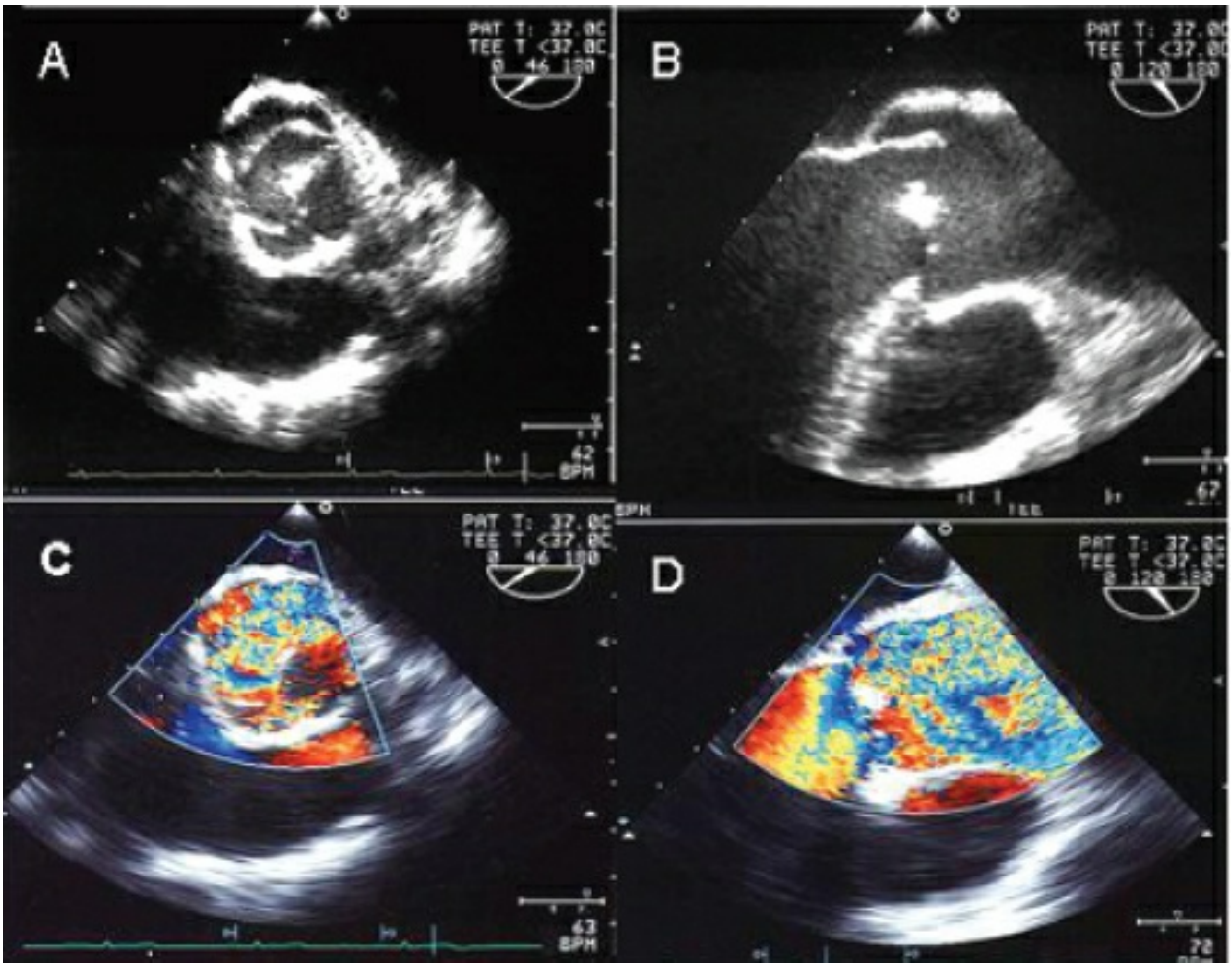


Figure 4.63: A patient with congenital bicuspid aortic valve. Note the eccentric orifice of the valve (panel A transverse section and panel B, longitudinal section). Panels C and D show the turbulent systolic flow across the valve due to severe degree of aortic stenosis.

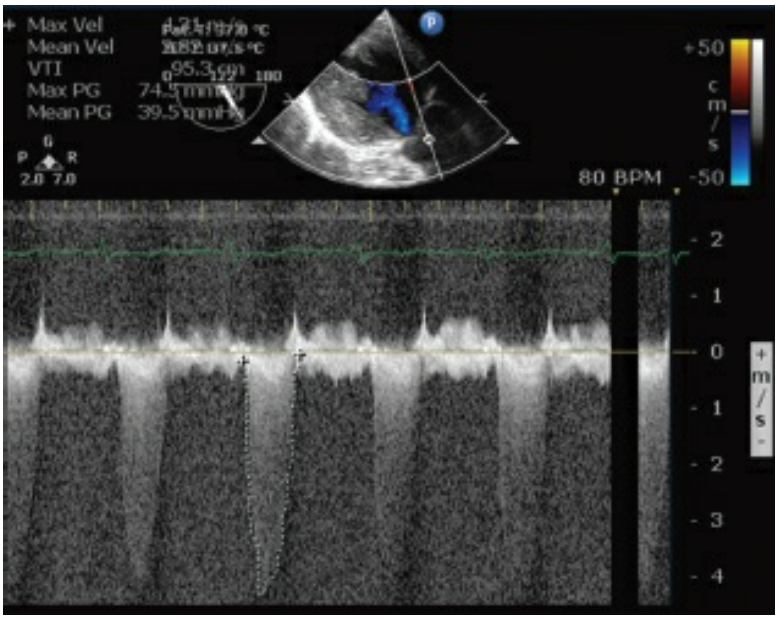


Figure 4.64: Trans-gastric view showing continuous wave spectral Doppler across the aortic valve with a flow velocity of around 4 m/s giving a peak gradient of around 64 mm Hg.

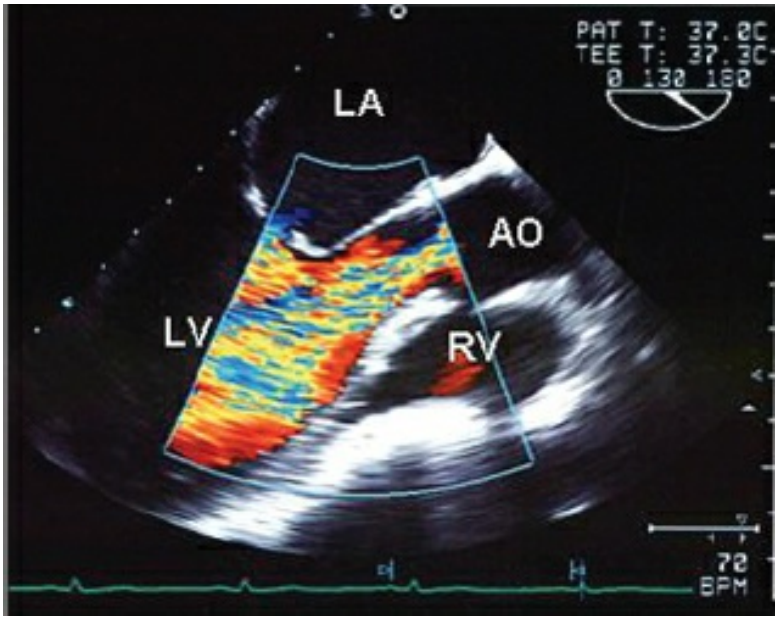


Figure 4.65: A patient with severe aortic regurgitation. Colour flow across the aortic valve shows the regurgitant flow in diastole (LA: left atrium, LV: left ventricle, AO: aorta, RV: right ventricle).

TOE as intraoperative diagnostic tool

TOE can reveal new diagnostic findings before incision leading to changes in the surgical management. A study involving 5016 patients revealed that prebypass TOE evaluation led to modification of the surgical procedure in 27 percent of patients undergoing coronary surgery and 11 percent undergoing

valve surgery.[98] Subsequent studies have reported similar findings, but the percentage of patients requiring change in the surgical plan have been variable.[99,100]

The diagnostic capabilities of TOE are also useful in rapid assessment of patients undergoing emergency surgery without adequate prior evaluation. Diagnosis of pericardial effusion, atrial septal defect, pulmonary venous drainage, atrial thrombi, valvular anatomy, aortic dissection and aneurysm can be made in the OT.

Examination of the aorta

The thoracic aorta can be divided into 4 sections; aortic root (AV to sinotubular junction), ascending aorta (sinotubular junction to innominate artery), arch (innominate artery to left subclavian artery), and descending aorta (distal to the left subclavian artery). The ascending aorta measures 7 to 11 cm, the aortic diameter is 35 ± 2 mm and the wall thickness is 1 to 2 mm. Evaluation of the athermatous disease of the aorta is extremely important during TOE examination. The presence of atheromas, especially grade 4 (protrudes > 5 mm into the aortic lumen), and grade 5 (mobile atheromas of any size), and the location is an invaluable piece of information to the surgeon. It can help the surgeon modify the technique (change in the site of aortic cannulation or cross-clamp, or avoiding the cross clamping altogether, choosing alternate technique of femoral-femoral bypass, total circulatory arrest or even replacement of the aorta)[101] in order to avoid major stroke. Figure 4.66 shows a grade 3,4 atheroma. The other important use of TOE is the diagnosis of aortic dissection. The TOE findings in aortic dissection are the presence of an undulating intimal membrane (flap) inside the aortic lumen (Fig. 4.67) that divides the aortic channel into two lumens (the true and the false lumens).[102] False lumen is usually larger than the true lumen. TOE has been found to be diagnostically superior and faster than aortography for detection of the aortic injury.[103] It is also a quicker and superior tool for the detection of aortic dissection.

Congenital heart disease

The management of congenital heart diseases (CHD) has been transformed by the noninvasive cardiovascular imaging. The haemodynamic assessment that is now possible with echocardiography has decreased the need for

invasive procedures such as cardiac catheterisation.

With the introduction of smaller probes to suit infants, TOE has now become an important investigative tool in the OT as well as ICTJ. Immediate on-line assessment of the CHD and its repair both intraoperatively and postoperatively have been greatly enhanced by the TOE.[104] The confirmation of the adequacy of repair of various congenital lesions by looking at the leaks across the patch repairs, calculation of gradients across the valves and conduits, diagnosis of any residual defects and haemodynamic monitoring is of great help in the successful performance of simple as well as complex surgical repairs. It has been reported that intraoperative TOE reliably detects residual cardiac defects in patients undergoing congenital heart surgery.[105]

De-airing of cardiac chambers and separation from CPB

It is an important step before unclamping the aorta in patients undergoing open-heart procedures. Despite careful de-airing methods that are adopted, air is invariably left in the LV cavity which might lead to systemic air embolisation. This is particularly so in patients undergoing reoperations in whom the LV cannot be adequately mobilised to assist in de-airing.

TOE can assist the surgeon to completely de-air the cardiac chambers and separate the patient from CPB. It is common to see cardiac chambers filled with micro air emboli. These should be removed as much as possible. The major concern however, is the presence of macroemboli of air inside the cardiac chamber. The macro-bubble creates at the blood-air interface a linear, dense and undulating echo-density. In addition, near total reflection of the ultrasound beam at the blood-gas interface results in complete shadowing behind the air collection (Fig. 4.68). Such collections of air should be removed under echocardiographic guidance by the surgeon via the aortic root vent by gently massaging the cardiac chambers while the aorta is partially clamped anteriorly. The dynamic tearing away of the small air bubbles from the surface of the air pocket into the cardiac chamber can be visualised. The intermittent bursting of microbubbles has been termed as the “Popcorn Sign”.[106]

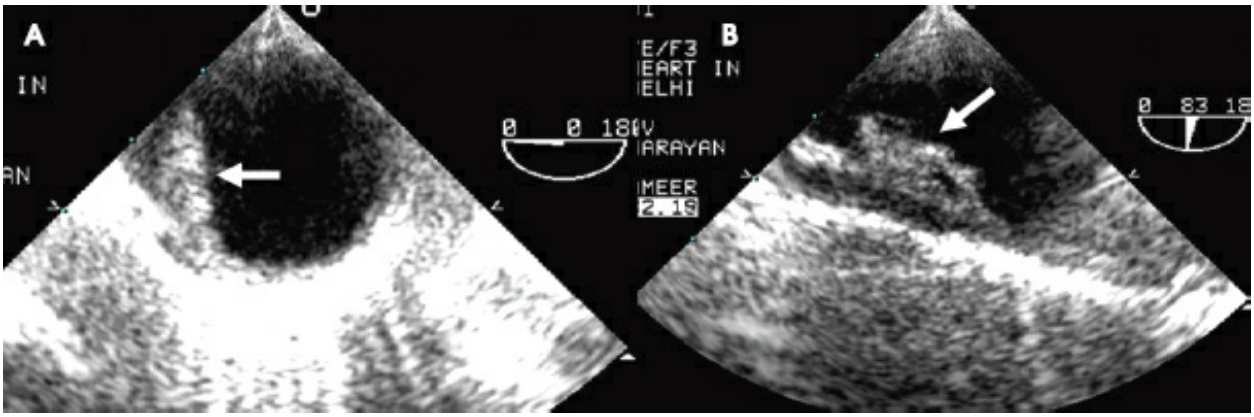


Figure 4.66: Intra-operative detection of a large aortic atheroma in descending thoracic aorta (arrow) in short-axis (A) and long-axis (B) views of aorta. Atherosclerotic lesions of aorta constitute a major cause of perioperative peripheral embolism and ischaemic events.

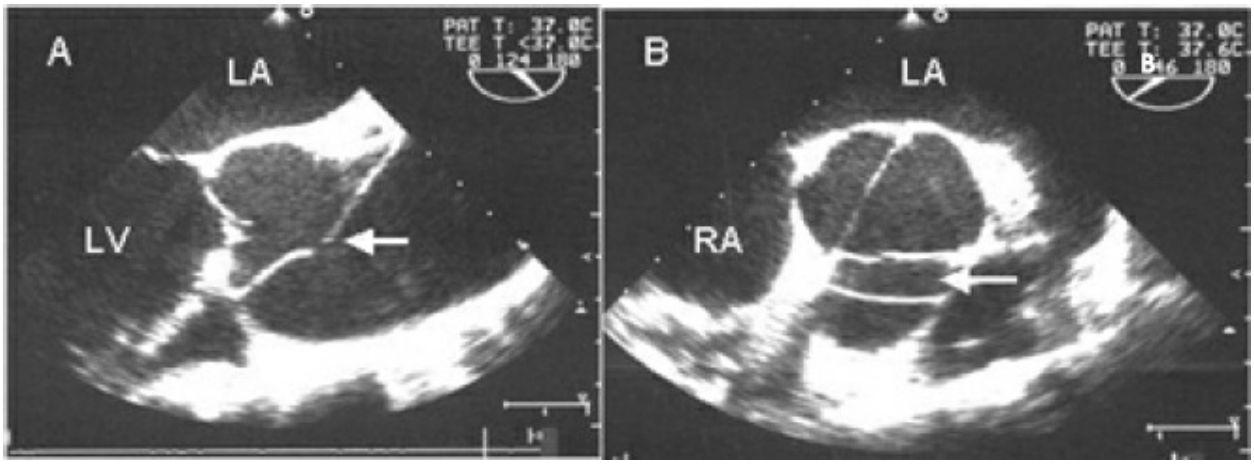


Figure 4.67: A patient with aortic dissection. Panel A shows the long-axis view of the ascending aorta with the dissection flap (arrow). Panel B shows the short-axis view; note the true and false lumina (arrow). (LA: left atrium, LV: left ventricle, RA: right atrium).

Separation from CPB can be facilitated by confirming the adequacy of the surgical procedure that has been performed. In this respect, identification of the prosthetic valve dysfunction, paravalular leaks, residual shunt/defects, MR secondary to ischaemia and SAM are important. Further, evaluation of the preload, contractility and RWMAs are crucial and can help to make appropriate choice of therapy before the CPB is terminated.

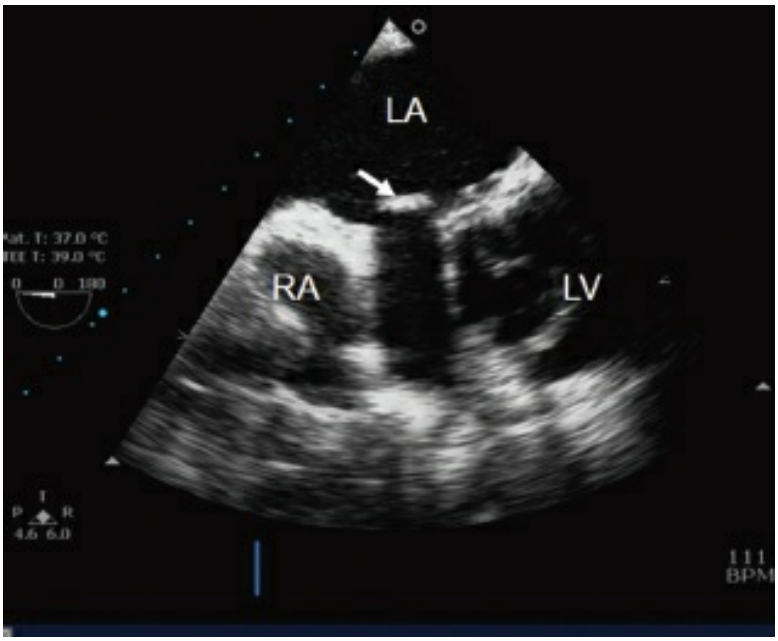
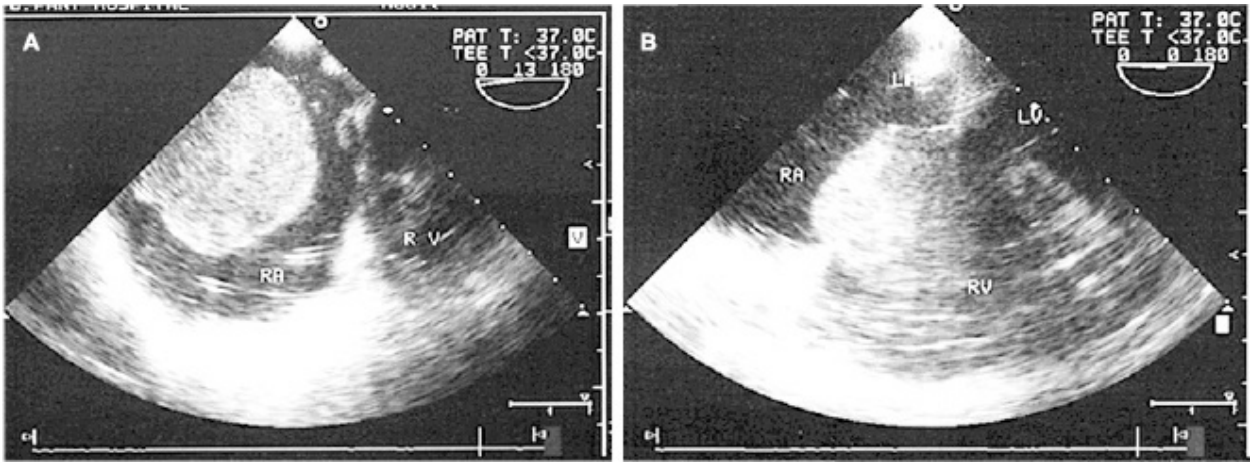


Figure 4.68: Mid-oesophageal modified 4-chamber view showing a linear echo density (arrow) caused by presence of air bubble in the left atrium. Also note the acoustic shadowing caused by air bubble that gives a deceptive appearance of a foreign body.

Other uses

Some other uses of TOE include the diagnosis of endocarditis (vegetation), intra-cardiac thrombi and masses, some rare defects and pericardial effusion (Figs 4.69 to 4.73). In addition, it can assist in positioning of the cannulae and other devices. In this respect, placement of the intra-aortic balloon catheter and coronary sinus catheter are important. In robotic off-pump coronary artery bypass procedures, cannulation of SVC, IVC and endo-aortic cross-clamp is also assisted by TOE.



Figures 4.69A and B: A large right atrial myxoma prolapsing across the

tricuspid valve in diastole (LA: left atrium, RA: right atrium, RV: right ventricle, LV: left ventricle).

Tissue Dopple imaging

Tissue Doppler echocardiography measures the velocity of myocardial tissue using low-pass filters to screen out higher velocities generated by blood flow. Tissue motion creates Doppler shift and the velocities rarely exceed 20 cm/s. During image acquisition, the temporal resolution is optimized by selecting as narrow an image sector as possible, which increases the frame rate.

Patients with normal global LV function have systolic velocities greater than 7.5 cm/s[107] whereas velocities $\leq$ 5.5 cm/s indicate LV failure.[108] The mitral annular motion is utilised for assessing the diastolic function. The tissue Doppler velocity measurements (mitral annulus) are less vulnerable to the effects of acute changes in loading conditions of the heart. The PWD sample volume is positioned at the lateral mitral valve annulus to obtain the tissue Doppler profile, which has a biphasic diastolic component that includes an initial early (E') and a late (A') diastolic tissue velocity (Fig. 4.74). The diastolic component thus obtained appears as a mirror image of the trans-mitral diastolic flow velocity except that the tissue velocities are much lower in magnitude (8-15 cm/s). In healthy patients, the peak E' is greater than A'. E' and E'/A' decline with age and are reduced in LV hypertrophy. E' remains reduced in impaired ventricular relaxation and pseudonormalisation suggesting relative preload independence. Thus, E' can be used as a discriminator between normal and pseudonormal pattern. This can be especially useful in the perioperative period when the loading conditions can vary considerably.

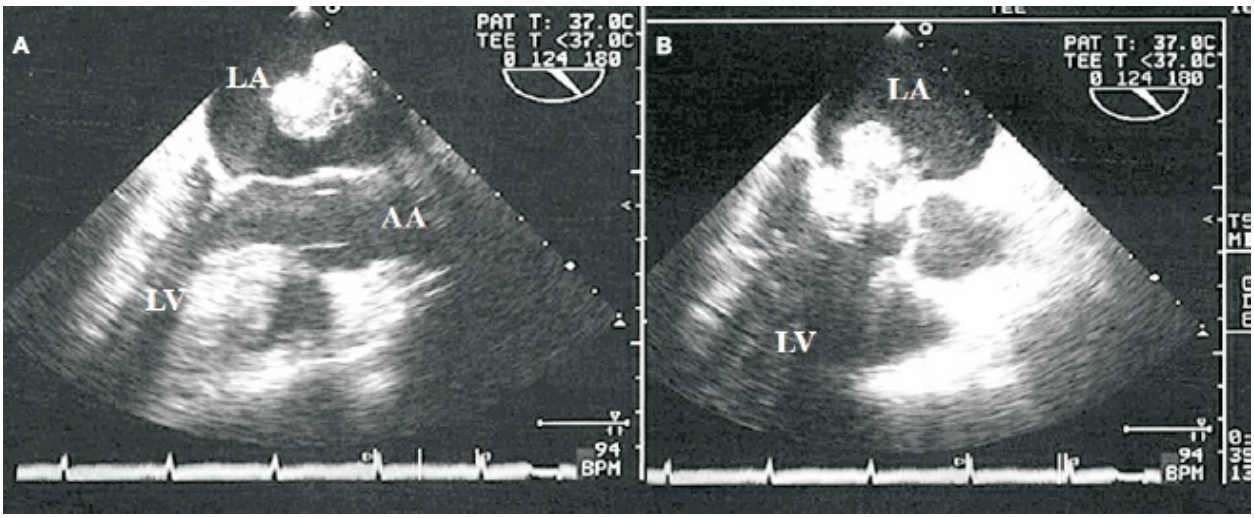


Figure 4.70: A mobile left atrial myxoma. Note the to and fro movement of the myxoma in the left atrium in systole (A) and diastole (B) causing mitral valve obstruction (LA: left atrium, LV: left ventricle, AA: ascending aorta).

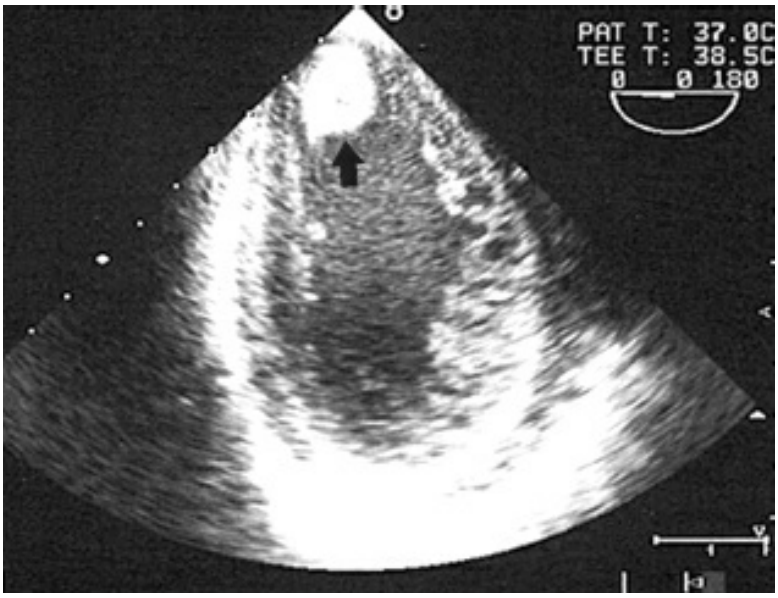


Figure 4.71: Trans-gastric short-axis view of the left ventricle in a patient with inferior wall myocardial infarction. Note the aneurysm in inferior wall with a thrombus (arrow).

Colour M-mode

Colour M-mode imaging is used to measure mitral-apical propagation velocity. After obtaining a clear view of LV inflow, colour flow Doppler is superimposed on the LV inflow. The M-mode scan line is displayed extending through the mitral valve opening to the LV apex. The propagation velocity is determined by measuring the slope of the aliasing velocity from the mitral inflow to about 3 to 4 cm into the LV cavity. The normal propagation velocity is more than 50 cm/sec, a decrease in velocity is a marker of LV diastolic dysfunction. It is useful for evaluating the diastolic function when the other parameters of diastolic dysfunction are inconclusive.

Three-dimensional transoesophageal echocardiography

Sequential multiplane 2-D TOE images can be used to reconstruct the three-dimensional (3-D) image. In the beginning, the sequentially acquired 2-D images were transferred to an off line computer for subsequent 3-D reconstruction. The present-day TOE machines are capable of 3-D reconstruction of the sequentially acquired 2-D images. Also, the time taken

to reconstruct the 3-D image has been drastically reduced. In order to minimise the artifacts in the 3-D reconstructed image, one should acquire images only in a particular phase of respiration. Editing and cropping of an image are required for the development of an image that can be used for interrogation.

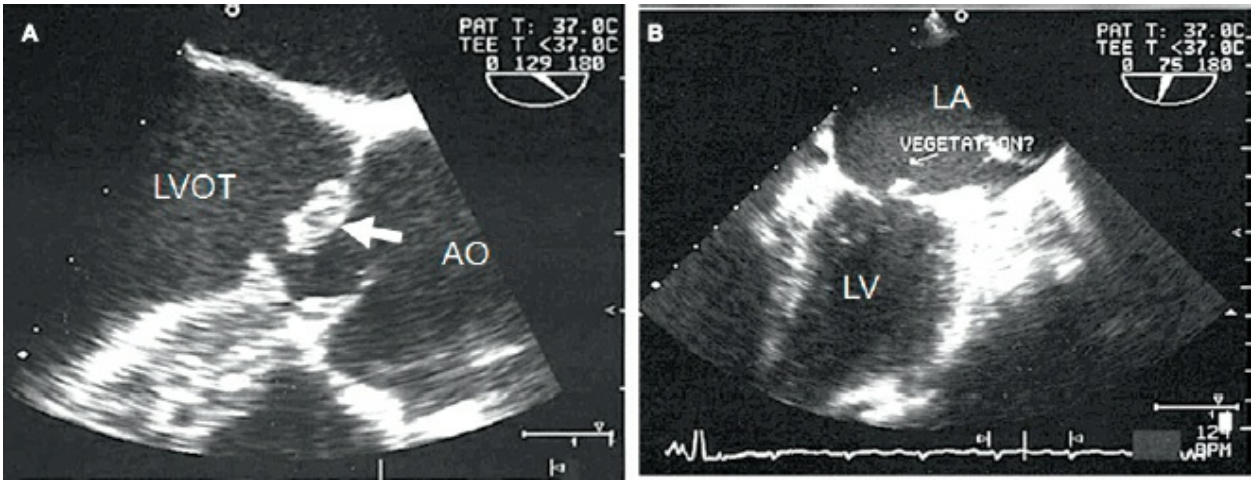


Figure 4.72: A: Vegetation (arrow) on the aortic valve in a patient with infective endocarditis. B: vegetation on the mitral valve in a patient with mitral valve prolapse with infective endocarditis (LA: left atrium, LVOT: left ventricular outflow tract, AO: aorta, LV: left ventricle).

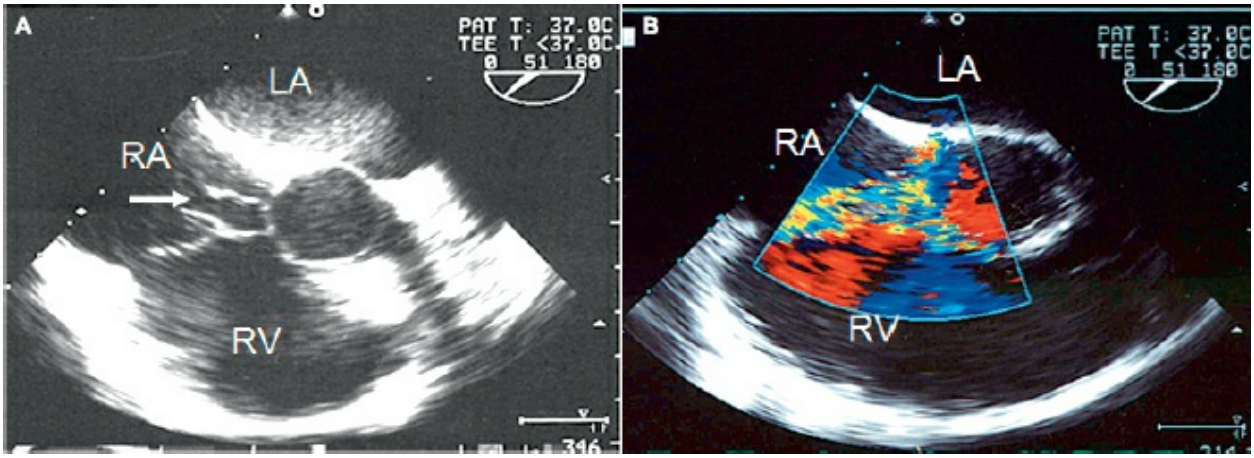


Figure 4.73: A patient with ruptured aneurysm of the sinus of valsalva. Note the track of the ruptured sinus in panel A (arrow). Panel B shows the turbulent flow across the sinus opening into the right atrium. (LA: left atirum, RA: right atrium, RV: right ventricle).

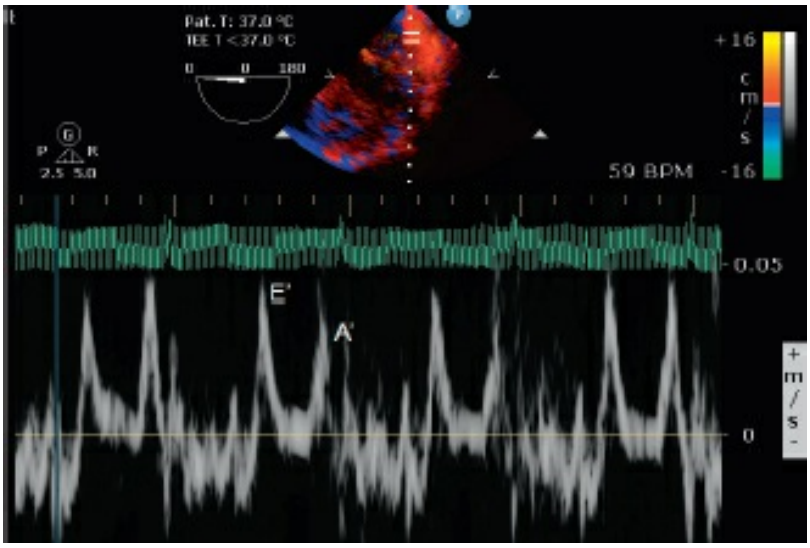


Figure 4.74: Mitral annular tissue Doppler velocities showing early (E') and late (A') diastolic velocities.

3-D TOE is superior to 2-D TOE, especially in detection of individual scallop/segmentprolapse of the mitral valve. Further, the en face view of the atrial surfaces of both leaflets can be visualised. Thus, 3-D TOE is of exceptional use during mitral valve repair. Likewise, the assessment of intracardiac masses, intracardiac defects, aortic dissection, and AV is remarkably improved. These aspects are of practical clinical importance. For instance, exact size of an atrial septal defect is crucial during percutaneous catheter closure of the defect. The en face view is used for guidance of the catheter across the defect as well as the assessment of device position.

3-D TOE is being increasingly used nowadays. A detailed discussion on the subject is beyond the scope of this book, and the reader should refer to the standard text books for the details.

Complications

Most of the complications of TOE occur in outpatient and are related to the stress response that the patients experience while swallowing the TOE probe. Minor oropharyngeal injuries and postoperative gastrointestinal complaints can occur after major surgery. Although, serious pharyngeal or oesophageal injury following TOE is rare,[109] a case of splenic laceration has been reported.[110] In infants the TOE probe may occasionally obstruct the airway distal to the endotracheal tube[111], or the subclavian artery.[112] Recently a 13 cm long submucosal dissection of the oesophageal wall has been reported

following TOE examination in a patient with Barrett's oesophagus.[113]

In conclusion, the utility of TOE in anaesthesia practice is largely confined to the cardiac OT. Confirming the adequacy of surgical repair of various congenital anomalies and valve repair, detection of aortic atheromas and monitoring of the myocardial performance and diagnosis of acute myocardial ischaemia remain the most important intraoperative applications of TOE. It also helps clear visualisation of the LA thrombus or mass. Although, these applications are presently being used mostly inside the cardiac OT, some of them can also be used in cardiac patients undergoing non-cardiac surgery. In addition, the same applications can be extended to the cardiac ICU as well as the general ICU.

Since the accurate interpretation is dependent on the quality of image that the operator is able to generate and some of the interpretations are likely to change the course of management, it is important that the operator is well experienced in the technique. The cardiac anaesthesiologist, thus, should obtain adequate training so that he is able to assist in the patient management with this fascinating tool.

Monitoring of Respiratory Function

Cardiovascular and respiratory systems have intimate relationship. An abnormality of one system can affect the performance of another. Due to this reason, monitoring of the respiratory function is as important as monitoring of the haemodynamic function.

Arterial blood-gas measurements continue to remain the gold standard for determining the adequacy of oxygenation and ventilation. The arterial pH, oxygen tension (PaO_2 carbon dioxide tension ($PaCO_2$) are measured with the help of pH electrode, oxygen electrode and carbon dioxide electrode. The remaining values in a blood-gas analysis are calculated from these three measured variables.

Bubbles in blood gas syringe may influence the results. The PO_2 of air is around 150 mm Hg and the PCO_2 of air is less than 1 mm Hg. A bubble in the blood gas syringe will equilibrate with the gases in the blood. Therefore, the PO_2 in the sample will be raised, if it is less than 150 mm Hg and lowered, if it is more than 150 mm Hg. The PCO_2 of blood will always be lowered.

Devices are available that are capable of continuous monitoring on a real time basis, of the blood-gas tension, oxygen saturation, haemoglobin and haematocrit in the blood passing through the bypass circuit. The cardiac anaesthesiologist should have thorough understanding of the acid-base balance because changes in acid-base balance can occur quickly in a patient undergoing cardiac surgery during the perioperative period. In addition, these changes may prove to be crucial in the ultimate outcome of the patient as they may influence important physiological functions of the body. The interpretation of the arterial blood gases and acid-base balance is briefly described in chapter 15, however, the reader may refer to the reviews on the subject for details.[114,115]

The pulse oximetry provides a reliable, real time estimation of arterial haemoglobin saturation. Its use, predictably, has led to a considerable increase in the diagnosis rate of the hypoxaemia (arterial oxygen saturation < 90 percent). The present generation pulse oximeters are extremely easy to use and require no calibration by the user. Pulse oximeters, thus provide a fairly accurate estimation of arterial oxygenation. They have gained wide acceptance mainly due to the reliability and convenience and have become standard component of anaesthesia monitoring. However, the main disadvantage is that the PaO_2 must fall below 100 mm Hg before the oximeter detects any change and below 60 mm Hg before rapid changes will occur.[116] Thus the device is not sensitive to changes in PaO_2 over a wide range.

End-tidal carbon dioxide

Continuous measurement of the expired CO_2 is possible. End-tidal gas monitors are now available that measure not only CO_2, but also anaesthetic gases. Accurate estimation of adequate CO_2 elimination is thus possible by use of these monitors. CO_2 has important cardiovascular effects and therefore, maintenance of CO_2 levels within normal range or even lower range is sometimes desirable and can be achieved with the use of end-tidal carbon dioxide monitor.

In summary, a vast range of invasive and non-invasive monitoring devices is available. The cardiac anaesthesiologist is equipped to derive haemodynamic information by using them. He should have knowledge to

understand and interpret these data, so that maximum benefit is provided to the patient.

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Chapter 5: Anaesthesia for Valvular Heart Disease

Lesions of the cardiac valves result in profound alteration in the cardiac loading conditions and ventricular contractility. The loading conditions may be in the form of either a pressure overload or a volume overload. However, the human heart possesses significant capacity to adjust and compensate for the abnormal stressful conditions imposed by the valvular disease. The compensatory mechanisms include ventricular hypertrophy and/or dilatation associated with alteration in the ventricular compliance. In addition, utilisation of the Frank-Starling mechanism and redistribution of the pulmonary blood flow also occurs. Unlike coronary artery disease (CAD), the symptoms are not related to the myocardial contractility, which may be normal or sometimes supranormal. Nevertheless, in due course, the compensatory mechanisms fail and the myocardial contractility declines.

There has been a significant progress in the management of valvular heart disease. The techniques of mitral valve repair continue to be refined and the success and safety of mitral valve repair is well established. In addition, newer techniques such as minimally invasive mitral valve surgery and trans-catheter mitral valve repair are evolving. Furthermore, trans-catheter aortic valve implantation (TAVI) to treat severe aortic stenosis (AS) is emerging as a viable option for high-risk patients who have high operative mortality for surgical correction under cardiopulmonary bypass (CPB). The mortality rates of cardiac valve replacements are much higher than mat of coronary artery bypass grafting (CABG) (3 to 10 percent for valves and < 1 percent for CABG).[1] In the developing countries, due to a variety of reasons, patients are often neglected during the course of their illness and many of them present at a fairly late stage at a time when compensatory mechanisms have nearly exhausted, and the circulatory system is failing. Rheumatic fever continues to

be the most common cause of valvular heart disease (VHD) and the patients are young and often suffer from cardiac cachexia. Nevertheless, surgery is still performed on them, as it leads to substantial symptomatic improvement. These patients, therefore, pose considerable challenge to the anaesthesiologist during the perioperative period. At G.B. Pant hospital, New Delhi, on an average 600 patients undergo valve surgery every year with an early mortality of about 5 to 8 percent.

Pathophysiology

Each valve lesion has a different haemodynamic profile and understanding of the pathophysiology is of absolute importance. This helps the anaesthesiologist in choosing the anaesthetic, muscle relaxant, and vasoactive drugs so that optimum haemodynamics are maintained during the perioperative period. The left ventricular (LV) pressure-volume loop depicts both systolic and diastolic ventricular performance and can be used to understand the pathophysiology of the valvular lesions. Figure 5.1 shows the normal LV pressure-volume loop that is constructed by plotting the ventricular pressure against volume during one cardiac cycle.

Mitral valve opens at point ‘A’ and ventricular filling begins. The segment AB illustrates the pressure-volume relationship during diastole. Mitral valve closes at point ‘B’ and ventricular systole begins. Segment BC depicts isovolaemic contraction, which ends when the ventricular pressure exceeds aortic pressure, and aortic valve opens at point ‘C’ This is followed by the ejection phase which ends at point ‘D’, when the LV pressure falls below the aortic and the aortic valve closes. Segment DA represents isovolaemic relaxation that ends at point ‘A’, when the mitral valve opens again. The segment AB represents the diastolic pressure volume relationship and point D represents the end-systolic pressure-volume relationship. Preload, afterload, ventricular compliance and contractility are frequently used terms, which must be understood.

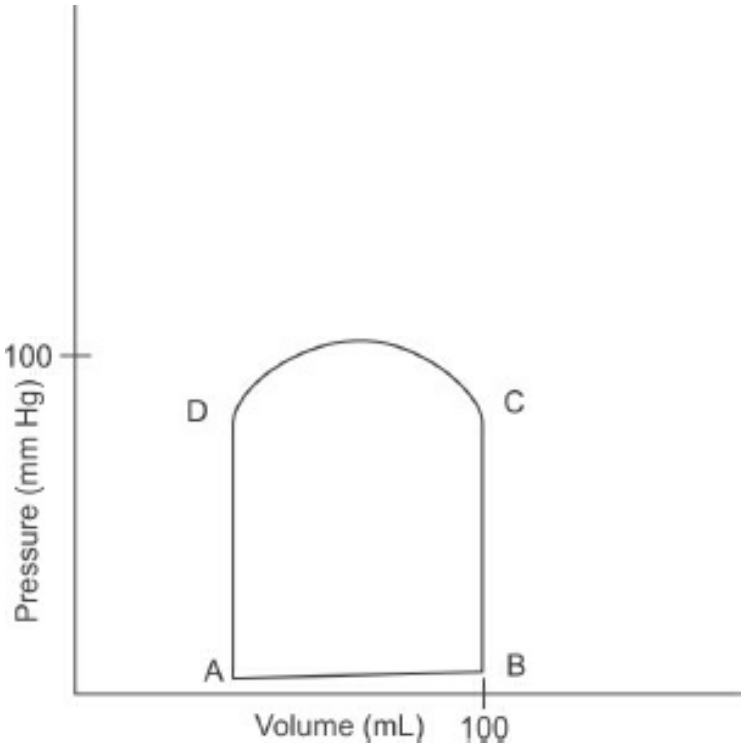

Figure 5.1: The diagram illustrates normal left ventricular pressure-volume loop. Refer to the text for details. (This is a diagrammatic and not an accurate representation.)

Preload and Afterload

Preload can be equated to the end-diastolic size or end-diastolic volume of the ventricle. The central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP) and left atrial (LA) pressure are often taken as the measures of preload. Afterload is defined as the tension or force per unit of cross sectional area in the ventricular wall during ejection.[2] In simple words it is the impedence to ejection. It is determined in part by the vascular resistance and points towards the pressure work the ventricle must do to complete the ejection. It can be calculated on the basis of Laplace's law[3] where the wall tension developed in a spherical chamber $= \frac{P \times R}{2h}$ where, P is the pressure, R is the radius, and h is the wall thickness. Thus ventricular afterload progressively changes as the intraventricular pressure and radius constantly change during each systole. The stroke volume (SV) progressively decreases as the afterload increases in the failing heart. In clinical practice, blood pressure or systemic vascular resistance (SVR) are often used as indicators of afterload.

Normally, increase in the afterload is compensated by increasing the

preload. Thus, when the afterload increases, the SV is maintained by increasing the end-diastolic volume (preload). This is called as preload reserve. However, preload cannot be increased beyond a limit and in an extreme situation, the ventricle over-distends with a fixed end-diastolic volume. Any further increase in the afterload cannot be compensated and leads to a decrease in the SV. This is called as afterload mismatch.

Ventricular Compliance

The relationship between the end-diastolic volume and end-diastolic pressure is the compliance of the ventricle. In the physiological range, the normal ventricle is extremely compliant so that there is a small ventricular pressure rise as the volume increases. In conditions with chronic volume overloading [mitral regurgitation (MR), aortic regurgitation (AR)], the ventricular compliance is maintained (by ventricular dilatation) so that substantial increases in ventricular volume are tolerated with a relatively little change in the end-diastolic pressure.

Myocardial wall thickness is an important determinant of the diastolic compliance. For instance, in conditions with chronic pressure overload e.g. AS, there is an increase in the LV wall thickness that is associated with a decrease in the diastolic compliance of LV.

Contractility

Myocardial contractility is an intrinsic property of the cardiac cell and is defined as the amount of work that the heart can perform at a given load.[4] Myocardial contractile function is one of the important determinants of the prognosis and it is of particular importance in decisions regarding the timing of surgical correction in patients with VHD. The most widely used clinical measure of ventricular contractility is the ejection fraction (EF). This method is popular as it is readily measurable by noninvasive methods such as echocardiography and radionuclide angiography. These methods are particularly useful in conditions that do not significantly alter ventricular loading conditions such as CAD.[5] However, they are not so reliable for assessing the contractile function in patients with VHD and at times may be misleading. For example, a patient with MR may have normal EF in the face of a poor contractile state, as a part of the ejection is easily pumped into the LA that is a low pressure cavity. On the contrary in a patient with AS, low EF

is really a reflection of the high afterload imposed by the stenotic valve. This means that a large proportion of the ventricular work is used up for pressure development (to overcome the resistance offered by the stenotic valve) and a small proportion will be utilised for the actual ejection of blood. Thus after restoring normal valvular function in patients with MR, the ventricular performance may be depressed as LA, the low pressure chamber is no longer available for ejection. After relieving the AS on the other hand, LV may perform vigorously, as the high afterload imposed by the stenotic valve is eliminated.

The use of end-systolic pressure-volume relationship (ESPVR) on the pressure-volume loop provides a more precise evaluation of the LV contractility. The pressure-volume loops are obtained at different filling volumes of the heart and the ESPVR is represented by a straight line connecting the upper left hand corners of the pressure-volume loops. All the end-systolic pressure-volume points fall on a single line, provided the contractility is held constant (Fig. 5.2A). Increases in the contractility are represented by a steeper line (ESPVR above and to the left of control), and decreases by rotation of the curve clockwise to the right (ESPVR below and to the right of control) (Fig. 5.2B). In other words, a stronger ventricle empties more completely (smaller end-systolic volume).

Mitral Stenosis

Clinical Presentation

As has already been emphasized, rheumatic heart disease is still common in the developing countries and is the commonest cause of VHD. In about 25 percent of patients with rheumatic heart disease, pure mitral stenosis (MS) is manifested and an additional 40 percent have combined MS and MR.[6]

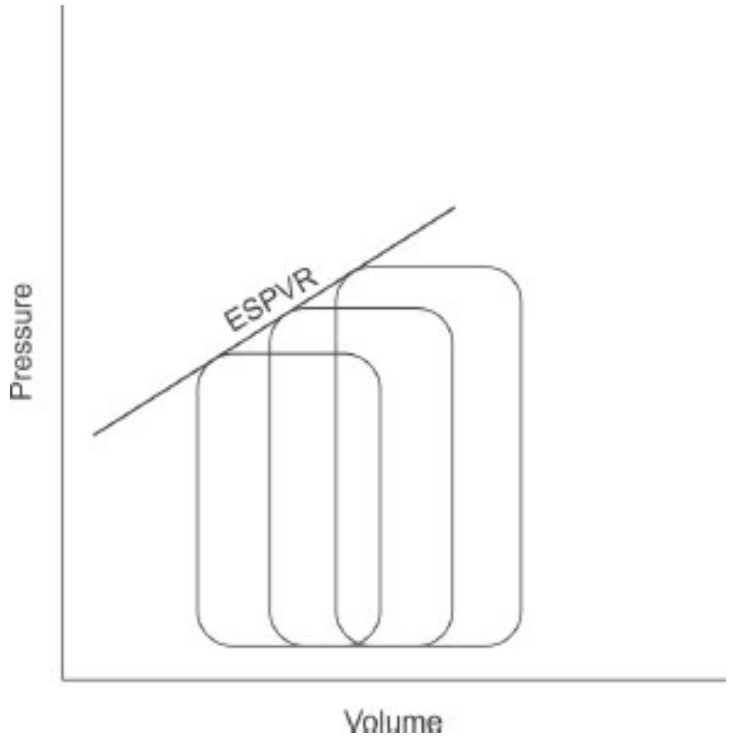

Figure 5.2A: The end-systolic pressure-volume relationship (ESPVR) is oPtained Py connecting the end-systolic points measured during a rapid decrease in preload. (This is a diagrammatic and not an accurate representation.)

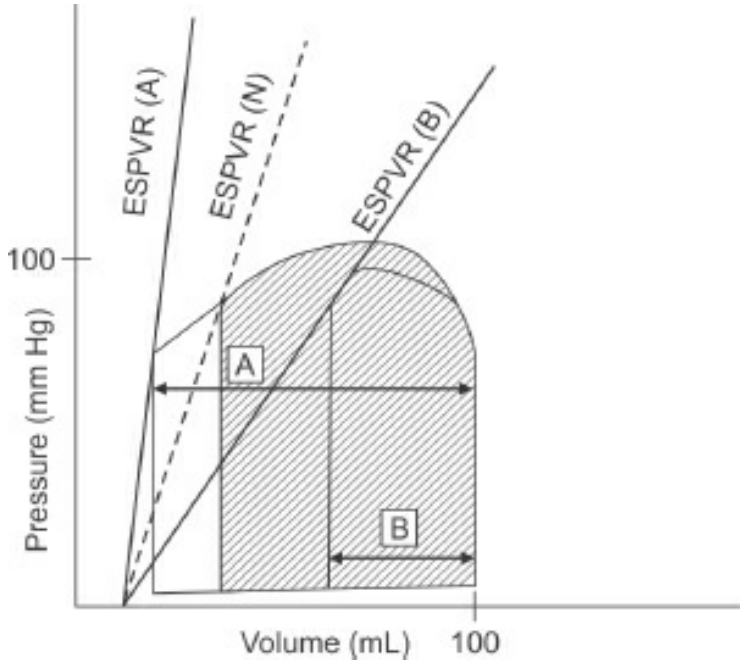

Figure 5.2B: End-systolic pressure volume relationship. Loop A and ESPVR (A) reflect increases in contractility. Preload and afterload remain the same as the normal (shaded loop), while stroke volume increases. Loop B demonstrates decreased inotropy with a decrease in stroke volume with same loading conditions. (This is a diagrammatic and not an accurate representation.)

Rheumatic inflammation causes thickening and calcification of the leaflets along with commissural fusion. The subvalvular apparatus can also be thickened and fused. This results in a narrowed, funnel shaped valve that obstructs the blood flow. In the developing countries, patients suffer from inadequate nutrition, sanitation and medical care. Consequently, many of them suffer recurrent episodes of endocarditis, and severe MS develops within 5 years of the initial episode. Patients with MS are, therefore, very young, usually in the second decade of life. In contrast, in the developed countries, the rheumatic fever is rare and there is a latency period of 3 to 4 decades between the initial bout of rheumatic fever and the onset of symptoms. Therefore, the patients present with signs and symptoms in the 4th to 6th decade of life. This is responsible for another major difference in the presentation of MS in the developing countries versus that in the developed countries, i.e. associated CAD is rarely present in patients with MS from the developing countries, as against those of developed countries. The rarity of MS in young patients in the developed countries was highlighted in an article in the British Medical Journal under the heading “Lesson of the week”.[7] The doctors failed to diagnose MS in young pregnant women of Asian origin until it was too late, as MS was not the differential diagnosis in these patients.

Dyspnoea is the most common initial symptom and is generally precipitated by some unrelated condition such as fever, pregnancy and thyrotoxicosis, which leads to an increase in heart rate (HR). Patients also develop pulmonary hypertension that leads to afterload stress on the right ventricle (RV) leading to RV dilatation and functional tricuspid regurgitation (TR). The end-stage picture of biventricular failure with pulmonary congestion, peripheral oedema and ascites follows, if the patient is left untreated.

Pathophysiology

The basic pathology is obstruction to the blood flow across the mitral valve generating a pressure gradient between the LA and the LV. This leads to abnormalities both proximal and distal to the abnormal valve. Due to restriction of the diastolic inflow to LV, it is underloaded and the preload reserve is limited (Fig. 5.3). Consequently, the left ventricular end-diastolic volume (LVEDV) and left ventricular end-diastolic pressure (LVEDP) are decreased and there is a corresponding reduction in the SV.

The LV contractility may be depressed. This can be seen in the immediate postoperative period and is attributed to a sudden increase in the diastolic filling of a chronically underloaded ventricle. In addition, rheumatic carditis can lead to an intrinsic myocardial depression[8] and angiographically demonstrable contraction abnormalities have been reported in 20 percent of patients.[9] The LV dysfunction related to the geometrical changes of LV have also been described. [10] Intrinsic compliance of the LV may also be reduced by the rheumatic disease process leading to impaired diastolic function.[11]

Vasodilators do not help as the diastolic underfilling is aggravated by the concurrent venodilatation.[12] However, they can be helpful in patients with severe pulmonary artery hypertension (PAH), where pulmonary vasodilatation reduces the RV afterload and the transpul-monary contribution to the ventricular filling is augmented.[13] As the LV is relatively thin walled, the afterload is increased. This also further compromises the LV ejection. Thus, abnormal loading conditions as well as intrinsic myocardial depression (due to rheumatic carditis) is responsible for the reduced contractile performance in patients with MS.

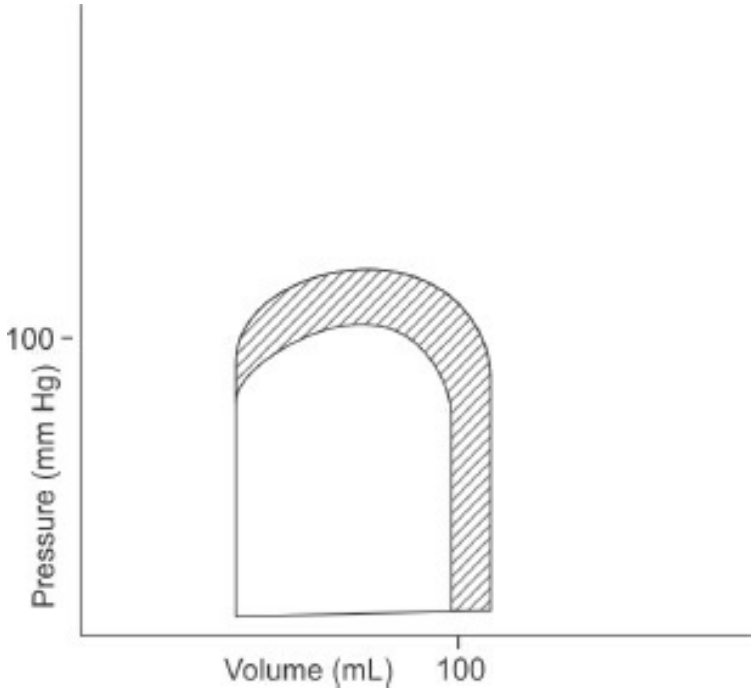

Figure 5.3: Pressure-volume loop in a patiet with mitral stenosis (clear area) against normal (shaded area). Note the “underloaded” left ventricle, both in terms of pressure and volume. (This is a diagrammatic and not an accurate representation.)

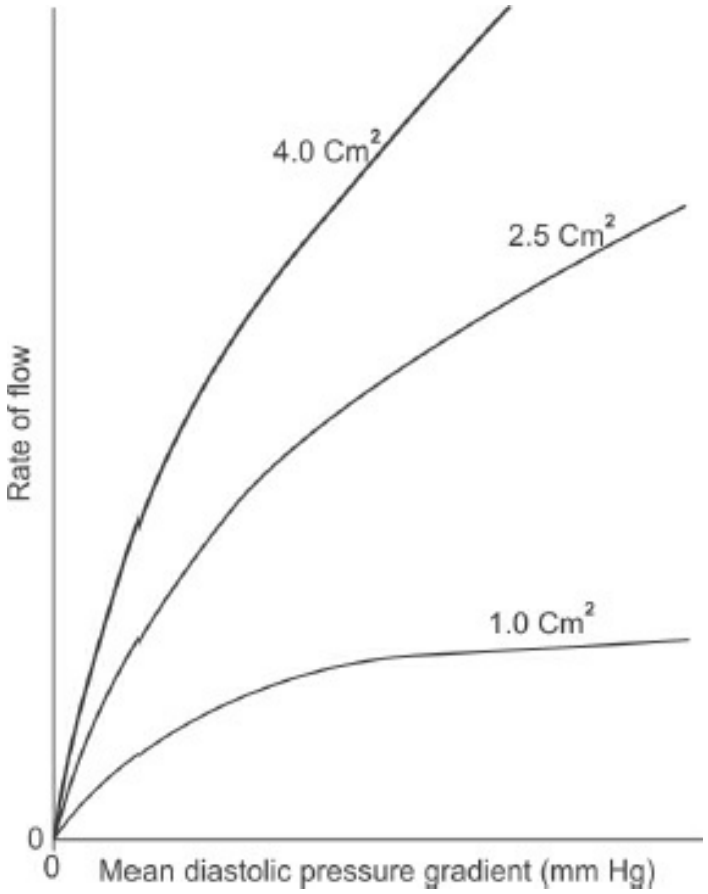

Figure 5.4: Rate of flow in diastole versus mean pressure gradient for three different mitral valve areas (4 cm^2,2.5 cm^2 and 1 cm^2). Note that there is a dramatic increase in the pressure gradient as the rate of flow is increased in a stenosed valve. (This is only a diagrammatic and not an accurate representation.)

Left atrial pressure overload

The area of the normal adult mitral orifice is 4 to 6 cm^2. This area is enough to allow the flow of blood into the LV during diastole without causing much pressure gradient. If the valve opening is narrowed, the diastolic flow into the LV can only be maintained by the development of an elevated pressure gradient across the mitral valve (Fig. 5.4). It can be seen from this figure that as the valve area is narrowed, the pressure gradient is increased to achieve the same rate of flow across the valve. As per the Gorlin formula,[14]

$$\left[\text{valve area} = \frac{\text{transvalvular flow rate}}{(\text{hydraulic constant} \times \sqrt{\text{pressure gradient}})}\right]$$

the pressure gradient varies directly as the square of the transvalvular flow rate when the valve area is constant. It is this relationship between the pressure gradient and the transvalvular flow rate that accounts for the

occurrence of symptoms in the presence of tachycardia in a patient with MS.[15] Tachycardia shortens the diastole, thereby decreasing the time available for flow across the mitral valve. Thus, in order to maintain the cardiac output (CO), the flow rate per unit time must increase, and the pressure gradient increases by the square of the increase in flow rate.[16] The resultant increase in the LA pressure leads to pulmonary congestion. It is because of this mechanism that tachycardia due to fever, pregnancy or thyrotoxicosis precipitates the symptoms of dyspnoea in otherwise asymptomatic patients with MS. As the time passes, the elevated transmitral pressure gradient leads to dilatation of the LA. In the developing countries, the patients often present at a very late stage and therefore, massive dilatations of the LA up to 10 to 12 cm, (normal up to 3.5 cm) can be observed (Fig. 5.5). The LA distention also distorts the depolarisation pathway leading to atrial arrhythmias [most commonly atrial fibrillation, (AF)]. The onset of AF can also be a precipitating factor for the symptoms to appear. It is, therefore, important to control the HR in patients with MS.

The increase in LA pressure is reflected back into the pulmonary circulation leading to PAH. Initially, the PAH is passive, but as the disease progresses, pulmonary arteriolar hypertrophy occurs leading to more permanent changes in the PAH. The increase in the pulmonary vascular resistance (PVR) leads to an increase in the RV afterload and RV dilatation and failure. This can further lead to TR, distended neck veins, hepatomegaly, peripheral oedema and ascites. The increased pulmonary blood volume[17] and increased extravascular lung water[18] also lead to decreases in lung compliance and exacerbation of the ventilation-perfusion inequalities.

The severity of MS can be assessed on the basis of several parameters such as mitral valve area, severity of PAH, and the LA size. In practice, the valve area is used to grade the severity of stenosis. Based on this parameter, the stenosis is graded as mild, moderate and severe, (valve area of 1.6 to 2.5 cm^2, 1.1 to 1.5 cm^2 and <1.0 cm^2 respectively). It is not uncommon to see patients having valve area of <1.0 cm^2 in the developing countries. These patients have a large LA, severe PAH and low CO. The PAH can often be equal to systemic pressure and the severity of PAH is evident on the radiological examination (Fig. 5.6).

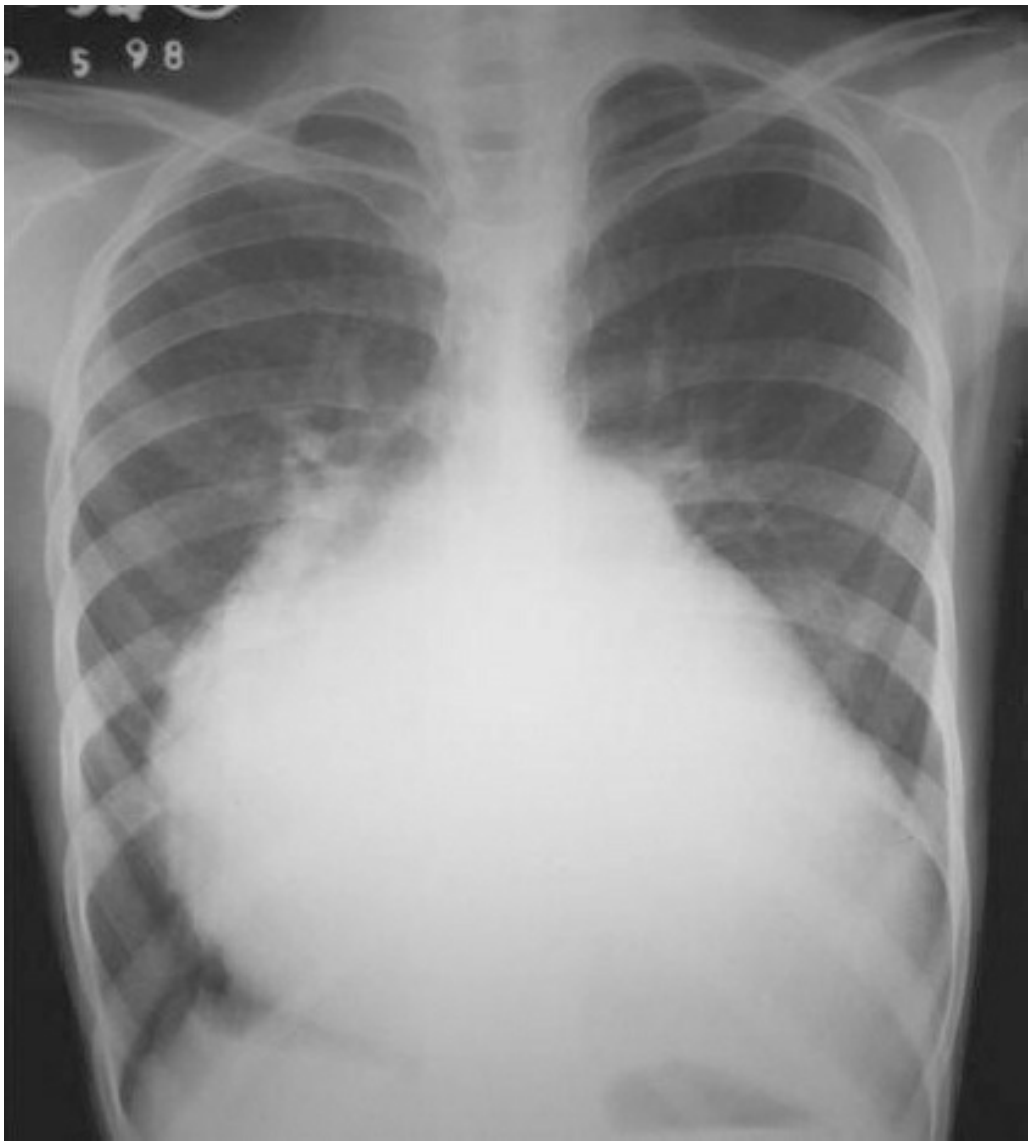

Figure 5.5: X-ray chest of a patient with severe mitral stenosis with severe mitral regurgitation and severe pulmonary artery hypertension. Note the massive enlargement of left atrium and left ventricle.

Echocardiography is the diagnostic modality of choice in MS.[19] The two-dimensional and Doppler echocardiographic techniques are particularly useful in calculating the pressure gradient as well as the mitral valve area. As the pressure gradient varies with the flow rate and diastolic period (heart rate), the severity of MS should be assessed on the basis of mitral valve area. This can be accomplished by pressure halftime technique, the continuity equation, planimetry of the valve orifice and proximal isovelocity surface area analysis. The other information obtained by the echocardiography includes the size and function of the ventricles and an estimation of the pulmonary artery pressure. A good correlation has been found between the

continuous wave Doppler calculated pressure gradients and that determined by the cardiac catheterisation.[20] With the result, cardiac catheterisation is almost unnecessary for the assessment of a patient with MS before surgery.[19]

Anaesthetic Considerations

Balloon Mitral Valvotomy

Percutaneous transvenous balloon mitral valvotomy (BMV), first described in 1984[21] is now widely performed with satisfactory results.[22,23] Encouraged by the success of this technique, the indications for BMV have widened considerably and only a thrombus in the LA or an associated severe MR is considered a contraindication by the cardiologist. However, unsuitable mitral valve anatomy such as heavily calcified valves or significant MR is likely to result in suboptimal valvotomy. The anaesthesiologist has a limited role to play in patients undergoing BMV as the procedure is mostly performed under light sedation. However, his services are required if the patient develops acute MR (one of the most serious complications of BMV) that necessitates urgent mitral valve replacement (MVR). This will be discussed under MR. The other situation when he is required is during the performance of an emergency BMV on very sick patients with critical MS (valve area $\leq$ 0.5 cm^2). These patients are in frank pulmonary oedema necessitating ventilatory support. The medical management does not lead to much improvement in such patients and often, opening the stenosed valve is the only alternative. The anaesthesiologist is needed in such situations to execute endotracheal intubation and initiate ventilation before BMV, and manage the respiration during transfer to the catheterisation laboratory, during the performance of BMV as well as the post-BMV period.

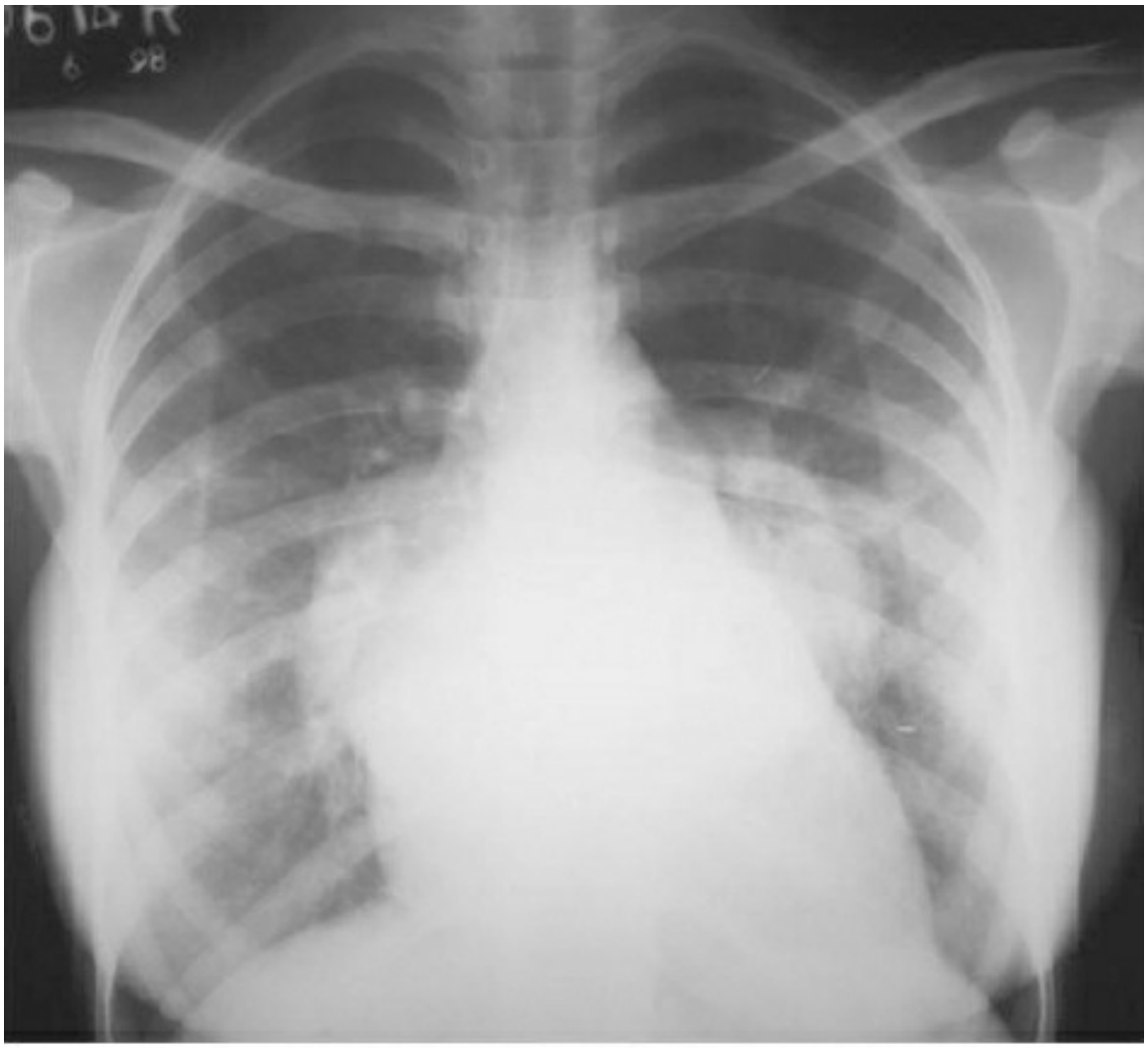

Figure 5.6: X-ray chest showing severe pulmonary artery hypertension in a patient with mitral stenosis. Note the enlargement of main pulmonary artery and right and left pulmonary arteries, also note increased pulmonary vascular markings.

BMV shortens the in-hospital stay and eliminates the risk imposed by thoracotomy and anaesthesia. The major drawback of BMV, however, is the fact that services of a skilled cardiologist backed by a team of cardiac surgeon and anaesthesiologist are necessary. Therefore, the number of centres, where BMV can be performed may be limited in the developing countries.

Closed mitral valvotomy/Open mitral valvotomy/Mitral valve replacement

Due to sheer number of patients and economic reasons, closed mitral

valvotomy (CMV) is still the preferred operation in the developing countries. The long-term results of this operation are reported to be satisfactory.[24,25] In a recent report comparing the results of CMV versus BMV at one week and one year after the procedure, it has been shown that the results of CMV are significantly better with regard to transmural gradient and mitral valve area at these times.[26] A significant decrease in the mean left atrial diameter and pulmonary artery pressure was observed in both groups. Open mitral valvotomy (OMV) is considered a better operation and is performed preferentially in developed countries. This is due to the fact that relief of valvular and subvalvular obstructive elements can be dealt with much better under direct vision.[27-30]

From the above discussion, it is apparent that in the developing countries, the choice of treatment for MS should be as follows: 1. BMV, if the facility is available; 2. CMV, if the facility for BMV is not available or there is a contraindication to BMV; 3. Open heart procedure such as OMV/MVR, if there is a contraindication to CMV, such as heavily calcified mitral valve or associated severe MR or other valvular lesion that needs open-heart procedure.

The main concerns in the anaesthetic management of patients with MS are to avoid tachycardia and hypovolaemia. Tachycardia should be avoided as it leads to an increase in the transmitral pressure gradient and hypovolaemia should be avoided as the patients have a limited preload reserve and it also leads to tachycardia. Preoperatively, majority of the patients will be in AF and receiving digitalis. It is necessary to continue digitalis preparations until the day of surgery and also to maintain normal potassium levels by potassium supplementation. Adequate premedication is necessary to prevent anxiety and tachycardia. Over-sedation also should be avoided as these patients may be sensitive to small doses of narcotics and hypnotics. Appropriate monitoring and supplemental oxygen therapy should be considered, if necessary. Morphine (0.1 to 0.2 mg/Kg) along with promethazine (12.5 to 25 mg) administered intramuscularly 1 to 2 hours before surgery is an adequate premedication for these patients. A small dose of benzodiazepine can be combined, but then the dose of morphine should be reduced. Scopolamine is also another choice as it has a direct action to slow the HR.[31]

Anaesthetic agents causing tachycardia or profound vasodilatation should be avoided. For CMV, thiopental administered slowly or a narcotic

(morphine 0.5 mg/Kg, fentanyl 5 to 10 μg/Kg) is a good choice. Due to the common practice of extubating patients at the end of CMV, there is a tendency to restrict the dose of narcotic to avoid excessive respiratory depression. However, it has been shown that elective ventilation for a few hours in the postoperative period should be preferred[32] and hence, higher dose of morphine/fentanyl that provides haemodynamic stability to these patients should be used for induction of anaesthesia. For selecting a neuromuscular blocker, it should be remembered that vecuronium when administered along with narcotics can lead to dangerous bradycardia.[33-35] Pancuronium is, therefore, generally preferred by most anaesthesiologists as a muscle relaxant in these patients, unless the basal heart rate is high.[35] Other muscle relaxants such as atracurium and rocuronium can also be used. Rocuronium also causes some increase in the HR due to its slight vagolytic action and has been shown to decrease the PA pressure.[36] It thus, appears to be a good choice for patients with MS. Benzodiazepines such as diazepam and midazolam should be used cautiously in small increments as they can lead to profound vasodilatation, especially if used with narcotics.[37] Maintenance of preload is another important goal and appropriate replacement of blood loss is desirable. For detailed discussion on the anaesthetic management of CMV, refer to chapter 8.

For patients undergoing open-heart procedures, high-dose narcotic technique with pancuronium or vecuronium should be preferred. It should be remembered that maintenance of haemodynamic stability is of prime importance and that this is more difficult and important if the disease is severe. Careful selection of drugs and their doses is important while anaesthetising a patient with severe MS (valve area <1 cm^2 and severe PAH). It is a good practice to administer increments of small doses of anaesthetic agents so that precipitous haemodynamic changes are avoided. It is also necessary to have a good venous access so that intravascular volume can be maintained properly and if necessary, quickly.

Intraoperative use of vasodilator therapy (nitroglycerin or nitroprusside, 0.5 to 1 μg/Kg/min.) is desirable in patients having severe PAH as it helps to off-load the strained RV and improves transpulmonary filling of the LV. It can be continued in the postoperative period.

Use of vasoconstrictors to treat transient episodes of hypotension should be performed carefully as it can lead to an increase in the RV afterload and RV

failure. An inotrope (dopamine, dobutamine, epinephrine) along with proper filling conditions is more appropriate.

Intraoperative monitoring should include electrocardiogram (ECG), direct arterial pressure and CVP. CVP provides valuable information about loading conditions, and the CVP catheter offers a means of transfusing inotropes and/or dilators. Pulmonary artery catheter (PAC) provides very useful information. PCWP, together with CO measurements offers a very good estimate of the overall ventricular function. However, PCWP overestimates the LVEDP because of pressure gradient across the mitral valve. PAC is also a useful means of monitoring the pulmonary artery (PA) pressure, which is especially desirable in patients having severe PAH with RV dysfunction. The PAC helps to evaluate the effects of therapeutic intervention. The use of LA catheter may be considered in postbypass period in patients in whom PCWP is not the reliable indicator of LA pressure.

In the postoperative period, it is important to avoid even mild hypercarbia (up to 48 mm Hg) which causes significant increase in PVR and RV end-diastolic pressure (RVEDP) suggesting RV stress.[32] It is, therefore, desirable to electively ventilate the patients in the postoperative period (even those who have undergone CMV) and maintain normocarbia at all times.[32] Increased pulmonary blood volume[17] and increased extracellular lung water[18] lead to decrease in lung compliance and exacerbation of ventilation perfusion inequalities in MS. These are, therefore, additional reasons for elective ventilation in the postoperative period. The inotropic support and the vasodilator therapy should be continued for a prolonged period (24 to 48 hours) in patients having severe PAH.

In summary, MS is a common valvular lesion and cardiac anaesthesiologist will frequently need to anaesthetise patients suffering from severe MS for cardiac surgery and sometimes for non-cardiac surgery. Avoidance of tachycardia and hypovolaemia are the key issues on which the selection of drugs should be based. Narcotic-based anaesthetic technique appears to be preferable. Aggressive haemodynamic monitoring and postoperative care may be necessary.

Mitral Regurgitation

Clinical presentation

Structural abnormality of the mitral valve leaflets, chordae tendinae and the papillary muscles leads to an incompetent valve. Excessive LV dilatation can produce mitral annular dilatation leading to functional MR. Mitral valve prolapse has been reported to be a common disease in the developed countries with the prevalence reported to be 2.4 percent according to the Framingham heart study.[38] In a large recent sample, however, the prevalence has been reported to be much less, 0.6 percent.[39] As already pointed out rheumatic fever continues to be the most common cause of MR in the developing countries, and it is frequently associated with MS. Myocardial infarction (MI) is also an important cause of MR and has been found to be present in almost one-third of patients undergoing angiography for CABG.[40] Although ischaemic MR is amenable to surgical repair, it has been controversial whether this intervention should be routinely performed along with CABG. A recent randomised trial has shown that MV repair in addition to CABG surgery adds a significant outcome advantage in terms of postoperative haemodynamics, ventricular function and degree of heart failure.[41] However, there was no short-term mortality reduction.

There has been a significant change in the surgical approach to mitral pathology over the past decade. The success and safety of MV repair has been established and valve repair is now preferred over valve replacement.[42,43] This holds true even in asymptomatic severe MR.[44] The application of transoesophageal echocardiography (TOE) has played a pivotal role in this transition and it is now considered a standard of care for these procedures.[42] The various techniques employed to repair the MV include, quadrangular resection, neochordae, and commissuroplasty. These may be performed singly or in combination. In addition, rigid mitral annuloplasty is also performed.

Advances have also taken place in minimally invasive mitral valve surgery via hemisternotomy or limited right thoracotomy.[45] Further, transcatheter mitral valve repair without CPB has been shown to be safe and feasible. These techniques include transcatheter edge-to-edge repair with mitral clips and trans-catheter mitral valve annuloplasty.[46,47]

The advantages of MV repair over MVR include enhanced survival, better preservation of ventricular function, and longer freedom from endocarditis,

thromboembolism and anticoagulant-related haemorrhage.[48] Therefore, mitral valve repair is recommended over MVR whenever possible.[48] However, feasibility of the repair and the expertise available should be a consideration in the final decision, as MVR is a reasonable alternative. There are patient subgroups that significantly benefit from MVR such as the elderly and complex mitral valve pathology. Preservation of the subvalvular apparatus during MVR is currently the preferred technique for improving the postoperative outcome.

Acute MR may result due to destruction of the valve (chordae) as occurs in the acute endocarditis and although rare, it can still be found in the developing countries. In addition, rupture of papillary muscles or chordae tendinae following acute MI can also lead to acute MR that is a fairly dangerous condition carrying a high mortality. Lately, however, another important cause of acute MR has emerged, that is traumatic disruption of the mitral valve during BMV.[22,49-51] The number of patients undergoing BMV has increased considerably. At G. B. Pant hospital alone, about 1000 patients undergo BMV every year. With about 1 percent incidence of acute severe MR during the procedure, a sizable number of patients will require surgical intervention and, hence, the cardiac anaesthesiologist should be familiar with all the aspects of acute MR in this group of patients.

In chronic MR, the symptoms depend upon the volume of regurgitation as well as the status of LV contractility. The LA is dilated and due to its compliance often protects the pulmonary circulation. The symptoms, therefore, appear quite late and acute pulmonary oedema is a relatively uncommon initial presentation.[52] The initial symptoms are those of a “forward” cardiac failure such as chronic weakness and fatigability. However, as the disease progresses, pulmonary congestion leading to breathlessness appears and is the predominant symptom. In acute MR on the contrary, LA pressure rises precipitously leading to acute pulmonary congestion as well as a decrease in CO.

Echocardiography with the capability of two-dimensional and colour-flow Doppler imaging is the diagnostic method of choice for the assessment of MR. Cardiac catheterization is rarely required. Some other diagnostic tests that are usually performed include ECG and chest radiograph. ECG findings such as AF, LA enlargement (tall or biphasic P wave), and ST segment abnormalities may be observed, but they are not specific. The chest

radiograph may reveal enlargement of left heart chambers and pulmonary vascular congestion.

Pathophysiology

Ventricular systole ejects blood into the aorta as well as the LA. The LA acts as a low pressure vent for the LV ejection. This blood returns to the LV with each successive diastole, thus causing volume overload of the LV. The ejection begins immediately with the onset of ventricular contraction so that there is no period of isovolaemic contraction (Fig. 5.7). The total SV consists of forward flow into the aorta and the backward flow into the LA. As the LA acts as a low pressure vent, EF may be normal even though the ventricular contractility is subnormal. The ventricular size and compliance increase so that large end-diastolic volumes can be accommodated without causing significant increases in the LVEDP. Thus, patients may tolerate the chronic compensated MR for many years as elevated preload maintains the LV ejection. The symptoms at this time are often related to reduced forward output and include fatigue and weakness.

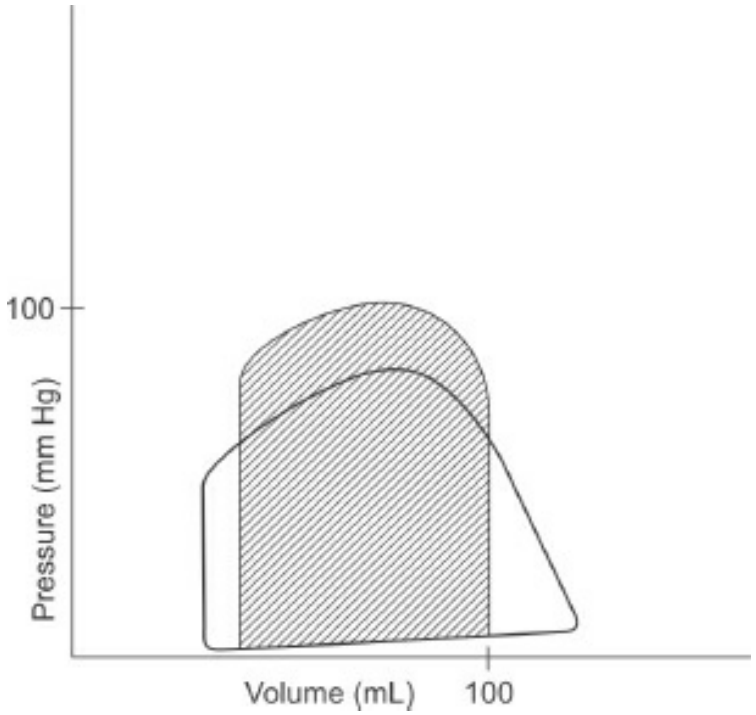

Figure 5.7: Pressure volume loop of mitral regurgitation. Note that there is no period of isovolaemic contraction. For details refer to the text (This is a diagrammatic and not an accurate representation.)

The LA enlarges, but the increase in LA pressure is related to the volume

of MR and the compliance of the LA. In some patients there is a dramatic increase in the LA compliance so that large increases in the LA pressure and pulmonary venous hypertension are prevented. If the disease is left untreated, however, eventually there is an increase in the LA pressure leading to pulmonary vascular congestion, PAH and RV dysfunction. Figure 5.8 demonstrates the radiological evidence of severe PAH in a patient suffering from severe MR. In such patients, the ventricular compliance also decreases and raised LVEDP along with massively dilated LVs are present. Ventricular dysfunction develops, but is often not apparent as the ventricular ejection is helped and accommodated in the LA that is a low pressure chamber. Therefore, EF may be a misleading estimate of myocardial contractility. In patients with severe MR, an ejection fraction in the range of 50 to 60 percent may represent significant LV dysfunction and is an indication for surgery.[53] The intrinsic depression of contractility is often not apparent until after MVR, when the competent prosthetic valve makes the LV contract against systemic resistance. This afterload mismatch imposed on a ventricle having significant preoperative contractile dysfunction can account for the decreased EF in the postoperative period.[54] Indeed, a marked impairment in global systolic pump function that correlated with the left ventricular afterload has been observed with the help of TOE.[55] However, the issue is controversial as some studies have not been able to document the expected increase in the end-systolic volume, if the afterload is increased.[56,57] Therefore, other aetiologies such as residual effects of past myocarditis and technical aspects of the operation itself may be operational.[58]

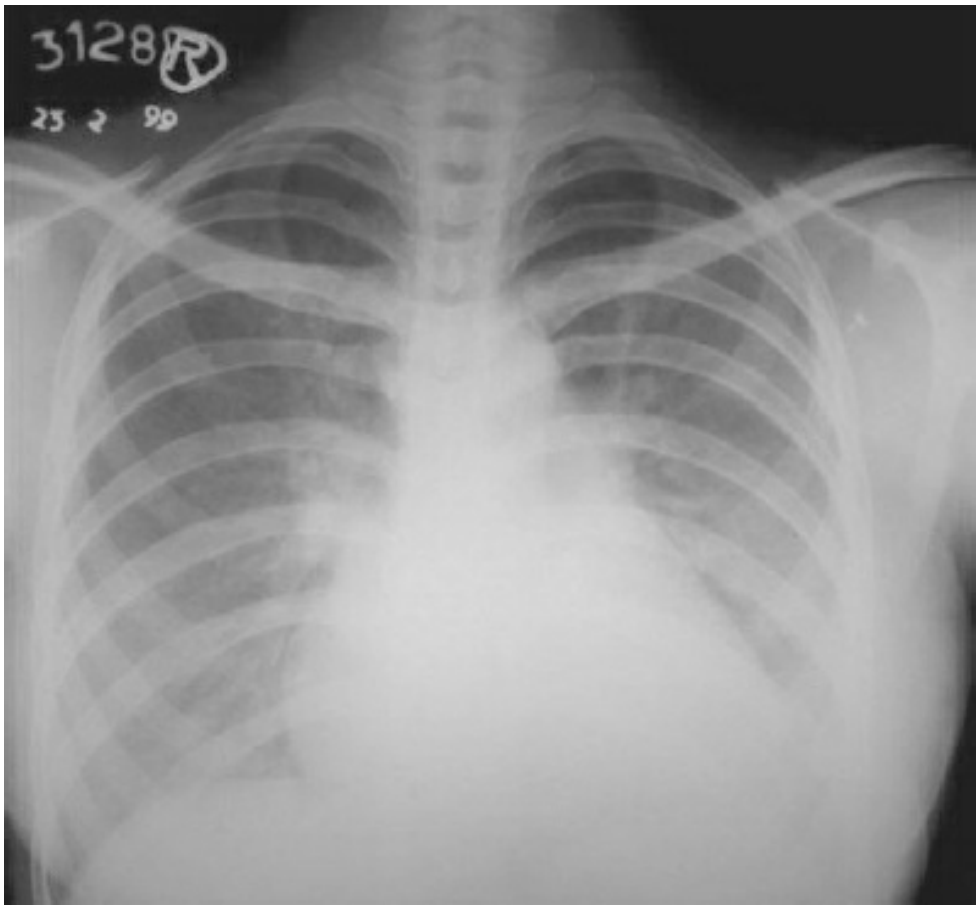

Figure 5.8: X-ray chest showing severe pulmonary artery hypertension in a patient with severe mitral regurgitation. Note the prominent main pulmonary artery and increased pulmonary vascularity.

There is a significant decrease in the heart size as well as the pulmonary hypertension (Fig. 5.9) following surgery in patients with severe MR.[59,60] However, the operative as well as the postoperative morbidity and mortality rates are higher for patients with MR.[61-63] In acute MR, there is no chance for the LA and LV to compensate for the acute volume load. Therefore, sharp increases in the LA and PA pressures are produced leading to acute pulmonary oedema. This may cause pulmonary hypertension and right ventricular failure that is often accompanied by catastrophic haemodynamic compromise.

Ischaemic Mitral Regurgitation

The MR occurring in patients with ischaemic heart disease without significant abnormalities of the valve leaflets or chordal structure is labeled as ischaemic MR. The incidence is quite common, and is detected by echocardiography in 39 to 75 percent of patients with acute MI.[64] The most

common pathophysiological basis of ischaemic MR is outward papillary muscle displacement.[64] The outward displaement of papillary muscles leads to apical displacement of the point of mitral leaflets coaptation resulting in valve tenting. Another cause is scarring and retraction of the papillary muscles leading to mitral leaflet feathering and incomplete leaflet coaptation. Papillary muscle rupture leading to acute severe MR is also included in the ischaemic MR, although a clear organic defect of the mitral valve is present.

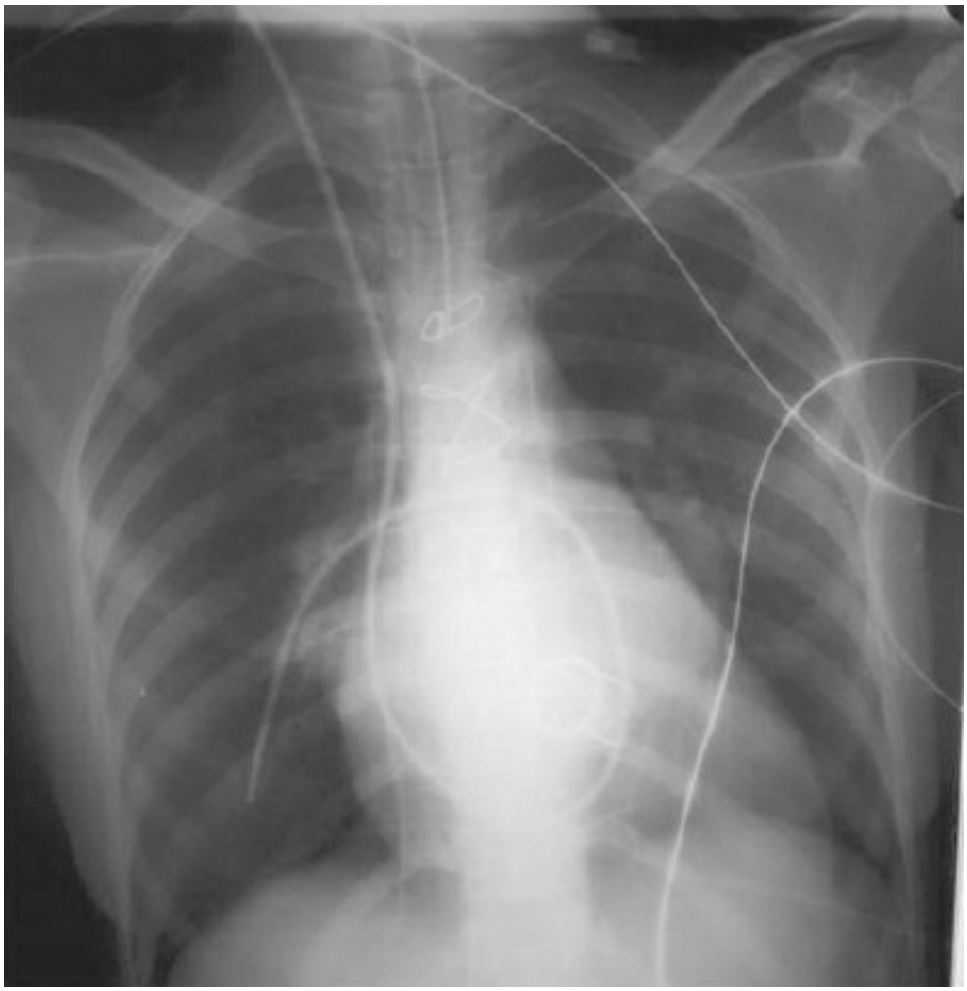

Figure 5.9: Postoperative chest X-ray of a patient who has undergone mitral valve replacement for severe mitral regurgitation. Note the decreased pulmonary vascularity.

Anaesthetic Considerations

The anaesthetic management is aimed at maximising the forward flow and reducing the regurgitant flow. In addition, RV function should be optimized by avoiding increases in PVR and pulmonary hypertension. A patient who experiences dyspnoea at rest or with minimal activity may have pulmonary

vascular congestion and compromised RV function. Right ventricular systolic pressure reported in the preoperative transthoracic echocardiography can help to identify such patients. Vasodilatation can improve the forward flow and significantly decrease the regurgitant flow. Both nitroprusside and nitroglycerin infusions can be used for this purpose. They can also produce sustained vasodilatation in the pulmonary circulation in a dose-dependent fashion[65] and therefore, can be useful in patients with PAH to lower the afterload of the RV. Prostaglandin E_1 is a better and more effective agent in this respect.[66] Inhaled nitric oxide is another alternative available for the treatment of RV failure in the setting of pulmonary hypertension. Nitric oxide dilates the pulmonary vasculature and is then immediately bound to haemoglobin and inactivated. It has an advantage that it does not cause systemic hypotension.[67] However, pulmonary vasodilators are not very useful once the RV failure sets in due to severe PAH. Therefore, strictly following the basic principles of anaesthesia, i.e. avoidance of hypoxia, hypercarbia and acidosis (all cause increase in PAH) are very important.

A slightly increased HR (80 to 100 beats/min.) is desirable as slower heart rates allow for larger filling volumes that can lead to LV distention and mitral annular dilatation. Thus, regurgitant volumes may increase at slower heart rates. Therefore, pancuronium bromide is the preferred muscle relaxant in these patients. Hypovolaemia should be avoided, in fact, it is preferable to have a slightly ‘fuller’ patient so that adequate preload is maintained at all times. This is particularly important as vasodilators are preferred in these patients and therefore, patients are susceptible to become hypovolaemic.

Another important consideration is the fact that afterload is increased after MVR as the low pressure chamber (LA) is no longer available for LV ejection. The LV dysfunction can therefore be precipitated in the postoperative period. Use of inotropes (to improve contractility) and vasodilators (to reduce the afterload) are quite important during the early postoperative period. It is a practice in the author’s unit to start infusions of nitroglycerin and inotropes (usually epinephrine) well before the bypass is terminated and the infusions are continued in the postoperative period. Alternatively phosphodiesterase inhibitors such as enoximone, milrinone or a combination of dobutamine and nitroglycerin may be used during this period. It has been shown that enoximone infusion causes increases in CO, blood pressure and HR that are similar to those caused by a combination of

dobutamine and nitroglycerin.[68] In addition, enoximone is more effective in reducing the PA pressure.[68]

Light premedication is preferable and a large-dose narcotic induction (due to its relative lack of myocardial depression) is used, as intrinsic myocardial dysfunction may be present in these patients. Alternatively, a combination of opioids and benzodiazepines can also be used to provide adequate haemodynamic stability. Combination of fentanyl and midazolam or sufentanil and midazolam administered either as a continuous infusion or intermittent bolus can be used. It has been shown that induction with sufentanil (up to 2 μg/Kg) and midazolam (0.05 to 0.15 mg/Kg); followed by a continuous infusion of sufentanil 3.6 μg/Kg/hour and midazolam 0.08 mg/Kg/hour provided haemodynamic stability similar to those of bolus administration.[69] This suggests that other drugs can also be utilised in the form of an infusion without compromising the haemodynamic stability. As has already been mentioned, pancuronium bromide is the preferred neuromuscular blocking agent but atracurium or vecuronium may be used depending upon the basal HR of the patient. Inhalational agents (halothane, isoflurane) may be used as both can produce vasodilatation. The use of nitrous oxide has declined in the USA and narcotic-oxygen technique is widely used.[70] Nitrous oxide can cause an increase in PVR[71] and therefore, should be used with caution in patients who have severe PAH. It is not used after the institution of CPB mainly due to the fear of expansion of air bubbles, but it can be used cautiously before CPB is instituted. This is possible after a good anaesthetic induction which leads to a decrease in the PA pressure. The CVP and PA pressure monitoring are important. The CVP is important to assess the RV function. The PA pressure measurements are useful for assessment of the intravascular filling and measurement of the CO. It is particularly useful in patients with severe PAH, in the sense that effects of therapeutic intervention on the PA pressure can be evaluated. TOE is useful to assess valve repair procedures as well as prosthetic valve function and LV dysfunction. It is also useful to confirm complete removal of air from the LV before the release of aortic cross clamp.

TOE is an excellent haemodynamic monitoring tool. It provides an objective measure of chamber sizes and contractility. In particular, appearance of systolic anterior motion (SAM) immediately after valve repair can guide the anaesthesiologist to institute appropriate therapy. SAM results due to reduced septal-anterior leaflet distance following repair creating a

narrowed channel that leads to pressure gradient across the outflow tract. The increased blood velocity creates a venturi effect that pulls the anterior leaflet of the mitral valve or the chordal structures into the outflow tract. This results in mechanical obstruction of the left ventricular outflow tract (LVOT) as well as MR. Beta-blockers or phenylephrine can be administered to correct the haemodynamic compromise. If the haemodynamic compromise persists after the therapy, the surgeon may choose to further repair or replace the mitral valve. A recent paper has described how the circumflex coronary artery can be visualised in the modified mid-oesophageal long-axis view of the aortic valve.[72] This can help to diagnose the possible complication of the mitral valve surgery, i.e. iatrogenic injury to the circumflex artery leading to compromised flow. The authors suggest that visualisation of the circumflex artery with their technique should be performed more frequently in patients undergoing mitral valve surgery.

It has been suggested that a subset of patients with severe PAH who undergo MVR may be at an increased risk of developing acute, isolated RV failure in the immediate postbypass period.[70] Acute pulmonary vasoconstriction of unknown aetiology leading to increase in PVR has been suggested to be the precipitating factor. However, in the author's experience, such a phenomenon is extremely rare. In fact, it has been shown that following MVR, in patients having severe PAH, the indices of RV stress such as PVR, RVEDP, mean pulmonary artery pressure (MPAP), etc. decline significantly and rapidly.[59,60] Nevertheless, manoeuvres that are known to induce increase in PVR like protamine administration should be performed carefully, and factors such as even mild hypercarbia should be avoided in the postoperative period in patients having severe PAH. This is important as there is no effective treatment available for the full blown syndrome of acute severe exacerbation of PAH leading to RV failure. Inhaled nitric oxide, adenosine, prostaglandins and phosphodiesterase-III inhibitors have been shown to be helpful in decreasing PAH and can be used in such a situation.

Acute Mitral Regurgitation

Rupture of the papillary muscle or chordae tendinae following acute MI can cause acute MR. Such a patient may enter the operating room in cardiogenic shock with pulmonary congestion necessitating intra-aortic balloon pump (IABP) support. The anaesthetic goals, however, remain similar. Hospital mortality rate in patients undergoing combined CABG and MVR has been

reported to be very high.[73,74] Therefore, some surgeons have advocated a conservative approach of CABG alone for patients with a moderate ischaemic MR. However, some authors have reported successful outcome in patients undergoing elective as well as emergency MVR plus CABG following acute MI.[75,76]

Results of emergency MVR following acute MR during BMV are not well reported. However, it has been shown that the indices of RV stress (PVR, MPAP, RVEDP) do not decrease early after surgery and hence, careful haemodynamic management is necessary for these patients.[51]

Finally, “transverse midventricular disruption” is the most dreaded complication after MVR and is usually fatal. The aetiological features include, implanting a disproportionately large valve, direct surgical injury and sudden overdistention of the LV after CPB.

Aortic Stenosis

Clinical Presentation

There is a left ventricular outlet obstruction at the level of aortic valve. Stenosis of the aortic valve may be either congenital or acquired. The acquired AS is most commonly of rheumatic origin in the developing countries. In the developed world however, it is non-rheumatic in origin and usually results from calcification or degeneration of a congenitally bicuspid or a previously normal tricuspid valve.[6] With the increasing longevity of life, more and more elderly patients are presenting with AS. Functional outcome after aortic valve replacement (AVR) in these patients is reported to be good.[77] The classic symptoms of the disease include angina, syncope, and congestive heart failure (CHF). Although, clinical symptoms do not correlate with the severity of AS, appearance of symptoms indicate that early treatment is necessary as the risk for development of complications is increased.[78]

Angina and CHF are related to the concentric hypertrophy of LV that increases the wall thickness and syncope is related to the decreased CO due to obstruction to the SV. Thus, patients with AS experience angina even without CAD. However, CAD is known to frequently coexist with AS, especially in older patients. A large study found that 14 percent of patients with triple-vessel or left main CAD and AS presented without angina.[79]

Identification of such patients is crucial, as combined CABG and AVR can be performed in them for better outcome.[80] Since, rheumatic AS occurs more frequently in younger patients in the devloping countries, associated CAD is a relatively rare phenomenon.

Advances in Doppler echocardiography allow for the completely noninvasive evaluation of the patients with AS. However, coronary angiography is indicated in patients over 50 years of age who have significant AS. Many centres follow the practice of routinely performing coronary angiogram in patients of > 40 years of age. Concomitant CABG may be necessary in patients who have CAD.

Pathophysiology

The normal aortic valve orifice is 2.5 to 3 cm^2 and severe AS is defined as an area of less than 1 cm^2.[81] As a result of obstruction to the LV outlet, the LV has to work against pressure (pressure overload) leading to concentric ventricular hypertrophy. The muscle mass is increased to cope with the pressure overload but the cavity size remains the same. It is this limitation of the cavity size that limits the SV and consequently the CO at the slow HR. The peak pressure generated during systole is much higher due to a high transvalvular pressure gradient (Fig. 5.10). The thickened LV wall is also responsible for decreasing the compliance of the LV and therefore, the diastolic pressure volume relationship is shifted upward, meaning thereby that small changes in the diastolic volume produce relatively large increase in the ventricular filling pressure. The ventricular filling depends upon adequate intravascular volume and atrial contraction. Therefore, normal sinus rhythm is very important in these patients as atrial contraction can contribute up to 40 percent of the ventricular filling (normal 15 to 20 percent).

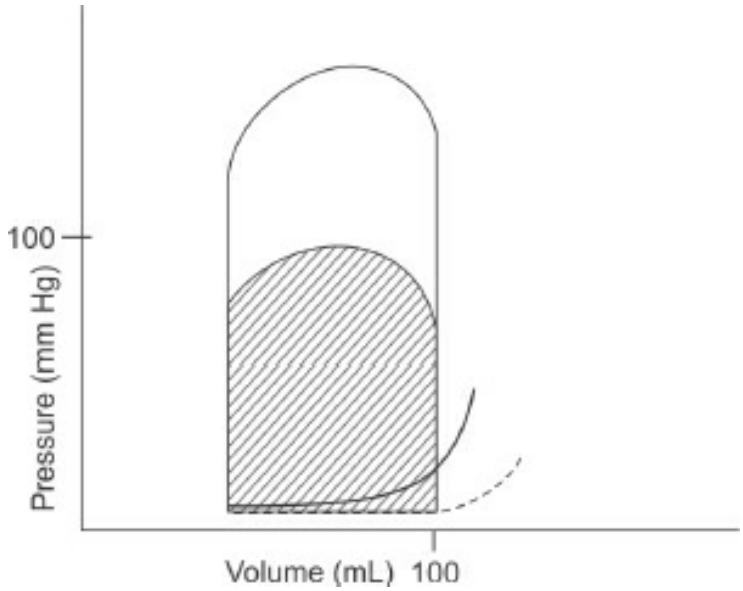

Figure 5.10: Left ventricular pressure volume loop in a patient with aortic stenosis. The diastolic pressure volume relationship is shifted upward and peak pressure generated during systole is much higher. Refer to the text for details. (This is a diagrammatic and not an accurate representation.)

Due to a decrease in the ventricular compliance, LVEDP is often elevated leading to pulmonary congestion and symptoms of dyspnoea. This is an example of diastolic dysfunction where symptoms of CHF are caused by the raised LVEDP due to a stiff ventricle (ventricle unable to relax during diastole) rather than the inability to empty (systolic dysfunction).

Myocardial ischaemia results because of decreased coronary perfusion pressure (CPP) due to a raised LVEDP (CPP = diastolic aortic pressure-LVEDP). With severe outflow obstruction, SV is decreased and the resultant systemic hypotension can further compromise the coronary perfusion. In addition, the coronary vascular reserve is decreased due to increased basal oxygen requirements of a thick pressure overloaded ventricle. Any associated CAD will compromise the situation further. Structural abnormalities of coronary circulation (coronary vessels not enlarging in proportion to the LV hypertrophy) may also be a contributory factor.

Myocardial contractility is usually well preserved with a normal ejection fraction until very late in the course of the disease. In fact, the hypertrophied LV is also hypercontractile to maintain SV in the presence of obstruction to flow. Late in the disease, however, contractility can decrease leading to a decrease in the gradient across the aortic valve.

Anaesthetic considerations

The anaesthetic management revolves around maintenance of the sinus rhythm and adequate intravascular volume and avoidance of systemic hypotension. It must be remembered that patients are susceptible to develop myocardial ischaemia and that resuscitation is extremely difficult in the event of ventricular fibrillation (VF).

As has been already highlighted, maintenance of sinus rhythm is crucial. Any arrhythmias such as AF or junctional rhythm can lead to severe hypotension. Since the SV is limited, the CO is rate dependent and bradycardia can cause a decrease in the CO. Tachycardia on the other hand can be tolerated for short periods but can lead to myocardial ischaemia by disturbing the myocardial oxygen supply-demand and by decreasing the time for coronary filling. The use of vasodilators is contraindicated as the stroke volume is relatively fixed across the narrowed valve. Vasodilatation reduces the SVR without any increase in the SV and leads to hypotension. However, it has been shown that vasodilator therapy with nitroprusside leads to decrease in PCWP and SVR and an increase in SV.[82] The dose of nitroprusside was carefully titrated to maintain mean arterial pressure (MAP) of 60 to 70 mm Hg in this study. Such a therapy may be used in patients with severe AS as a temporary bridge to AVR.[82]

Patients with AS generally have lower systemic blood pressure. Occasionally, increase in systemic blood pressure during intubation or surgical stimulus can occur leading to severe increase in the LV systolic pressure. The severity depends upon the gradient across the aortic valve, e.g. if the gradient is 80 mm Hg, the LV pressure is 180 at a systolic blood pressure of 100 mm Hg. Slight increases in the systemic blood pressure can therefore, cause substantial increases in the LV pressure (presuming that flow across the valve remains constant) and therefore, increase wall tension in the LV leading to ischaemia.

Due to the reasons cited above, a very precise control of haemodynamics during anaesthesia is important in patients with AS. Adequate premedication with morphine or benzodiazepine is required to reduce the likelihood of preoperative anxiety and tachycardia. Narcotic based induction is desirable to avoid haemodynamic disturbances. It ensures good analgesia and adequate depth of anaesthesia during intubation so that the reflex sympathetic responses to intubation are blunted. For intubation, a muscle relaxant devoid of cardiovascular effects is desirable. Metocurine has been found to produce minimal increase in the HR and mild vasodilatation when used in patients

with AS, who are anaesthetised with morphine and diazepam.[83] Pancuronium can be advantageous if used with narcotics as it counters the bradycardia produced by narcotics. Vecuronium and atracurium are reasonable alternatives but they can potentiate bradycardia produced by narcotics. It may be useful to take into consideration the basal HR of the patient for appropriate choice of the muscle relaxant. The adverse haemodynamic response to intubation should be treated by administration of increments of thiopental (if hypertension occurs) and a beta-blocker (if tachycardia occurs) after intubation. Low concentrations of inhalational agents may be used and continued to maintain anaesthesia. Another alternative to control persistent hypertension is the infusion of nitroglycerin as the risk of myocardial ischaemia is always present in these patients.

Intraoperative hypotension, regardless of the cause should be aggressively treated. A direct alpha adrenergic agonist such as phenylephrine or norepinephrine can be used in order to maintain coronary perfusion pressure. The primary cause of hypotension (e.g. hypovolemia, arrhythmia), should also be tackled aggressively. If necessary, CPB should be instituted as soon as possible.

Induction of anaesthesia can be really dangerous in patients who have critical AS with LV dysfunction. Such patients have low transvalvular pressure gradients and the operative mortality is increased. However, AVR is associated with improved functional status.[84] Percutaneous femoro-femoral bypass under local anaesthesia can be instituted before the administration of general anaesthesia to prevent the haemodynamic disturbances.[85]

Intraoperative monitoring should include standard ECG leads, including the V5 lead. CVP is a poor estimate of the LV filling as the LV compliance is reduced. PAC can be very useful in these patients, but can sometimes induce arrhythmias. Loss of sinus rhythm compromises the diastolic filling of a poorly compliant LV resulting in hypotension. However, PAC provides the measurement of PCWP that is a fairly good indicator of LV filling in patients with AS, and helps in the fluid management of patients. In addition, CO measurements along with the calculated haemodynamic parameters can also be carried out. Therefore it, appears worthwhile to accept a small risk of arrhythmias in these patients. In any case, if there are persistent arrhythmias, the PAC can be withdrawn and replaced with an ordinary central venous catheter through the sheath that is used for the insertion of PAC.

The risk of intraoperative myocardial injury in these patients also needs to be considered and utmost care in the myocardial preservation should be observed. The retrograde cardioplegia via coronary sinus along with an initial dose of antegrade cardioplegia can be used.[86] Irreversible ischaemic contracture termed as “stone heart” is reported to occur following AVR in patients with severe LV hypertrophy.[87,88] Such a complication is rare these days mainly due to the improvements in myocardial preservation techniques. However, in the author’s experience, severe LV dysfunction following AVR in patients having severe concentric hypertrophy is not unknown. These patients have a raised LA pressure and need prolonged support on CPB before it can be terminated. Occasionally, IABP support is also necessary. Calcium channel blockers (verapamil, nifedipine) are known to improve the diastolic performance in patients with hypertrophic states[89,90] and can also be helpful. It is also justified not to use calcium to improve the inotropic state of the heart in these patients.

Percutaneous balloon aortic valvuloplasty

Percutaneous balloon aortic valvuloplasty has limited applications and has two main indications: 1. very old patients with surgical risks, and 2. critically ill patients in whom the procedure is most often used as a bridge to surgery. It has been shown in a large series of 180 elderly patients that the technique is able to efficiently palliate the symptoms and improve survival.[91] Balloon aortic valvuloplasty is a low-cost and low-risk procedure in experienced hands requiring only local anaesthesia and a short hospital stay. Anaesthesiologist is generally requested to remain standby during the procedure to manage resuscitation, if necessary.

Trans-catheter aortic valve Implantation

The recent development of TAVI to treat severe AS has emerged as a viable option for high-risk patients, who are likely to have high operative mortality for surgical correction during CPB. Retrograde transfemoral AVR can be performed under local anaesthesia plus sedation, whereas antegrade transapical AVR is performed under general anaesthesia. General anaesthesia facilitates the use of TOE. Recent clinical studies have proven the feasibility of TAVI with early improvement of the global LV performance.[92-94] Two major systems are available, the Edwards SAPIEN and the Medtronic Core

Valve.

The procedure involves performance of a balloon aortic valvuloplasty followed by placement of the valve. The valve containing application system is positioned under the TOE and fluoroscopic guidance. The valve is instantaneously implanted after rapid inflation of the balloon. The implantation sheath and guidewire are then retrieved. The correct valve position is confirmed by a single shot aortic root angiography and TOE. Rapid ventricular pacing (RVP) with the rate of 180 to 220 beats/min is initiated both during valvuloplasty as well as valve implantation.

The anaesthesia should include adequate premedication followed by opioid based induction. In addition to usual monitoring, TOE probe should be inserted and external defibrillator pads should be placed. The specific anaesthetic challenges of this procedure are as follows.[95]

- Preparation for emergency CPB: Femoral venous and arterial wires should be placed to initiate emergency CPB.
- Avoidances of hypothermia: External convective warming devices and warm intravenous fluids should be used.
- Haemodynamic and volume management: Adequate volume should be infused in order to maintain CVP above 10 cm H_2O and MAP above 65 mm Hg. Inotropes (epinephrine in presence of LV dysfunction and non-epinephrine in patients with normal LV function) should be infused in order to maintain MAP of > 65 mm Hg. The MAP should be increased to 75 mm Hg before RVP in order to avoid the significant decline in MAP seen post-RVP.
- Rapid ventricular pacing: The pacing is instituted during balloon valvuloplasty and aortic valve implantation in order to decrease the systolic arterial pressure to below 60 mm Hg. The pacing is terminated once the balloon is adequately deflated.
- TOE monitoring: The entire TAVI procedure should be monitored by TOE. The mid-oesophageal long-axis view and the mid-oesophageal short-axis view of the aortic valve are used to assess the valve position and function. Measurement of aortic annulus diameter is essential for valve size selection. In addition, volume status and LV function should be monitored by TOE.
- Postoperative management: This entails maintenance of haemodynamics and offering adequate pain relief. Early extubation is attempted in all

patients.

As already mentioned, the procedure can be performed via trans-femoral route and transapical approach using a minithoracotomy incision. In presence of contraindication for transfemoral TAVI, the procedure can be performed via transaxillary approach.[96] The complications of the procedure include local bleeding, obstruction of the coronary ostia, and neurological insult due to embolization of sclerotic material.[97] AR due to paravalvular leak or inadequate device expansion can also occur. Renal dysfunction may occur if excessive contrast medium is used. Heart failure and atrioventricular block requiring a pacemaker are the most frequent cardiac complications. Further, the success of the procedure depends on a successful valvuloplasty. Thus, if the valvuloplasty fails, (e.g. densely calcified AV), the procedure may have to be abandoned or converted to the conventional AVR under CPB.

Hypertrophic Obstructive Cardiomyopathy

Hypertrophic obstructive cardiomyopathy (HOCM) is a rare familial disorder in which there is marked hypertrophy of the histologically abnormal sarcomeres with disproportionate involvement of the inter-ventricular septum.[98] It is a common cause of sudden cardiac death in young people. The hypertrophy of the basal septum leads to narrowing of the LVOT and a pressure gradient across it. The progressive compensatory hypertrophy narrows the outflow tract and worsens the gradient. This can lead to occurrence of SAM. The degree of LVOT obstruction is dynamic and is exacerbated by increase in the contractility and heart rate. The other terms used to describe this condition are, idiopathic hypertrophic subaortic and muscular subaortic stenosis. However, the term hypertrophic cardiomyopathy is the preferred description and applies to patients with ventricular hypertrophy but without an obvious cause such as hypertension or AS.[99] The nonoperative treatment options include placement of an intracardiac defibrillator and alcohol ablation[100] of the septum. Surgical treatment includes myotomy-myomectomy, and MVR has also been used with good results as it abolishers the SAM.[101] Therefore the anaesthetic management revolves around fluid management and pharmacological interventions to

decrease the degree of obstruction. Generally, inotropic agents should not be used. The hypertrophied ventricle usually has reduced compliance and is load sensitive. Optimization of the preload and ventricular filling is important. Afterload reduction worsens the obstruction and should be avoided. Increase in the afterload decreases the trans-outflow tract gradient leading to reduction in SAM and LVOT obstruction. Therefore, vasoconstrictors such as phenylephrine are useful. Finally, reducing the heart rate by beta-blockers should also be considered.

Aortic Regurgitation

Clinical Presentation

AR is usually chronic and of rheumatic aetiology in the developing countries. Non-rheumatic causes of AR are bicuspid anatomy, infective endocarditis, connective tissue disorders (Marfan's syndrome) or trauma.

The natural history of chronic AR is characterised by a long asymptomatic period with a relatively rapid downhill course after the onset of cardiac symptoms.[102] Many indicators for the necessity and timing of valve replacement have been described, however, there are no gold standards. The surgical results, both in terms of mortality and reversal of LV dysfunction are reported to be unfavourable in patients who are in New York Heart Association class IV before surgery. However, in developing countries, patients may present for treatment at such a late stage and surgery is performed on them, as substantial clinical improvement is still possible.

During the asymptomatic interval, the valvular incompetence and secondary ventricular enlargement become progressively more severe.[103] The most common symptoms are those of CHF. Syncope and angina are rare. The severity of symptoms and their duration may correlate poorly with the degree of haemodynamic and contractile impairment.[104] The life expectancy for patients with clinically significant AR is about nine years.[105]

The patients with acute AR (endocarditis, trauma) usually present in intractable pulmonary oedema. They are hypotensive and respond poorly to medical management. Coronary perfusion pressure may be severely impaired by the combination of low arterial diastolic pressure and the markedly increased LVEDP. Immediate surgical intervention is necessary.

Pathophysiology

The blood ejected into the aorta flows back into the LV during diastole resulting in volume overloading of the LV. The degree of volume overload is determined by the regurgitant flow that depends upon the degree of incompetence, the aorto-ventricular pressure gradient during diastole and the duration of diastole. The ventricle adapts to this load by increasing the chamber size as well as the wall thickness (eccentric hypertrophy). The result is an increase in the end-diastolic volume and stroke volume (Fig. 5.11). The end-diastolic volume can increase 3 to 4 times the normal. The stroke volume is increased in proportion to the regurgitant flow so that the forward stroke volume is maintained. There is no isovolaemic relaxation as the LV starts filling during early diastole from the aortic valve before the mitral valve opens. If the contractility is impaired, ejection fraction and stroke volume decrease.

The slowly developing volume overload is tolerated much better by the heart as against the pressure overload (as in AS). The ventricular compliance is increased and large volumes can be accommodated without causing a significant increase in the LVEDP until very late stage of the disease. The LV hypertrophy can be severe in patients with long standing AR. Progressive volume overload can reach a point where compensatory hypertrophy is no longer sufficient and a decline in systolic function occurs. Preoperative end-systolic diameter of > 55 mm (on echocardiography) is taken as a risk factor in these patients.[106] The ACC/AHA guidelines suggest that ejection fraction less than 25 percent or the endsystolic diameter greater than 60 mm indicate that irreversible myocardial changes are likely to have occurred.[53] Surgical treatment before significant ventricular decompenstion offers excellent recovery with early regressions and remodeling of the LV.[53] Therefore valve surgery is recommended in asymptomatic patients with LV dysfunction or LV dilatation with normal ejection fraction.[53]

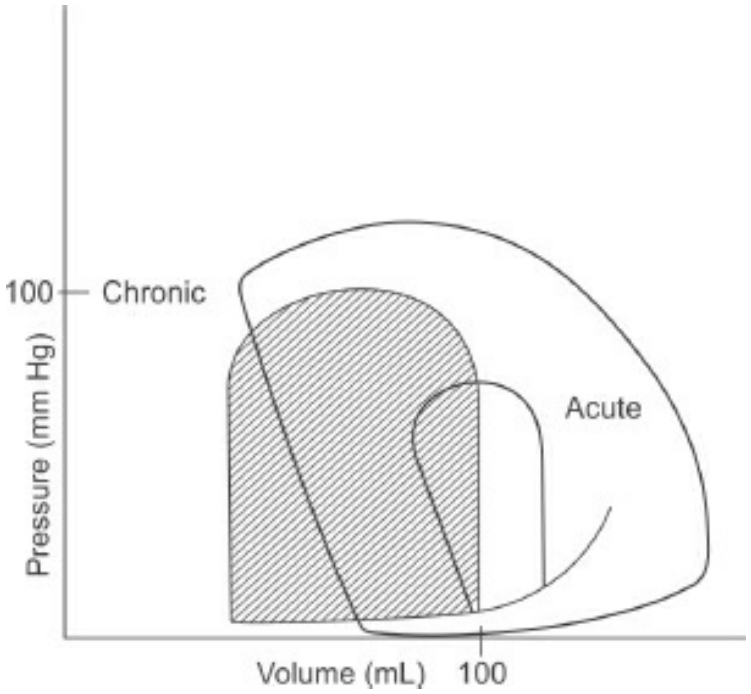

Figure 5.11: Left ventricular pressure-volume loop in a patient with aortic regurgitation (AR). Note the increase in end-diastolic volume and stroke volume. There is no isovolaemic relaxation, The end-diastolic pressure-volume relationship is maintained in chronic AR (not so in acute AR). For details refer to the text. (This is a diagrammatic and not an accurate representation.)

Myocardial ischaemia is relatively rare in patients with chronic AR. The contractility and wall tension that determine the oxygen consumption are usually normal (not elevated) in chronic AR. However, ischaemia may sometimes occur due to reduced oxygen supply caused by abnormalities of the coronary circulation resulting from LV hypertrophy.

In order to reduce the regurgitant flow, there is usually a compensatory tachycardia which reduces the diastolic time. A decrease in HR is not well tolerated as the diastolic time is increased and the LV filling continues to occur through the regurgitant valve. This might increase the LVEDP precipitously leading to myocardial ischaemia and arrhythmias.

Anaesthetic considerations

Patients with moderate AR (surgery is usually not performed in mild AR) without massive cardiomegaly or failure generally tolerate surgery well. Theoretically, vasodilatation and increase in HR decrease the regurgitant flow and therefore, should be the goals of safe anaesthesia. In particular, avoidance of bradycardia is important as it prolongs diastolic time and hence increases regurgitant flow and LVEDP. Consequently, the coronary perfusion pressure

decreases and a rapid LV dysfunction can set in. Vasodilatation by decreasing SVR on the other hand, decreases the diastolic pressure gradient across the aortic valve and reduces the regurgitant fraction of the SV.[107,108] It should be remembered, however, that adequate preload should be maintained during vasodilator therapy, otherwise, decrease in the venous return will produce further decrease in the SV. In addition, myocardial depressants should be avoided, if the patient also has LV dysfunction. Inotropic therapy should be instituted without wasting much time in these patients. Patients having an end-systolic LV dimension of > 55 mm are likely to be susceptible to myocardial depressants.

A light premedication will do well for patients with AR as myocardial depression is avoided and tachycardia, if any, is useful in these patients. Narcotic based induction is preferred to ensure haemodynamic stability. Pancuronium is the preferred muscle relaxant as it causes the beneficial increase in HR. The timing of surgery in patients with AR is controversial and it is still debated whether asymptomatic patients with AR should be subjected to surgery. However, in the developing countries, patients may present very late for surgery. Such patients will usually have long standing moderate to severe AR with severely hyper-trophied LVs. In addition, the LV contractility may be decreased necessitating careful management. It has been shown that 50 percent of patients do well after AVR in spite of preoperative contractility impairment.[109,110] The remaining 50 percent have a less satisfactory outcome following AVR. Such patients can be usually identified preoperatively based on their clinical symptoms and echocardiographic examination. Severity of preoperative symptoms especially, recurrent CHF along with a hypertrophied LV (end-systolic dimension of > 55 mm and end-diastolic dimension of > 70 mm) should alert the anaesthesiologist.

Careful titration of the narcotic dosage and fluid balance are important. Maintenance of faster HR is especially valuable and bradycardia should be promptly treated. Either nitroprusside or nitroglycerin infusion can be used for vasodilatation in these patients. Inotropes (dobutamine, epinephrine) should be used to improve the systolic function. The LV is prone to distend before placement of the aortic cross clamp, if it is not ejecting or being vented. This is so, as during this period, systemic cooling may induce bradycardia or arrhythmias. Cross clamping the aorta or venting the LV will correct this problem.

Another peculiar problem that may be encountered in these patients is the

inability to restore rhythm after release of the aortic cross clamp. This leads to excessive LV distention creating further difficulty in defibrillating the heart and restoring normal rhythm.[111] Use of LV venting through the LA or directly through the LV apex in order to restore beating empty state of the heart is recommended in these patients.[111] Simultaneous use of high dosage of inotropes to improve the LV contractility is also desirable. In a rare situation of persistent VF following aortic cross clamp release, amiodarone injection in the root of the aorta for successful defibrillation has been reported.[112]

As usual, the intraoperative monitoring should include ECG, direct arterial pressure and CVP. PAC can be useful, especially in patients who are known to have LV dysfunction. The measurement of CO and other haemodynamic parameters is also possible with PAC that may provide valuable information in terms of preload and afterload so that the vasodilator therapy can be tailored to the patient's needs. This information provided by the PAC is especially desirable during termination of the CPB and immediate postoperative period. TOE is, of course, a fascinating monitoring tool and if it is available, can be utilised to monitor the LV contractility and LV volumes.

Aortic valve repair

AVR has been the standard surgical management for the aortic valve disease. However, in the recent times, improvements in the aortic valve repair techniques have taken place, which provide an alternative to AVR. The advantages of the aortic valve repair include the avoidance of the risk of prosthetic valve complications such as thromboembolism, endocarditis, bleeding and structural deterioration. The choice of surgical technique for repair is determined by the nature of the AR. For instance, in presence of the dilatation of the sino-tubular junction (Type IA according to EL Khoury classification[113]), the dilated sino-tubular junction is remodeled to normalise the aortic cusp coaptation. Other techniques include, excision of the dilated sinuses of valsalva and a valve sparing root replacement, subcommissural annuloplasty, sinotubular junction annuloplasty, repair of cusp perforations by bovine pericardium, correction of the aortic cusp prolapse, shaving and decalcification of restricted aortic cusps, and sub-commissural annuloplasty.[114-117] It has been shown that aortic valve repair is feasible and safe and offers clinical outcome that is superior to the currently available data

for prosthetic AVR[114,118] Similar outcome results in terms of 10-year survival or freedom from reoperation at 5 years and at 10 years have been reported even in patients undergoing bicuspid aortic valve repairs.[119,120]

The TOE has been crucial for the success of the valve repair procedures and the recent guidelines strongly support its role in the aortic valve repair procedures.[121] A study has confirmed the utility of TOE in the aortic valve repair.[122] The risk factors for predicting the aortic valve repair failure are, residual AR, level of aortic cusp coaptation that is below the aortic annulus, and a short coaptation length (< 4 mm).[123]

In summary, aortic valve repair has come a long way and looks promising especially in younger adults with bicuspid or tricuspid valve. It may not be useful in patients who have valves with extreme degeneration and calcification.

Thoracic Epidural in Valve Surgery

Use of thoracic epidural anaesthesia (TEA) has been reported in a relatively large series of patients undergoing CABG. In contrast, there is a striking scarcity of patients in whom TEA has been reported during valvular cardiac surgery. This may be related to the fact that in the absence of coronary lesions, the benefit from optimisation in the redistribution of coronary blood flow and reduced demand for oxygen secondary to sympathetic block produced by TEA, is not necessary. In addition, the patients with valve disease are often on oral anticoagulants before and after surgery. However, some authors believe that certain other benefits of TEA such as excellent analgesia, early recovery of consciousness and spontaneous ventilation, attenuation of the stress response, early extubation and haemodynamic stability can still be useful in patients undergoing valve surgery. TEA in combination with general anaesthesia in patients undergoing valve surgery has been described.[124-126] The authors have reported extubation in the operation theatre in a substantial number of patients without any neurological complications. Patients suffering from mitral valve disease often have accompanying PAH and it is believed that elective postoperative ventilation is beneficial in them. However, in a series of 305 patients reported by Canto et al,[124] 63 percent patients had PAH with 14 percent having severe PAH (pulmonary systolic pressure > 70 mm Hg). One must be very cautious before

using TEA on a routine basis based on these reports and perhaps await more prospective randomised studies. TEA has also been used to perform awake AVR in an elderly patient with severe chronic obstructive pulmonary disease[127] and sick octogenarian patients.[128] Epidural anaesthesia without tracheal intubation in these patients permitted the avoidance of general anaesthesia and allowed continuous evaluation of cognitive function.

Mixed Valvular Lesions

While in clinical practice a single type of valvular lesion can be seen, mixed and multiple valvular lesions also occur very commonly. The commonest lesion in the developing countries is MS. Associated functional TR is very common in these patients. Isolated disease of the tricuspid valve is very rare and the organic disease of tricuspid valve (usually rheumatic) is almost always associated with the disease of other valves. By itself TR is not harmful, and the volume overload imposed on the RV is usually well tolerated. However, TR in the presence of PAH is not so well tolerated as regurgitant fraction is increased and the forward stroke volume is decreased. The functional TR associated with MS resolves after correction of the MS, and no treatment is generally necessary for TR. However, in the presence of severe PAH, medical management of PAH is important in order to improve cardiac performance in the postoperative period. The placement of PAC in presence of TR may be difficult and hence, may not be available as a monitoring tool in some patients with mitral valve disease.

The other types of mixed lesions are MS plus MR, MS plus AR, MR plus AR, AS plus AR etc. Almost all types of combinations can be seen necessitating replacements of more than one valve at a time. Combined stenotic and regurgitant lesions impose extra burden on the heart. For instance in a patient with AS plus AR, the increased stroke volume needs to be pumped against the resistance of the stenosed aortic valve. Where two different valves are affected in the same patient, the risk criteria of both the lesions should be considered during the perioperative management. However, more severe lesion amongst the two or stenotic lesion (if both are equally severe) should be given more importance.

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Chapter 6: Anaesthesia for Coronary Artery Bypass Surgery

The last decade has seen significant advances in the treatment of coronary artery disease (CAD). The emergence of drug eluting stents and off-pump coronary artery bypass grafting (OPCAB) have emerged as the alternative methods of coronary revascularization that avoid the use of cardiopulmonary bypass (CPB). The avoidance of CPB during OPCAB has made the operation equivalent to any other major noncardiac surgical procedure. This has led the cardiac anaesthesiologist to believe that elective postoperative ventilation may not always be necessary in these patients. The anaesthetic management has been modified to suit this requirement and a change-over from the high-dose opioid technique to a low-dose technique and reliance on inhalational anaesthetic agents or propofol for maintenance of anaesthesia is already noticeable in the cardiac anaesthesia practice.

The advances in the stent technology have resulted in more and more patients being subjected to percutaneous coronary interventions (PCI) rather than surgery. Thus patients who were formerly surgical candidates,, are undergoing PCIs. This has led to a decrease in the number of patients undergoing CABG as well as a change in the spectrum of patients undergoing coronary artery bypass grafting (CABG). In general, older and sicker patients with multi-vessel disease, often undergoing repeat procedure or having compromised left ventricular (LV) function associated with many co-morbid conditions are undergoing CABG nowadays. The newer surgical techniques such as robotic surgery and port-access surgery have been introduced, and although, they have not gained wide popularity, they are still being practiced. All these factors have posed additional challenges to the cardiac anaesthesiologists. He is expected to keep abreast with the current developments in the treatment of CAD and be familiar with their anaesthetic

requirements.

The monitoring of the patient inside the cardiac operation theatre (OT) has also seen a significant change. The most noteworthy being the widespread application of the transoesophageal echocardiography (TOE). This chapter deals with the anaesthetic management of patients undergoing CABG emphasising the recent developments.

Pathophysiology of Coronary Artery Disease

Anatomy

The right and left main coronary arteries originate from their respective sinuses of Valsalva at the aortic root. The left main coronary artery bifurcates into the left anterior descending (LAD) and circumflex branches (Fig. 6.1). The proximal LAD artery passes along the anterior intraventricular groove and gives off 4 to 6 septal perforators and continues further giving off branches (1 to 3 diagonal vessels) to supply the anterior and lateral walls of the LV. The circumflex artery proceeds in the left atrioventricular (AV) groove. Up to four obtuse marginal (OM) arteries arise from the circumflex artery and supply the lateral wall of the LV. When the circumflex gives rise to posterior descending artery (PDA), the circulation is called as left dominant and the entire interventricular septum and the AV node is supplied by left coronary circulation.

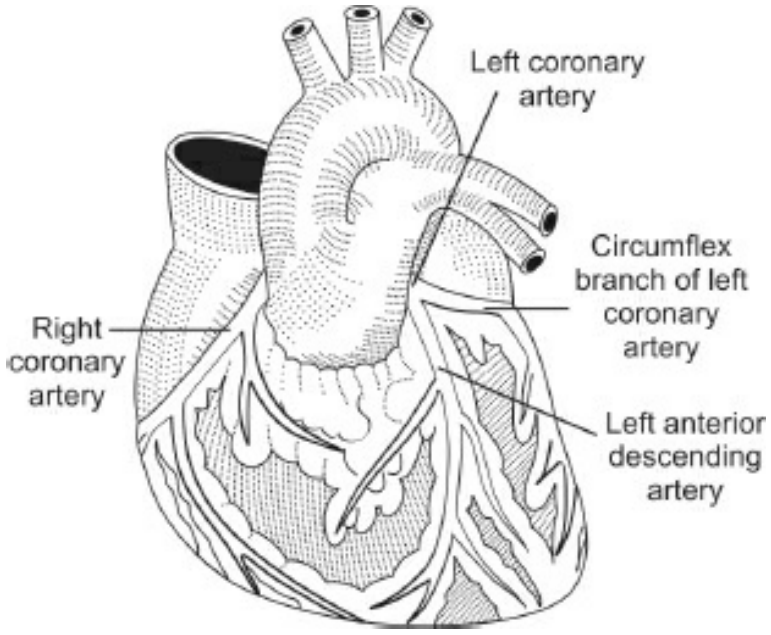

Figure 6.1: Anterior view of the heart showing right and left coronary arteries. The left coronary artery branches into left anterior descending artery and circumflex artery.

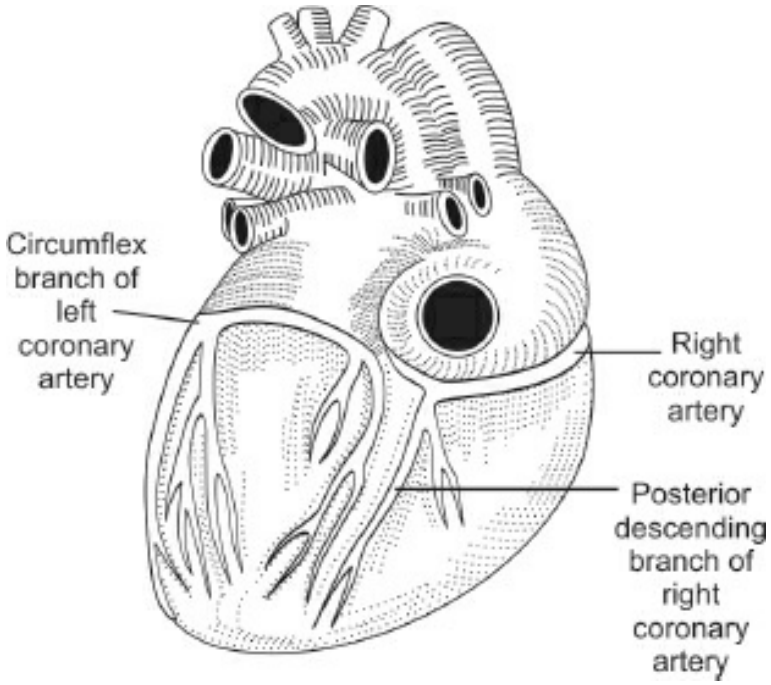

Figure 6.2: Showing posterior aspect of the heart. Note that the circumflex branch of left coronary artery running in the left atrio-ventricular groove and giving off marginal branches and continuing as distal circumflex artery. Right coronary artery descends in right atrioventricular groove and gives off posterior branch of the right coronary artery.

The right main coronary artery originates from the sinus of Valsalva of the right coronary cusp and traverses in the right AV groove. It gives off an acute

marginal branch and then continues to bifurcate into PDA and posterolateral branches (Fig. 6.2). When the PDA originates from distal right coronary artery, the circulation is referred to as right dominant, which is observed in about 85 to 90 percent of population.

These large epicardial vessels give rise to small intramural branches that are located within the myocardium. These small vessels are capable of altering the resistance of the circulation by altering their dimensions. Venous drainage of the myocardium is mainly to the coronary sinus, but a small fraction goes directly into the right atrium or other cardiac chambers via the thebesian veins.

Myocardial Ischaemia

In a normal individual, coronary blood flow (CBF) is autoregulated. Autoregulation signifies that the CBF is independent of the perfusion pressure but is related to the tissue oxygen demand. If there is progressive obstruction of a coronary artery, dilatation of the capillary bed beyond the obstruction occurs in order to maintain adequate blood supply. Coronary flow reserve is eventually exhausted and autoregulation begins to fail. Failure of autoregulation signifies that CBF is solely dependent on pressure gradients and the capacity to increase the flow by dilatation induced by metabolic control is lost. Subendocardial ischaemia is first to occur as autoregulation fails in the subendocardium first.[1] Autoregulation of CBF, however, cannot be maintained at all systemic pressures and at lower systemic pressures, the autoregulation begins to fail. In animals, this lower limit of pressure has been found to the be 38 to 40 mm Hg.[2] In addition, an increase in the heart rate (HR) can also affect the autoregulation in the sense that tachycardia increases the lower level of systemic blood pressure (BP) at which autoregulation fails. Tachycardia increases the myocardial oxygen consumption as well as reduces the diastolic time during which coronary perfusion occurs. Thus, both demand and supply of oxygen are affected.

Coronary Steal

An increase in the myocardial blood flow in one region that causes reduction in the flow in another is referred to as coronary steal.[3,4] When a coronary vessel develops stenosis, the microvas-culature distal to it may be maximally dilated. In addition, collaterals may develop between this ischaemic zone and

an adjacent non-ischaemic area that is supplied by another vessel. The collateral vessels have a high resistance unless they are fully developed. When vasodilatation occurs (exercise or pharmacological), it occurs mainly in the non-ischaemic zone, as the ischaemic zone may be already fully dilated. This results in a decrease in pressure in the non-ischaemic zone and flow across collateral vessels that have high resistance is reduced resulting in coronary steal. Steal-prone anatomy was found in 23 percent of patients in one study.[5]

The classical symptom of myocardial ischaemia is pain. However, myocardial ischaemia frequently occurs withoutpain and is called silent ischaemia. Silent myocardial ischaemia is known to occur frequently in preoperative period. In one study as many as 87 percent of preoperative ischaemic episodes were clinically silent.[6]

Myocardial ischaemia occurs when there is an imbalance in the determinants of oxygen supply and demand (Table 6.1). Whether it is silent or symptomatic, it leads to myocardial dysfunction with depressed contractile function and characteristic electrocardiographic (ECG) changes. As the myocardial ischaemia frequently occurs without haemodynamic changes, the anaesthesiologist must be watchful in detecting and aggressively treating it.

Table 6.1: Factors determining myocardial oxygen supply and demand

Myocardial oxygen supply	
Oxygen content	Haemoglobin
	Haemoglobin saturation
Coronary flow	Vascular resistance
	Diastolic pressure gradient
	Diastolic time
Myocardial oxygen demand	
Contractile state	Initial fibre length
	Intrinsic fibre shortening property
	Resistance to shortening

Preoperative assessment of coronary artery disease

Chest pain is the most common symptom and it is useful to be familiar with the type of pain that the patient has. He may have uncomfortable sensation, heart burn or shortness of breath. The location of the discomfort also differs and the patient's account of the suffering is an important information. If similar discomfort occurs on arrival in the OT, it should not be ignored. The severity of pain does not have relation to the magnitude of the vessel blockade. However, unstable angina carries a higher risk in terms of myocardial infarction (MI) or death. Based on simple clinical parameters, it was shown that the presence of resting ST depression, hypertension, prior MI or marked limitation of activity in patients with stable angina are associated with increased mortality.[7] More recently, it has been shown that the severity of illness characteristics, such as, LV dysfunction and emergency admission increase the risk of mortality.[8] Physical examination should be aimed at detecting evidence of LV dysfunction and associated systemic diseases (particularly respiratory and vascular disease) that might affect the anaesthetic care. Precordial heave, laterally displaced point of maximal impulse or presence of fine basal crepitations suggest LV dysfunction.

The patient with CAD is generally investigated in great details by the cardiologist. The cardiac anaesthesiologist is thus fortunate in the sense that extensive evaluation of the cardiovascular system has already been done and sufficient information about the cardiovascular system is available. Noninvasive studies such as chest radiograph, ECG, echocardiography, stress testing, nuclear imaging as well as invasive studies such as coronary angiography have usually been performed on them. Amongst these, angiography is the 'gold standard' for defining the extent of CAD. Vessels suitable for bypass are identified on the basis of a coronary angiogram. In addition, the LV angiogram is informative about the contractile function of the LV. The important information that the anaesthesiologist should look for is the distribution of lesions, LV ejection fraction (EF) and LV end-diastolic pressure (LVEDP). Normal LVEF is 50 to 75 percent. Generally LVEF of <

35 percent is labelled as poor LV function. An enlarged LV size on X-ray, EF of < 30 percent and presence of areas of abnormal motion, (hypokinesia or dyskinesia) on echocardiography are suggestive of a high risk.

After completing the physical examination and reviewing all the investigations, the anaesthesiologist should form an opinion about the nature and extent of the disease. Information such as number of grafts that will be necessary, the LV function of the patient and the presence of associated systemic illness should be noted. Presence of diabetes mellitus, renal failure, hypertension, vascular disease or pulmonary disease is particularly important. This helps him to work out a proper anaesthetic plan for the patient. It is reasonable to believe that more information about cardiac function means better treatment and improved outcome. Therefore, the cardiac patients should be fully investigated. The knowledge and understanding of the cardiac function as well as the management of haemodynamic disturbances form the basis of successful anaesthetic management of a cardiac patient.

The important risk factors that have been identified in patients undergoing CABG are, advanced age (more than 75 years), reoperation, emergency state, female gender, LVEF less than 30 percent, presence of diabetes and dialysis dependence.[9-12]

It is now well known that the population presenting for CABG is changing. This is mainly due to the advances in the techniques of PCIs. The debate on the subject such as PCI versus CABG is beyond the scope of this book and it is sufficient to say that patients with more extensive CAD are now presenting for CABG surgery.

Preoperative Drug Therapy

Nitrates, beta-blockers and calcium antagonists are the mainstay of treatment of angina. In addition, anticoagulant or platelet inhibiting drugs are also prescribed in order to prevent acute thrombotic events at the site of coronary stenosis. These drugs are likely to be continued up to the time of surgery in order to prevent episodes of myocardial ischaemia.

Nitroglycerin

Nitroglycerin (NTG) is generally administered sublingually for the treatment of acute angina. However in patients with unstable angina, an infusion of NTG can be used. This therapy should be continued up to the time of surgery,

since acute withdrawal can precipitate myocardial ischaemia. The ability of nitrates to reduce the preload by venodilatation must be appreciated and induction of anaesthesia by withdrawing sympathetic tone can induce profound hypotension in these patients.

Beta-blockers

The perioperative use of beta-blockers has been controversial. However, it is being increasingly utilised particularly in the high-risk group of patients undergoing major noncardiac vascular surgery. By virtue of decreasing myocardial oxygen demand, increasing diastolic perfusion time and reducing the frequency of arrhythmias, beta-blockers are expected to decrease myocardial ischaemia and hence, perioperative myocardial infarction. The initial randomized trials by Mangano et al,[13] and Poldermans, et al[14] are the prominent ones that demonstrated the utility of beta-blockers in providing long-term benefits to the patients undergoing noncardiac surgery. A reduction in perioperative mortality in CABG patients by beta-blocker therapy was demonstrated by a few studies.[15,16] The beneficial effect of beta-blockers was more pronounced in high-risk sub-group of patients.

The controversies regarding the type and dose of beta-blocker as well as the target heart rate continues, but the use of beta-blockers is beneficial for most CABG patients. They significantly decrease the myocardial oxygen demand and the incidence of atrial and ventricular arrhythmias.[17]

Calcium channel blockers

The utility of calcium channel blockers in decreasing the cardiac events in patients undergoing CABG is a controversial topic. A metaanalysis has suggested that they are effective in reducing mortality in CABG patients.[18] However, randomised controlled trials in this area are lacking. It appears reasonable to continue them in patients taking them chronically.

Angiotensin converting enzyme inhibitors

The angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor antagonist have become an integral part of management of patients with hypertension, congestive heart failure, and chronic renal disease. They are prescribed after acute MI and they decrease the damage after ischaemic reperfusion and cause ventricular remodeling. Many patients undergoing

CABG are receiving ACE inhibitors. The controversy regarding their perioperative use revolves around the significant hypotension following anaesthetic induction and after separation form CPB leading to increased requirement of vasoconstrictors, if they are continued[19], and hypertension leading to wound bleeding, arrhythmias and increase in ischaemia related events, if they are discontinued.[20] One study in patients undergoing CABG has reported that omitting ACE inhibitors before surgery did not have sufficient advantage to be recommended routinely.[21] A recent study that included a cohort of 45,291 patients has shown that ACE inhibitors in combination with diuretic therapy was significantly associated with hypotension (mean arterial pressure, MAP < 70 mm Hg) and vasopressor requirement.[22] It seems therefore, that there is not enough evidence to discontinue ACE inhibitors before surgery, but withholding ACE inhibitors on the morning of surgery and restarting in the postoperative period only after the patient is euvolaemic is practiced by many.

Statins

The use of statins in the cardiac patient has increased during the recent times. They have been shown to decrease cardiovascular morbidity and mortality in patients undergoing PCI, cardiac surgery, vascular surgery and non-cardiac surgery. Majority of the studies have been retrospective and observational in nature. A recent meta-analysis that included over 30,000 patients (mostly CABGs) has shown that there was a significant reduction in mortality, atrial fibrillation and stroke[23] in patients taking statin. However, there was no decrease in the incidence of MI. Thus, the decrease in mortality was perhaps, not due to decrease in the MI. This may be related to variation in restarting the statins early in the postoperative period, as postoperative statins withdrawl is linked with an increased risk of cardiac mortality.[24] Despite the beneficial effects of statins, the current use of statins in patients with CAD admitted for cardiac surgery is suboptimal, with only 40 percent receiving them.[25] The current evidence indicates that statins should be continued is those patients who are already receiving it, and it should be restarted early in the postoperative period. There is no evidence to empirically start it in all patients.

Anti-platelet agents

Patients with CAD are generally administered aspirin for its platelet inhibiting effects.[26] It is a well recognised component of primary and secondary prevention strategies for all patients with ischaemic heart disease.[27] Aspirin leads to platelet dysfunction, and CPB induced platelet dysfunction is considered to be an important cause of post-bypass coagulopathy. For this reason, at many centres, elective CABG is not performed on patients who are taking aspirin. However, there are conflicting reports in terms of postoperative bleeding associated with aspirin therapy. Some authors have shown an increase in the postoperative chest drainage in patients receiving aspirin therapy,[28,29] while others have shown no difference in bleeding or re-exploration rate in patients taking aspirin.[30,31] Moreover, it has been shown that preoperative aspirin use appears to be associated with a decreased risk of mortality without significant increase in haemorrhage, blood product requirements or related morbidities.[32] The Society for Thoracic Surgeons guidlines[33] recommend that, in high-risk group (those with unstable angina or recent MI) requiring urgent or emergent CABG, aspirin should be continued until the time of surgery. For elective patients in whom active platelet aggregation is less likely to be a critical factor in precipitating ischaemia, discontinuation of aspirin for 3 to 5 days pre-operatively is recommended with early reinsti-tution in the postoperative period.

The thienopyridines, ticlopidine and clopidogrel are other anti-platelet agents that form a part of the standard medical therapy for patients with CAD. Clopidogrel has replaced ticlopidine, as it has a lower incidence of thrombocytopenic purpura. It has been shown to be beneficial in patients with acute coronary syndromes undergoing PCI, if administered on a long-term basis for a period of 9 months.[34] Another study has shown that the freedom from MI and death can be extended by continuing the clopidogrel for a period of two years in patients with drug eluting stents.[35] The current practice is to continue dual anti-platelet therapy (aspirin and clopidogrel) for a period of at least one year after placement of drug eluting stent and 3 months after placement of bare-metal stent.

Some of the patients with acute MI may be referred for urgent surgery, while a few others who are taken for stent placement may become surgical candidates due to failure of the procedure. All these patients would have received clopidogrel and pose an increased bleeding risk during surgery. Amongst other patients who are scheduled for elective CABG and who are

receiving clopidogrel, it should be discontinued for a period of 3 to 5 days, unless platelet aggregation is a critical factor in them. This decision regarding the need to continue clopidogrel in some patients should be taken in consultation with the cardiologist and should be based on the nature of the coronary lesion and the type of angina.

Heparin and thrombolytic therapy

In patients with unstable angina, heparin infusion is administered. It is generally stopped 6 hours before surgery, but in some cases it may be continued up to the time of surgery. This might result in excessive anticoagulation, if usual doses of heparin are administered during surgery. In some patients, heparin therapy may induce heparin induced thrombocytopaenia while in others, it may cause a relative deficiency of antithrombin-III. These factors should be taken into account for the management of anticoagulation of these patients so that inadequate anticoagulation or excessive heparin dosage are avoided. In patients with heparin induced thrombocytopaenia requiring emergent surgery, the results obtained by using low molecular weight heparin appear promising.[36] Bivalirudin is another safe alternative.[37,38] The patients with antithrombin-III deficiency will need administration of fresh frozen plasma that contains antithrombin III.

Some patients with acute MI who have received thrombolytic therapy may be subjected to emergency surgery. Thrombolytic agents (streptokinase, urokinase) decrease the plasma fibrinogen concentration by activating plasminogen and these patients are likely to develop coagulopathy after CPB. Increased postoperative bleeding is known to occur in these patients[39] and their requirement of fresh frozen plasma and cryoprecipitate (which is rich in fibrinogen) is also increased. An antifibrinolytic agent such as epsilon aminocaproic acid or tranexamic acid can also be useful in these patients. The anaesthesiologist should anticipate all these problems and ensure adequate supply of blood products well in time.

Premedication

The goals of premedication are to reduce apprehension and fear, to provide some analgesia for vascular cannulations that are performed before induction, and to provide some degree of amnesia. A good premedication is essential in

order to prevent the occurrence of potential ischaemic events in the preoperative period. A commonly used drug combination is oral diazepam (0.1 to 0.15 mg/Kg), with intramuscular morphine (0.1 mg/Kg) and scopolamine (0.2 to 0.4 mg).[40] The dosage should be appropriately reduced in elderly or debilitated patients. On the other hand, if the patient arrives in the OT with inadequate sedation, supplemental intravenous sedation should be provided either with benzodiazepines or opiates. Scopolamine provides amnesia in addition to providing sedation. It is a usual practice in the author's unit to administer morphine (0.2 mg/Kg) and promethazine (25 mg) intramuscularly 1 to 2 hours before surgery. Other opioids such as fentanyl can also be used for premedication, but due to the short duration of action, should be administered about 30 min. before the operation. Oral benzodiazepines alone (diazepam 0.1 to 0.15 mg/Kg or lorazepam 2 to 4 mg) are also used as effective premedicants, but they may produce significant hypotension during induction of anaesthesia. In addition to providing anxiolysis and amnesia, the anaesthesiologist must ensure the administration of appropriate cardiac medication on the morning of surgery with sips of water.

Anaesthetic Management: Induction and Maintenance

Before the patient is wheeled into the OT, the anaesthesiologist must ensure that adequate preparations for anaesthetic induction are carried out. This mainly includes, checking the anaesthesia machine, ventilator, laryngoscope, endotracheal tube and anaesthetic drugs. In addition, facilities to promptly initiate resuscitation (defibrillator, inotropes and syringe pumps, etc.) in the event of a cardiac mishap should also be available.

The choice of anaesthetic drugs is wide and the anaesthesiologist is expected to use the technique which he is most familiar with. Nevertheless, their usage must be modified according to the good, poor or extremely poor condition of the LV.

Induction of anaesthesia should take place in a relaxed atmosphere in a quiet OT. Undue conversation amongst the OT personnel can disturb the patient and add to his anxiety. It is a usual practice in most centres to initiate ECG monitoring and establish a venous access and radial arterial cannulation

under local anaesthesia before the induction of anaesthesia. A central venous catheter (CVC) or a pulmonary artery catheter (PAC) should be inserted and a wide bore venous access should be established before induction in patients who have poor myocardial function.

The selection of induction agents as well as their dosage is based on the objective of preventing an episode of myocardial ischaemia. This includes avoidance of tachycardia and hypertension as well as precipitous hypotension. In order to achieve this goal, the LV function should be taken into consideration. Hypertension and tachycardia is more likely to occur in patients with normal LV function whereas patients with poor LV function may require pharmacological support to maintain the blood pressure. It is a good practice to restrict the doses of anaesthetic agents in patients having poor LV function, and use modest doses in those having good LV function. Further doses of anaesthetic agents may be administered in increments to obtund the hyperdynamic response, if it occurs during stressful stimulation such as intubation.

High-dose opioid anaesthesia has been a popular technique since the time the safety of high-dose morphine was demonstrated in patients with compromised cardiac function [41] Vasodilatation from histamine release, necessitating fluids and vasoconstrictors, prolonged respiratory depression and lack of amnesia were clear disadvantages of high-dose morphine technique. In 1979, the use of high-dose fentanyl for CABG was described.[42] This was followed by sufentanil and alfentanil, none of which release histamine. Amnesia is not guaranteed, however, and surgical stimuli can cause tachycardia and hypertension. The use of opioids still continues to be popular, mainly due to its lack of any direct effect on the heart and relatively pain free postoperative course, albeit at the cost of delayed postoperative awakening. Opioids also cause bradycardia which is advantageous in patients with CAD. Nevertheless, superiority of any particular opioid over others in terms of haemodynamic stability is not clearly demonstrated.

With the recent trend towards fast-tracking, early extubation has become a goal at many centres. This has led to reduction in the doses of the opioids used during cardiac surgery. Some clinicians use infusions of shorter acting agents (propofol, sufentanil, remifentanil) and others even use volatile anaesthetic-based techniques.

Hypnotics such as thiopental and propofol, benzodiazepines such as midazolam and diazepam can also be used for induction. However, thiopental

and propofol alone are clearly unsuitable, as they lead to myocardial depression and peripheral vasodilatation. However, they can be used in smaller doses as adjuvants to opioids. Propofol is a favoured agent over thiopental at most centres. Diazepam (0.5 mg/Kg) and midazolam (0.2 mg/Kg) have been used effectively as induction agents. However, the induction dose and speed of induction vary from patient to patient and haemodynamic responses to intubation and surgical stimulation are not abolished with benzodiazepines alone. Etomi-date appears to be devoid of any cardiovascular effects and its use for induction in cardiac patients with impaired LV function is common and increasing. In patients with normal LV function, blunting of the adrenergic response to intubation is poor and may result in hypertension and tachycardia.[43]

From this discussion, it is apparent that opioids should form a “base” and hypnotics and/or benzodiazepines in small doses may be used as supplemental agents during induction of anaesthesia. This, not only assures amnesia, but also obtunds the haemodynamic response to intubation or surgical stimuli. In this respect, benzodiazepines should be used carefully as they are known to cause precipitous vasodilatation leading to hypotension when used along with opioids.[44] For this reason, it may be useful to administer them following intubation, if a hypertensive response is observed. The dose of opioids may be appropriately reduced in order to achieve the goal of early extubation. It is prudent to say that most hypnotics, opioids and volatile agents in different combinations have been successfully used by experienced anaes-thesiologists.

Muscle Relaxants

Adequate intubating conditions during CABG can be obtained with most of the muscle relaxants that are currently available. Succinyl-choline (1 to 1.5 mg/Kg), pancuronium (0.08 to 0.15 mg/Kg), vecuronium (0.08 to 0.2 mg/Kg), atracurium (0.5 to 1 mg/Kg) and rocuronium (0.6 mg/Kg) can be used. Amongst these, rocuronium appears to be a good choice if high-dose narcotic technique is used, since the bradycardia produced by opioids is effectively countered. Pancuronium is widely used but can sometimes cause dangerous tachycardia and the anaesthesiologist must be watchful in its prompt detection and treatment. Vecuronium in particular, should be used cautiously as it may lead to dangerous bradycardia or asystole when used

with high-dose opioids.[45,46] While using atracurium, its ability to release Wstamine should be considered.

The newer relaxants such as doxacurium and pipecuronium are longer acting than pancuronium and provide stable haemodynamics during opioid/benzodiazepine anaesthesia.[47,48] Mivacurium has been used in patients undergoing CABG. A dose of 0.15 mg/Kg was shown to produce changes of small magnitude in BP and systemic vascular resistance (SVR), but a dose of 0.2 mg/Kg produced significant decreases in BP and SVR and suggested histamine release.[49] A survey performed in 2002 has revealed that despite availability of newer short acting muscle relaxants, pancuronium was the most commonly used agent.[50] With growing emphasis on fast-track cardiac surgery, early extubation is being increasingly used. In this respect, longer duration of pancuronium is a potential disadvantage. Shorter acting agents such as cisatracurium or rocuronium are recommended to avoid residual paralysis and to allow early extubation.

In summary, when the patient arrives in the OT, ECG should be connected and patient is assessed for the effect of premedication. If it is inadequate, additional bolus (morphine 3 to 5 mg or fentanyl 25 to 50 μg) should be administered intravenously after establishing a venous access. Arterial cannulation should then be performed (usually left radial artery) to provide invasive BP monitoring. Patients with good LV function can be induced at this stage, but in patients having poor LV function (EF < 35 percent), a CVC or PAC should be inserted under local anaesthesia, and a venous access with a wide bore cannula (14 G) should be established before induction (Fig. 6.3). Morphine (0.5 to 0.75 mg/Kg) or fentanyl (8 to 10 μg/Kg) should then be administered, followed by muscle relaxant (usually pancuronium 0.08 to 0.15 mg/Kg). Benzodiazepines (midazolam 2.5 to 5 mg) can also be administered before intubation to ensure amnesia. In patients with poor LV function, however, benzodiazepines may be withheld till intubation is accomplished and hypertensive response is observed. Small boluses of thiopental or propof ol can also be used to control the hypertensive response. If tachycardia is accompanied by hypertension, beta-blocker (metoprolol 1 mg increments) may also be administered.

Maintenance of Anaesthesia

As has been discussed, a “base” of opioid is obtained by administering a

modest dose at the time of induction. In case of fentanyl and sufentanil, it is better to administer a bolus dose (fentanyl 8 to 10 µg/Kg, sufentanil 1 to 2 µg/Kg), followed by a continuous infusion of the drug (fentanyl 0.1 to 0.5 µg/Kg/min. and sufentanil 0.01 to 0.02 µg/Kg/min.). Majority of anaesthesiologists prefer to administer intermittent doses over continuous infusion. For maintenance of anaesthesia, it is a usual practice to supplement anaesthesia with a low dose of inhalational agents, benzodiazepines or propofol. Nitrous oxide has been used as an adjunct to general anaesthesia for a long time. Although, its use has continued in many European centres, it has almost vanished from North America. In the developing countries, however, it is still being widely used, but its use is declining. In any case, nitrous oxide should be discontinued once the CPB is instituted.

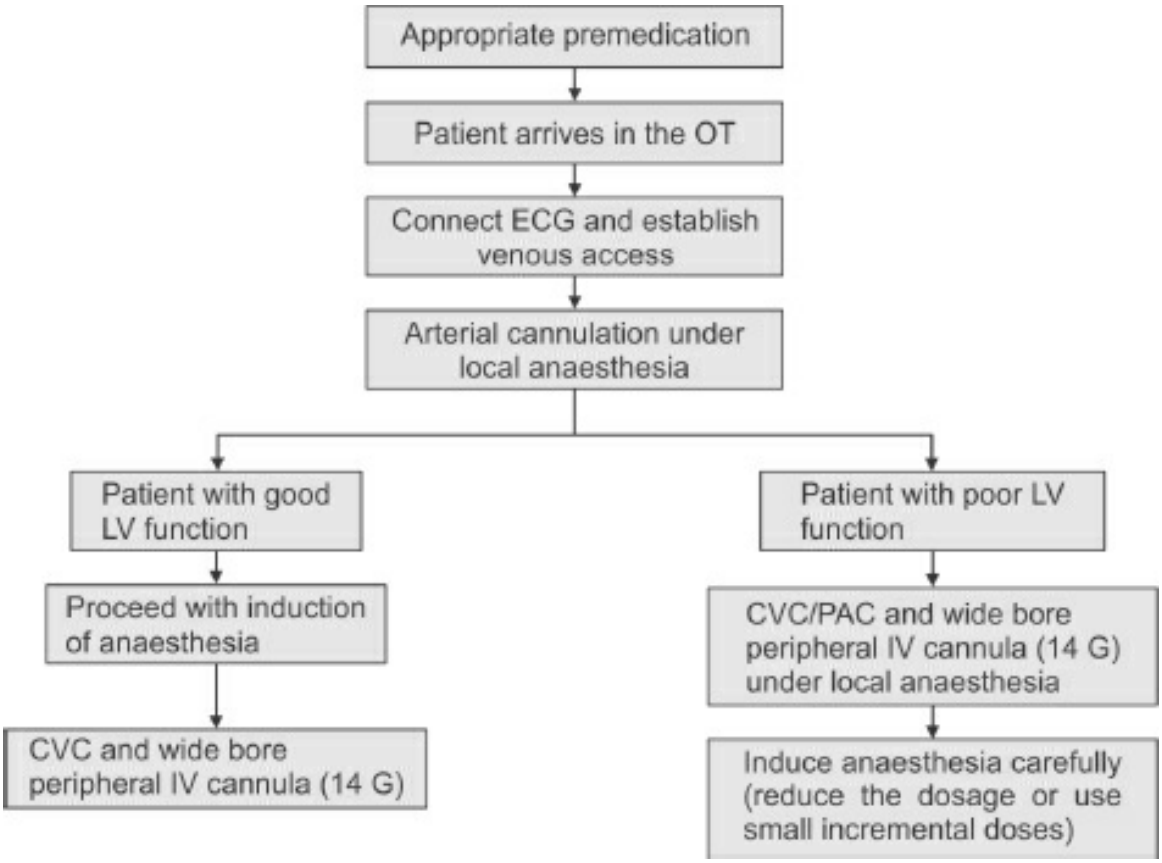

Figure 6.3: Schematic representation of the induction of anaesthesia in a patient undergoing coronary artery bypass grafting. (OT: operation theatre, LV: left ventricle, CVC: central venous catheter, PAC: pulmonary artery catheter, IV: intravenous)

The supplemental agents help to ensure complete anaesthesia and also permit reduction in the total dose of opioid. In addition, their dosage (isoflurane, halothane, or propofol) may be increased temporarily to deepen

the level of anaesthesia, especially during increased surgical stimulus such as sternotomy or dissection around the ascending aorta. Inhalational agents are particularly useful to control hypertension during prebypass period in patients having normal LV function.

Volatile Anaesthetics

Isoflurane has been discussed a lot, as its coronary vasodilatory property can lead to coronary steal causing myocardial ischaemia. The detailed discussion on this issue can be found in chapter 2. There is evidence suggesting that isoflurane does not increase the incidence of ischaemia in patients undergoing CABG.[51,52] The clinical evidence proposes that isoflurane is safe to use in patients with CAD and if hypotension is avoided, it is safe even in patients with steal-prone anatomy.

The other volatile agents, halothane, enflurane and sevoflurane are not coronary vasodilators and therefore, do not cause coronary steal. They also can be used as supplements to general anaesthesia in patients undergoing CABG.

Inhalational agents cause myocardial depression and peripheral vasodilatation. These may have beneficial effects on myocardial oxygen balance, thereby providing myocardial protection. However, increasing experimental evidence accumulated over the past two decades has indicated that the volatile anaesthetic agents have cardioprotective properties that cannot only be explained by their beneficial effects on the myocardial oxygen balance. Initial reports suggested that inhalational agents provide myocardial protection when administered before myocardial ischaemia.[53-55] This is termed as anaesthetic preconditioning (APC), which refers to the phenomenon where exposure of the heart to a volatile anaesthetic before myocardial ischaemia results in protection against the deleterious effects of myocardial ischaemia and reperfusion. This is similar to ischaemic preconditioning (IPC), which refers to the phenomenon wherein a brief period of ischaemia is able to protect the myocardium against the reversible and irreversible consequences of a subsequent longer period of ischaemia.

APC has a clear advantage over IPC of not requiring ischaemia to produce the protective effect. Subsequently, it was shown that myocardial protection is provided even when the volatile agents were administered before and after the ischaemia as well as throughout the procedure.[56-58] A recent meta-

analysis also has suggested that volatile anaesthetics may reduce mortality in cardiac surgery.[59] The myocardial protective effect was attributable to mechanisms such as myocardial oxygen balance, free radical scavenging, negative inotropism, formation of nitric oxide, and calcium blocking or direct interaction with actin-myosin function.

The beneficial effects of volatile anaesthetic agents have been demonstrated in OPCAB. Conzen et al[60] and Guarracino et al[61] administered volatile agents throughout the procedure during OPCAB and showed that troponin-I concentration increased significantly more in patients receiving total intravenous anaesthesia than in patients receiving sevoflurane or desflurane. Bein et al[62] reported echocardiographic evidence of preserved myocardial function with sevoflurane in patients undergoing minimally invasive direct coronary bypass (MIDCAB). Others too showed similar beneficial effects with sevoflurane and isoflurane.[63,64]

Majority of the studies have thus far shown the beneficial effect on the myocardium by reduced levels of troponin-I, troponin-T or brain natriuretic peptide. The cellular mechanisms responsible for such protection are not yet fully understood. There is little convincing evidence to show that the use of volatile agents was associated with an improved outcome by way of a reduction in perioperative MI and mortality. Further, it is not clear as to which one of the inhalational agents and at what dosage provides the most beneficial effects. This needs to be confirmed by well-designed, large-scale, randomized controlled trials. Until such time, it is prudent to use the volatile agents as the part of anaesthetic technique in patients undergoing CABG.

Haemodynamic Monitoring

Since the detection and aggressive management of ischaemia is an important goal of anaesthesia, ECG monitoring is of vital importance. Slogoff and Keats demonstrated that the adverse outcome as measured by postoperative MI was increased in patients who developed pre-CPB ischaemia.[65,66] Subsequently, however, it was demonstrated that ischaemia that occurs prior to CPB may not be as predictive of outcome as was once thought.[67,68] Majority of the episodes of ischaemia are also not associated with haemodynamic changes. These findings do not suggest that tight haemodynamic control is unnecessary.[69]

ECG

A multilead ECG system is useful in managing patients with CAD. The American Heart Association recommends that ischaemia should be diagnosed when a 0.1 mV horizontal or down-sloping ST segment depression occurs 60 to 80 milliseconds after the 'J' point.[70] For unipolar leads, lead V5 has the greatest sensitivity (75 percent) and the combination of leads V4 and V5 has greater sensitivity (90 percent) than either a single lead or the combination of leads II and V5 (sensitivity 80 percent).[71] Monitors having online ST segment analysers with trending facilities that are currently available can be useful in patients undergoing CABG.

Arterial pressure

For arterial pressure monitoring, radial artery is usually cannulated. Sternal retraction during internal mammary artery (IMA) dissection compromises the flow in the radial artery. Therefore, at some centres, the radial artery opposite to that of the proposed IMA dissection is cannulated. With the growing popularity of total arterial revascularisation, one or both radial arteries may be used for myocardial revascularisation. In such a situation, femoral artery should be cannulated. Accurate, beat to beat monitoring of BP is essential, as many important decisions regarding drug selection and anaesthetic depth are based on BP readings. After hypothermic CPB, radial arterial pressure may be less than the central aortic pressure. For this reason, at some centres, both radial and femoral arterial cannulations are performed. Femoral arterial cannula also provides a ready access for the insertion of intra-aortic balloon pump (IABP) catheter during post-CPB period, if the need arises.

Central venous pressure

The placement of CVCs is a standard practice for measurement of central venous pressure (CVP) as well as infusions of inotropes or other medications. A single multi-lumen catheter or 2 single lumen catheters can be inserted through the right internal jugular vein (IJV).

Pulmonary Artery Catheter

When the LV fails and dilates or becomes ischaemic and less compliant, the pressure required to fill it to the same degree rises. In such a situation, left atrial (LA) or pulmonary capillary wedge pressure (PCWP) will increase, but

the CVP may be unchanged. The LV filling pressure in the left heart failure can be measured by monitoring the PCWP. PACs have thus, become a routine at many centres. Studies on PAC use have demonstrated that they do not have any effect on outcome[72,73] or may even lead to adverse outcome in terms of higher risk of mortality, longer length of stay and higher total costs.[74] Whereas another study has suggested that a more selective use of PACs (in patients with multiple cardiac risk factors) is safe.[75] The existing literature is inconclusive and it is not possible to give clear guidelines regarding the PAC use in CABG surgery. However, most cardiac anaesthesiologist would agree that PAC provides useful information that can change the management strategies, especially in patients having poor LV function, having high-risk of intraoperative ischaemia, severe comorbidities, emergency surgery, combined procedures and reoperation. The PACs are also commonly used is patients undergoing OPCAB. Pre-induction placement of the PAC provides valuable, objective information to the cardiac anaesthesiologist without incurring significant risk to the patient.[76] However, it has been shown that placement of PAC before the induction of anaesthesia consumes more time and fails to improve haemodynamic stability or lessen vasoactive drug use during the induction of anaesthesia in patients with normal LV function undergoing elective CABG.[77]

PACs having specialised functions, such as pacing port, continuous cardiac output (CO) and mixed venous oxygen saturation (SVO_2) monitoring facility and right ventricular ejection fraction measurement capacities are also available. The SVO_2 PACs have not been shown to provide any additional benefit over the routine PAC.[78]

Transoesophageal Echocardiography

Segmental wall motion abnormalities occur within seconds of coronary occlusion and are the earliest indication of myocardial ischaemia. These can be easily detected on TOE, however, TOE requires considerable expertise for reliable interpretation. The short-axis mid-papillary view is commonly used, because it includes the myocardium supplied by three major coronary arteries. Assessment of global and regional LV function using this view has been shown to be an effective method in patients undergoing CABG.[79] It also provides an accurate estimate of LV preload by measuring LV end-diastolic area.[80] TOE provides valuable information in terms of the preload and

contractility. It gives a far more accurate estimate of the preload as compared to the PAC. In addition, TOE can be used to verify PAC location, placement of retrograde cardioplegia cannula, LV vent or IABP tip, detection of atheromas in the ascending aorta, intracardiac air, and valve function. Therefore, the use of TOE is increasing rapidly. The PAC derived haemodynamic data can also be obtained by TOE, but PAC insertion will still be required for the postoperative management in the intensive care unit (ICU). The requirement of specialised training and the cost of equipment are two major hurdles in its use as a routine monitoring tool inside the OT. Nevertheless, more and more cardiac centres are now using TOE routinely during cardiac surgery.

Anaesthetic Management of Patients with Poor Left Ventricular Function

Poor LV function is not uncommon in patients with CAD and anaesthesiologists will have to frequently anaesthetise them. Surgery is performed on these sick patients with the objective of prolonging and improving the quality of life. The anaesthesiologist should be aware of the pathophysiology of poor LV function and modify the anaesthetic technique along with meticulous attention to myocardial preservation and cardiovascular support.

Pathophysiology

LV dysfunction is generally described in terms of EF (assessed by echocardiography or angiography). A LVEF of less than 50 percent is regarded as abnormal, but even patients having EF of as low as 20 percent are subjected to surgery. In addition, patients may have wall motion abnormalities or raised LVEDP.

Left Atrial Pressure

The LV is much more powerful and thicker than the right ventricle (RV), as it has to pump blood against the SVR that is much greater than the pulmonary vascular resistance (PVR). For this reason, the systolic pressure in the LV is much higher than the RV. When the LV fails, CVP may remain unchanged,

but the LA pressure or PCWP will rise. LV compliance can change rapidly due to ischaemia or following CPB and aortic cross clamping so that the means of assessing LV filling are useful. Therefore, PAC is useful in these patients, which determines the PCWP and forms a good guide for LV filling pressure (preload). Alternatively, LA pressure can be measured directly by inserting a catheter into the LA by the surgeon. LA pressure is a guide to LVEDP and to the safety of increasing blood volume without causing pulmonary congestion and oedema. With the availability of PACs and TOE, the practice of inserting the LA line by the surgeon in declining.

LV compliance also determines the rate of filling during diastole. In a normal individual, the rapid ventricular filling phase of diastole accounts for 80 percent of the next stroke volume. Atrial systole that follows the rapid filling phase, thus contributes less than 20 percent of LV filling. When ventricular compliance is diminished the atrial component becomes much more important. Maintenance or restoration of sinus rhythm [from nodal rhythm or atrial fibrillation (AF)] is therefore, extremely important in these patients. The atrial component can also be restored by sequential pacing, where both the chambers (atrium and ventricle) are paced so that the normal relation between atrial and ventricular contraction is preserved.

The anaesthetic and pharmacological agents used to support circulation in patients with poor LV all have a bearing on the myocardial oxygen balance. The anaesthesiologist should aim to minimise oxygen demand and maximise oxygen supply whenever possible (Table 6.1). Monitoring of various cardiovascular variables during the perioperative period is essential. But a background knowledge of the pathophysiological processes of the poor LV is essential to optimally manipulate the circulatory system. However, maintenance of haemodynamics can be quite demanding at times.

Anaesthesia

Anaesthetic premedication, induction and maintenance must be modified according to poor or extremely poor condition of the LV. Any premedicant which may adversely affect the ventricular performance should be omitted. In general, the doses of premedicants should be reduced or omitted altogether if the patient is in congestive heart failure (CHF) or is orthopnoeic. Any mechanical circulatory support (IABP) or drug infusion (inotropes and dilators) should be continued during transfer of the patient to the OT. Oxygen

should also be administered and if the patient is orthopnoeic, he should be propped up. The preparation of anaesthesia must include availability of resuscitation drugs and the surgical and perfusion team should be ready during anaesthetic induction.

Anaesthetic drugs

The selection and dosage of anaesthetic drugs should be modified according to the known pharmacological effects on the heart and circulation that are accentuated in the presence of LV failure. The dosage of all anaesthetic drugs must be reduced. In the presence of opioids, it is best to omit the benzodiazepines. Drugs used to obtund cardiovascular responses to intubation are likely to adversely depress the heart and circulation. When the LV is very poor, these should be avoided. If the circulation is depressed during induction, inotropes should be appropriately started. Propofol for induction as well as for maintenance should be avoided when LVEF is really low. Pancuronium is a good choice for muscle relaxation as it counters the bradycardia produced by opioids. With the onset of muscle relaxation and commencement of positive pressure ventilation, the patient's CO and BP can decrease dramatically. Again, inotropes (epinephrine) must be promptly administered during such situations. In extreme situations, a judicious bolus dose (100 to 200 μg) of epinephrine (1 mg diluted in 10 mL) is very useful and must be considered necessary even for patients with CAD as maintenance of BP is extremely important.

Myocardial Preservation

Myocardial preservation is even more important when the LV has already been damaged. Newer techniques of myocardial preservation, blood cardioplegia (either cold or warm), retrograde cardioplegia, etc. can be used. For details, refer to chapter 13.

Cardiovascular Support

The various issues in relation to the cardiovascular support that should be considered are summarised in Table 6.2. During termination of CPB, sinus rhythm and a rate of 80 to 90 beats/min. should be obtained. The AV sequential pacing should be used, if necessary. Antiarrhythmic drugs with least ventricular depression should be preferred. It may sometimes be necessary to reinstitute CPB and unload the heart, while normal rhythm is

being restored. It appears that a heart which is not dilated is less likely to develop rhythm disturbances and the early use of inotropes or inodilators may reduce the incidence of such disturbances.

Table 6.2: Cardiovascular support

Arrhythmia management
Volume
Myocardial contractility
Afterload control
Coronary vasodilatation
Inotropes
Mechanical assistance

It is a good policy, therefore, to commence inotropic support before the termination of CPB. By this, myocardial contractility is improved, cardiac distention is minimised and coronary perfusion is optimised. All this is achieved at the expense of increased myocardial oxygen demand, but is essential for successfully terminating the CPB as coronary perfusion pressure (CPP) is important soon after CPB. Dobutamine to increase the contractility (beta-1 effect) seems to be a useful drug at this stage. LA pressure measurement or PCWP is desirable in order to understand the LV filling conditions as well as the LV performance. TOE is especially useful in such patients.

Table 6.3: Inotropes

Epinephrine	Levosimendan
Dobutamine	Milrinone
Dopamine	Amrinone
Dopexamine	Enoximone
Norepinephrine	
Isoprenaline	

Newer inotropes have been introduced and there is a wide choice of them (Table 6.3). Amongst these are the inodilators; (amrinone, milrinone and

enoximone) and calcium sensitizer (levosimendan) that may be useful.

There is no consensus that any one or two of the inotropes amongst those listed are the drugs of choice in a particular situation. Dobutamine and dopamine are frequently quoted in the anaesthetic literature. Nevertheless, epmephrine at a dose of 0.02 to 0.08 µg/Kg/min. is predominantly beta agonist and it is only with a higher dosage that peripheral constriction occurs. Many units (including the author's) still regard epinephrine as the inotrope of choice at the termination of CPB. Others prefer dobutamine or an inodilator or a combination of noradrenaline and a vasodilator. Levosimendan is the latest introduction and may soon find a place, especially in very poor LVs with down-regulated beta receptors. By administering it a day before the surgery in high-risk patients it has been shown that Levosimendan improved cardiac index and stroke volume as compared to placebo.[81]

Vasodilators

If SVR is increased, a reduction should allow the ventricle to empty more easily, thus increasing the stroke volume and CO. Coronary vasodilatation in the presence of CAD and myocardial ischaemia should reduce ischaemia and improve compliance and contractility of the ventricle. A reduction in RV preload reduces RV pressure and improves compliance of the LV by reduction of right sided pressure on the ventricular septum. These are the reasons for which vasodilators are used in patients with poor ventricle. However, their application may be unsafe in the presence of hypotension.

Intra-aortic Balloon Counterpulsation

An IABP catheter may have been inserted preoperatively or sometimes may need to be inserted in a hurry during the induction of anaesthesia. More commonly, it is inserted before termination of the CPB because of severe LV dysfunction. Although, the indications for its use vary from place to place, in general, IABP catheter should be inserted when CO and BP are low and LA or PCWP is high (>15 mm Hg), despite moderate doses of inotropes (usually 2). Itis advantageous to use it early, rather than increasing pharmacological support and risking sternal closure at a marginally adequate cardiac performance.

Other methods of ventricular support include centrifugal pump with partial bypass and extracorporeal membrane oxygenation, cardiac assist devices and

ultimately a total artificial heart and heart transplant.

Myocardial ischaemia

One of the fundamental objectives of management of patients with CAD is the prevention and treatment of myocardial ischaemia. The majority of ischaemic events are not induced by haemodynamic changes, while the anaesthetic techniques may have little bearing on the incidence of ischaemia[82] and outcome of surgery.[83] However, there is an association between tachycardia and the development of ischaemia.[84,85] The association of tachycardia with hypotension or increased LV filling pressure (both of which reduce CPP) is an undesirable combination. It follows, therefore, that close attention to haemodynamic control and rapid treatment of haemodynamic abnormalities is an important issue during intraoperative management of the patient with CAD. As the incidence of ischaemia does not decrease following revascularisation, careful monitoring must continue after bypass and in the ICU.

Treatment of Myocardial Ischaemia

Hypotension should be treated with volume and/or inotropes. Hypertension in response to surgical stress should be treated by deepening anaesthesia or administration of vasodilators. NTG infusion is beneficial for coronary circulation and should be the preferred treatment if the depth of anaesthesia is adequate. However, being primarily a venodilator, it may not always be effective in decreasing the BP and it may be necessary to administer inhalational agents such as isoflurane to produce the desired effect. If hypertension is accompanied by tachycardia, beta-blockers (metoprolol, atenolol, esmolol) should be used. Sinus rhythm should be restored if AF is present. This can be effectively performed by direct current (DC) cardioversion, if the sternum is open. Similarly, sequential pacing should be used in case of junctional rhythm. Intravenous NTG was used during CABG in 1976[86] and is the treatment of choice for perioperative myocardial ischaemia. It decreases the LV filling (preload) by venodilatation and reducing systemic BP. It is also a coronary vasodilator and thus, helps to improve the LV performance and can be used before, during and after CPB as an infusion at the rate of 0.5 to 2 μ/Kg/min.

Calcium channel antagonists: Calcium channel antagonists can be used to prevent and treat intraoperative myocardial ischaemia, coronary artery spasm,

and hypertensive episodes.

Nifedipine is not available for parenteral use and hence is not suitable during surgery. Diltiazem can be used in infusion form especially in those patients who have arterial revascularisation (radial and/or IMA). It can be administered as a bolus of 10 to 20 µg/Kg followed by an infusion of 5 to 10 mg/hour. It does not increase the coronary blood flow or decrease the coronary vascular resistance. However, it can cause hypotension and, hence, the infusion needs to be titrated constantly.

Nicardipine is another short acting calcium antagonist that can be administered intravenously. It has coronary antispasmodic and vasodilatory effects and also produces systemic vasodilatation. Studies have shown that nicardipine produces rninimal myocardial depression and a significant improvement in diastolic function in patients with ischaemic heart disease.[87,88] Due to its rapid onset and cessation of action, it is an attractive drug for the perioperative management of hypertension and myocardial ischaemia.[89]

Esmolol: Esmolol is an ultrashort acting cardioselective beta-1 blocker with a half-life of 9 minutes. It is extremely useful for the management of tachycardia and hypertension during perioperative period. It has been used effectively even in patients having poor LV function.[90] Its major role during CABG appears to be the control of tachycardia and hypertension. Adequate depth of anaesthesia must, however, be ensured before esmolol is administered. It can be used as a bolus of 0.5 to 1.5 mg/Kg followed by an infusion at the rate of 50 to 200 µg/Kg/min.

Myocardial protection

Although, currently, the focus of attention in myocardial protection is ischaemic and/or pharmacological preconditioning, the standard techniques of cardioplegia should be rigorously applied. In this respect, retrograde cardioplegia[91] and continuous nonmothermic cardioplegia techniques[92-94] are important in patients with poor LV function. For details of these techniques, refer to chapter 13.

Fast Tracking

The policies of cost containment, efficient resource utilisation and the

pressure on ICU beds have influenced the development of techniques of fast-track cardiac anaesthesia. A generally accepted definition of fast-tracking is not existent and what is fast to some may be slow to others. Indeed, published definitions have ranged from extubation on the operating room table followed by 2 to 4 hours stay in the recovery area to extubation within 12 hours and ICU stay as long as 24 hours. Nevertheless, a reasonable benchmark for defining early extubation appears to be extubation within 4 to 6 hours of the ICU arrival. Clearly, it appears that the hospitals want to do more and more cases at reduced cost. Thus, those hospitals that are not hard pressed to operate more cases may not necessarily follow the techniques of fast-tracking.

Since the major determinant of cost is length of stay, the aim is to extubate the patient early, remove the chest tubes early, and transfer the patient from the ICU and subsequently discharge from the hospital as soon as possible. It is needless to emphasize that in doing so, there should be no added risk to the patient. A metaanalysis has revealed that fast-track anaesthesia is safe and no significant outcome differences were found in 30-day all cause mortality, MI, sepsis, wound infection, stroke, acute renal failure, prolonged ICU stay, or surgical re-exploration for bleeding.[95] Reducing the total amount of opioid administered to enhance extubation within a few hours of ICU arrival has been the hallmark of fast-track cardiac anaesthesia. In order to do so, shorter acting anaesthetic agents that can be adrninistered in infusion form have been used. These include, midazolam, fentanyl, sufentanil remifentanil alfentanil, propofol and even inhalational agents such as isoflurane.

Although early extubation is the main concern of fast-tracking, it is not the anaesthetist alone who can achieve it. A focussed cardiovascular oriented surgical, anaesthetic and nursing team with common goals is essential. It is important that the surgical team is efficient as there is little room for surgical mishap that leads to prolonged CPB, coagulopathy and haemodynamic instability, all of which can come in the way of early extubation. Patients should not be actively cooled during CPB, but the body temperature should be allowed to drift to 32°C. Hypothermia in the postoperative period is the most important factor that makes early extubation difficult, if not impossible. Although some centres follow the policy of including all the patients in the fast-track protocol,[96] it is reasonable to consider high-risk patients with poor EF, low CO, CHF, etc. as less optimal candidates for early extubation.[97-99] Avoidance of intraoperative complications such as inadequate myocardial

revascularisation or inadequate myocardial protection is important as they may all lead to low CO syndromes. Intraoperative complications or inadequate surgery most commonly require extended mechanical ventilation.

Anaesthetic Technique

Extubation of the patient at the end of surgery in OT is possible. However, this practice is likely to prolong OT time. The better option is to move the patient to the ICU as soon as possible after skin closure, and allow the postoperative care team to manage the extubation. Various techniques have been used to shorten the time to extubation. These include the use of mainly inhalational agents, or reducing the dose of opioids in conjunction with propofol, or epidural[100] and intrathecal[101] techniques. Propofol is increasingly used as a supplement to the low-dose opioid anaesthesia.[102] Infusions of remifentanil or sufentanil have also been successfully used.[103-105] These techniques necessitate carefully planned postoperative pain management. In addition, failure of the fast-track protocol leading to readmission to the ICU is a possibility that should not be forgotten. The main reason for the failure, is respiratory distress, and the risk factors are age > 65 years, peripheral arterial disease, and drainage > 500 ml.[106]

In summary, early extubation after cardiac surgery is becoming the need of modern practice. However, reducing the mechanical ventilation times and ICU stay are not the only considerations. It is also important to look at the morbidity and mortality as well as the total hospital stay. The fast-track protocols mayneed to be individualised to institutional needs for economic as well as safety reasons. The cardiac anaesthesiologist is perhaps the most important member and he should actively participate in the team approach and tailor the anaesthetic management to achieve early awakening and extubation.

Off-Pump CABG

The mortality following conventional CABG with CPB has decreased to an acceptable level, but the morbidity in the form of stroke, neuro-cognitive dysfunction, atrial fibrillation and transfusion related complications still continues. Since, CPB has been one of the major contributors to these complications, it was believed that avoiding the CPB altogether may decrease

the incidence of these complications. This has been the driving force in the genesis of CABG without the use of CPB, i.e OPCAB. However, OPCAB is not a new technique and it was performed first in St Petersburg in 1964 when a left IMA was anatomosed to OM on a beating heart.[107] During this period, rapid developments were taking place in the CPB and cardioplegia techniques, and, hence attention was focused on these issues.

In the early 1990s, cardiac surgeons started doing 'MIDCAB', a term used to describe the CABG performed via "mini-thoracotomy" incision placed in the fourth or fifth intercostal space. Myocardial revascularisation is achieved with arterial grafts (either IMA or inferior epigastric artery) without using the CPB. Most commonly, the left IMA is anatomosed to the LAD coronary artery approximately 2 to 3 cm past the first diagonal branch or the right IMA is anatomosed to the distal right coronary artery. This surgical technique initially required one-lung ventilation and induced bradycardia to improve the operating conditions. Nowadays, this is almost abandoned as it allows only a single or two vessel surgery, it is technically demanding, and is a cause for considerable postoperative pain.

In the late 1990s, many surgeons started using a special stabilising retractor (Medtronic Octopus System) to accomplish myocardial revascularisation without CPB, the OPCAB. Jansen and coworkers in 1998 reported the design, experimental evaluation and the first clinical use of this suction based stabilising system.[108] The technological advances in the suction based stabilising systems allow access to all the areas of the myocardium making complete revascularisation of the myocardium possible. These coronary stabilizers (CS) minimise the myocardial movement and stabilise the coronary artery for anastomosis. The apical positioner is applied at the apex of the heart and is used to retract the apex of the heart. It is used in conjunction with the CS to provide access to the lateral myocardium. One such device, Guidant stabilization system (Guidant Corporation, Santa Clara, CA, U.S.A.) is shown in Fig. 6.4. The transition from MIDCAB to OPCAB surgery has eliminated the need for both one-lung ventilation and induced bradycardia. The CS is placed on the epicardium over the arteriotomy site to provide regional immobilisation. The Guidant stabilization system consists of two suction paddles connected to mobile arms. The suction paddles are placed adjacent to the arteriotomy site. The suction is applied via tubing connected to a regulated vacuum source to immobilise the surgical field. A saline and/or carbon dioxide irrigation system is also used to maintain a clear

surgical field. The CS can reach all sides of the heart and multiple vessel revascularisation can be performed. Thus, CABG on the beating heart has become a real alternative to conventional CABG with CPB. Single or multiple coronary arteries can be grafted through a variety of graft conduits that include IMA, saphenous vein, and radial artery.

OPCAB is the single greatest change in CABG technique in the past two decades. It can be performed in almost all patients except those with intracavitory thrombi, malignant ventricular arrhythmias, deep intra-myocardial vessels, combined procedures (valve replacement) and emergency CABG in a haemodynamically compromised patient. However, it is still not a widely practiced technique, and is performed in about 20–25 percent of patients undergoing CABG. This is likely to increase further, especially for high-risk patients with serious comorbidities.

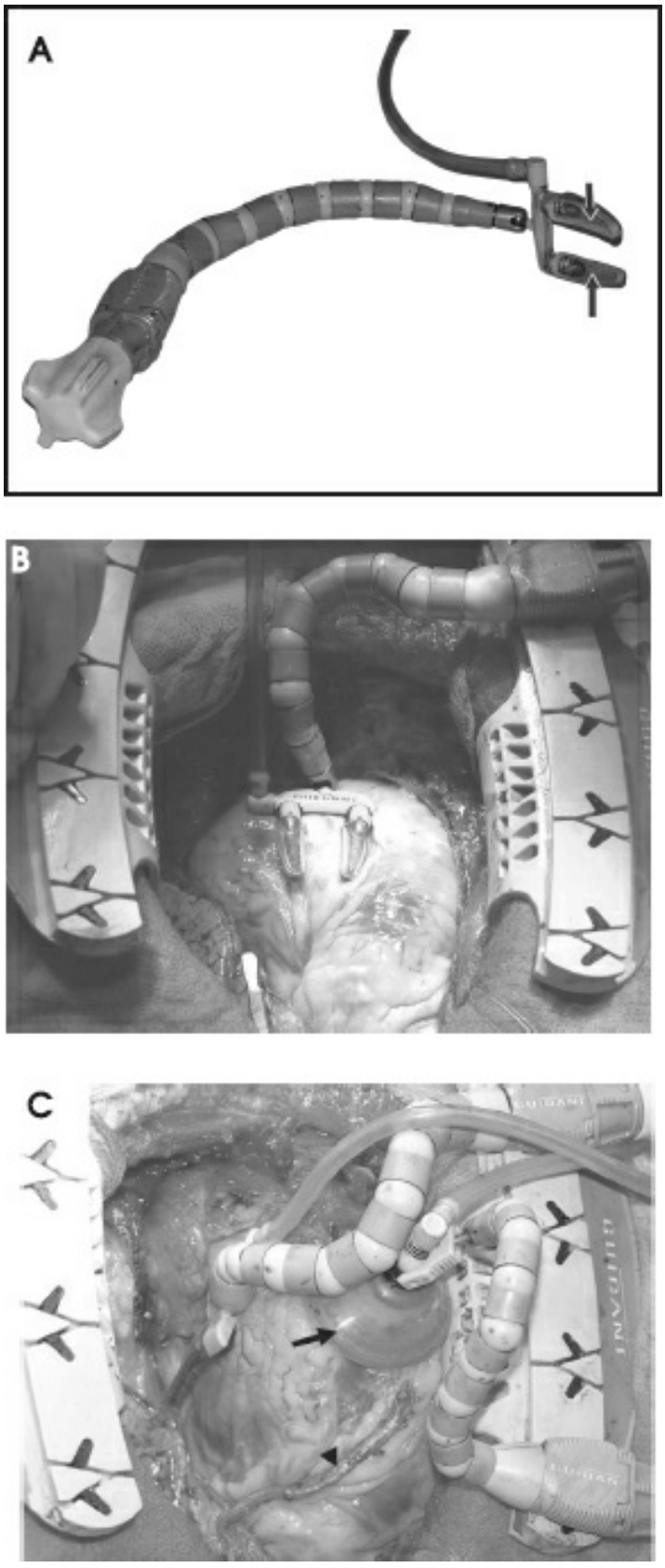

Figure 6.4: (A) Guidant stabilization system showing suction paddles (arrows), (B) The device being

used to stabilise the left anterior descending coronary artery, (C) The Guidant Axius™ Xpose™ Device 3 (arrow) being used in conjunction with Guidant stabilization system to provide surgical access to the lateral myocardium. The suction cup conforms to the heart and is mounted to the interlinking arm that can be used to position the heart as desired.

Anaesthetic Considerations

With the avoidance of CPB, the OPCAB can be considered equivalent to any other major noncardiac surgical procedure. Consequently, the need for elective ventilation is not there, and the patients can be extubated at the end of the operation or soon thereafter in the ICU. The anaesthetic technique needs to be modified to meet this goal. The changes in the anaesthetic techniques that have emerged in a patient undergoing OPCAB are summarised in Table 6.4. Shorter acting anaesthetic agents or inhalational agents are used more commonly to accomplish early extubation. In addition, hypothermia should be actively avoided by the use of warming blankets, fluid warming, and heat exchanger on fresh gas flow. As the patients are extubated early and the opioids are used in smaller doses or not used at all, the postoperative pain management becomes an important consideration and must be addressed appropriately. In summary, the goals of the anaesthetic management are, monitoring for and prevention of coronary ischaemia, maintaining anaesthetic depth and haemodynamic stability, and appropriate plan for postoperative care such as extubation and pain relief. A survey of 46 studies for main anaesthetic agents used during OPCAB has revealed that fentanyl was the most common agent (67 percent) followed by propofol (54 percent) and isoflurane (41 percent). The other agents such as sufentanil and remifentanil were used much less frequently (24 and 15 percent respectively), and the epidural technique was used in only 9 percent of the studies.[109]

Haemodynamic alteration

During OPCAB, frequent and multiple manipulations of the heart are required so that optimum exposure of the targeted vessels is obtained. These manoeuvres are likely to cause haemodynamic instability leading to hypotension, ischaemia, and arrhythmias. Therefore, the cardiac anaesthesiologist has to be more attentive during the anastomosis (unlike the conventional CABG performed under cardioplegic arrest) and has an important role to play in the maintenance of haemodynamic stability. In a prospective, observational study performed on 500 patients undergoing

OPCAB, Mishra and colleagues have reported that there is 18 percent decrease in the MAP and 66 percent increase in the CVP. In addition, the stroke volume and cardiac index decreased by 35 percent and 45 percent respectively.[110] These haemodynamic disturbances are related to frequent manipulation of the heart (verticalisation) as well as the compression effect of the CS.

Table 6.4: Changes in the anaesthetic technique that have emerged in a patient undergoing off-pump coronary artery bypass grafting.

• Reduction in the dosage of opioids • Use of shorter acting opioids • Administration of opioids in the form of an infusion • Maintenance of anaesthesia with inhalational agents or propofol • Use of thoracic epidural analgesia • Use of intrathecal opioids • Intensive monitoring and maintenance of haemodynamics • Early extubation • Intensive pain management in the postoperative period

Some authors have aimed at raising the blood pressure to offset the haemodynamic disturbances during cardiac manipulation. This is usually accomplished by using a phenylephrine infusion.[111] The systolic pressure is raised as high as 150 to 160 mm Hg before cardiac manipulation. In addition, the OT table is placed in the Trendelenburg position and rotated to the right to increase the cardiac preload. This manoeuvre also helps in visualisation, dissection and grafting of the distal coronary arteries. The decrease in CO and MAP depends on the operative location for revascularisation. Access to inferior and posterolateral myocardium by sternotomy demands lifting of the heart partly out of the pericardium and out of the thoracic cavity. Nierich et al[112] have shown that by placing the patient in 30° Trendelenburg position, the acceptable haemodynamic levels are usually restored within 30 seconds without the use of vasoactive medication. However, a bolus dose of ephedrine, 5 to 10 mg may be necessary. If restoration of acceptable haemodynamics is not possible with these methods, Nierich et al[112] further recommend that the heart must be released and a low dose of dopamine (less

than 5 μg/Kg/min.) should be administered during the next manoeuvre.

A few authors recommend the use of infusion of alpha agonist such as norepinephrine, phenylephrine or phenylephrine plus epine phrine that helps to maintain the pressure at a uniform desired level.[113,114] However, since the BP is maintained by increasing the SVR, transient decreases in CO to dangerous levels can occur. At times, the cardiac index can decrease to as low as 1.2 to 1.4 L/min/m^2. In patients with coexisting MR, the haemodynamic changes can be more severe. Cardiac index can decrease significantly with increase in the MR and mean pulmonary artery pressure. Milrinone has been used effectively in such patients to stabilize the haemodynamics.[115]

Over the years, the surgeons and anaesthe-siologists have improved their expertise, and the technological advances have taken place. In particular, the apical suction device used for access to the lateral and inferior walls of the myocardium is noteworthy. The results of Xpose access device in a report of 5 patients were published by Dullum et al.[116] The authors reported that the device provided easy access and grafting of all target vessels including lateral and inferior walls. In addition, the patients maintained stable haemodynamics with minimal or no inotropic support. Less severe haemodynamic changes were also reported with apical suction device during obtuse marginal grafting.[117]

Nowadays the haemodynamic derangements during OPCAB are not as severe as they used to be earlier. In the author's experience, the decrease in MAP is amenable to fluid therapy and the Trendelenburg position in most patients, with few patients requiring the use of inotropers. Nevertheless, severe haemodynamic derangements can occur and therefore, a perfusionist with a 'dry ready' CPB machine should always be on stand-by. The generally accepted criteria for conversion to CPB are, cardiac index < 1.5L/min/m^2, SVO_2 < 60 percent, MAP < 50 mm Hg, malignant arrhythmias, ST change > 2 mm, and complete cardiovascular collapse.[109] In patients with severe LV dysfunction (ejection fraction < 20 percent), OPCAB can be performed under assistance of IABP in order to avoid conversion to CPB.[118] In summary, infusion of volume and Trendelenburg position (to maintain preload) with or without the use of inotropes is required to maintain satisfactory haemodynamic status during the distal anastomosis. Overall, the requirement of inotropes has decreased and the choice of agent varies from place to place.

Surgical technique and myocardial ischaemia

Heparin should be administered before the placement of CS. The prescribed dose has varied between 1 to 3 mg/Kg with a goal of achieving an activated coagulation time (ACT) greater than 300 seconds. ACT is assessed every 30 minutes, and additional heparin (1 mg/Kg) is administered to maintain a level greater than or equal to 300 seconds. The heparinisation prevents thrombus formation in the native arteries and bypass grafts and allows emergent institution of the CPB if needed.

The surgeon places silicon elastic tapes deep in the myocardium, proximal and distal to the site of anastomosis. The CS is then placed over the site of anastomosis and arteriotomy is performed. At this stage the silicone elastic tapes are pulled tighter to provide a bloodless field. This would constitute the ischaemic time. The patient's ability to tolerate the procedure is continuously assessed and infusion of inotropes and fluids may be necessary to maintain BP while the anastomosis is being performed. IPC technique can be utilised before manipulating the target coronary artery. Preconditioning is a rapid adaptive response to a brief ischaemic insult. This adaptive response (conditioning) can slow the rate of cell damage during a subsequent prolonged period of ischaemia. A brief period of coronary occlusion (2, 3 or 5 min.) followed by a similar time for reperfusion in the target vessel is carried out. The regular use of IPC is however, not popular, and the groups describing large series of OPCAB have not reported the use of IPC.[119,120]

The development of intra-coronary shunts (DLP, Grand Rapids, MI) has added considerably to the safety and convenience during OPCAB surgery. The intra-coronary shunt provides a bloodless operative field while providing the blood flow to the distal myocardium. The blood flow through the intra-coronary shunt will be affected by the degree of narrowing of the native coronary artery to be bypassed as well as the CO, which may also be hampered during manipulation of the heart. The potential benefits of the intra-coronary shunt are; elimination of the need for IPC, prevention of arrhythmias and haemodynamic compromise. However, these benefits have not been proven by prospective randomised studies. As discussed earlier, inhalational anaesthetic agents can be used to provide pharmacological preconditioning in order to reduce the myocardial injury. The ischaemia during OPCAB may not be easy to assess. When the heart is lifted and rotated for exposure of circumflex and right coronary arterial distributions,

the ECG signal is changed and echocardiographic imaging of the heart is significantly hampered due to the placement of surgical sponges behind the heart.[111]

After completing all the distal anastomoses, the proximal anastomosis is performed by placing the partial clamp on the proximal ascending aorta. The BP should be lowered to 100 mm Hg systolic at this stage. The functioning of the grafts can be assessed by visual examination and palpation of the graft or Doppler ultrasound that shows phasic flow with dramatic augmentation and prolongation of the diastolic phase.[111] The use of a new generation infra-red camera has been described for the assessment of the anastomotic status.[121] The authors suggest that this non-invasive technique provides an effective and real-time evaluation in the OT that is likely to result in more successful OPCAB. Most of these new methods involve expensive technology and are not practical in many centres. TOE is now available in many cardiac centres and can be used to assess myocardial perfusion and graft patency in a relatively easy manner. Contrast echocardiography using sonicated albumin ultrasound contrast medium has been described.[122]

Protamine is given and the pericardium and sternum are closed, as would be done in conventional bypass surgery. It should be remembered however, that OPCAB may be converted to conventional CABG with CPB at any point, should the patient not tolerate the period of ischaemia required to complete the anastomosis or the surgeon encounters any technical difficulty or there is significant haemo-dynamic instability during cardiac manipulation. Therefore, the OT should be prepared as for a standard CABG and the perfusion team should be readily available.

Monitoring

Standard monitoring techniques including an intra-arterial line (radial artery) and central venous line and a continuous 3 to 5 lead ECG monitoring and ST segment analysis should be performed. However, as stated earlier, the ECG signal can change during cardiac manipulation. Likewise, TOE imaging of the ventricle from gastric or oesophageal views is difficult, but is considered an important monitoring tool during OPCAB. TOE is beneficial for the assessment of regional wall motion abnormalities and the volume status of the patient. The coexisting MR can increase during the verticalisation of the heart for anastomosing the lateral coronary vessels. TOE is commonly used

in most centres nowadays. If TOE is available, use of PAC may be avoided, instead, central venous access can be obtained by placing an 8.5 F or 9 F introducer sheath in the internal jugular vein. PAC can be inserted through the introducer sheath at a later stage, if necessary.

The haemodynamic data is affected by cardiac manipulation leading to elevation in the pulmonary artery pressure, PCWP, CVP and a decrease in CO. Therefore, a new baseline should be established after the heart is in position for each anastomosis. The maintenance of stable BP during OPCAB poses a greater challenge for the anaesthesiologists than conventional CABG with CPB.

Continuous cardiac output and mixed venous oxygen saturation

The continuous cardiac output (CCO)/SVO_2 PAC automatically calculates the CO by a blood warming technique with a heating coil around the PAC. It provides a trend in CO during the entire surgical period and is a useful monitoring tool in patients in whom grafts on the posterior or far lateral myocardial wall are necessary. More than CO, the online SVO_2 measurement is an excellent method of detecting abrupt changes in cardiac performance caused by surgical manipulation of the heart. The SVO_2 represents both delivery and consumption of oxygen and depends upon haemoglobin, arterial oxygenation and CO. The changes in SVO_2 during cardiac manipulation represent changes in CO, because haemoglobin and oxygenation remain stable. In general, SVO_2 of more than 60 percent is accepted before any interventions are performed.

Depth of anaesthesia

Monitoring the depth of anaesthesia is an important consideration as in an attempt to extubate patients early, doses of opioids and anaesthetic agents are minimised. Monitoring bispectral index (BIS) can be useful to prevent awareness from occurring. A BIS of less than 60 indicates adequate depth of anaesthesia.

Temperature control should be achieved with suitable methods during the intraoperative period. The various techniques that can be employed are

passive humidifiers, fluid warmers, warming blankets and maintaining adequate OT temperature.

Anaesthetic Agents

The anaesthetic technique should consist of a balanced anaesthesia with the same goals as conventional CABG with CPB. However, the selection of anaesthetic agents should be based on the objective of facilitating early extubation, unless some adverse event occurs during the perioperative period. Anaesthetic induction agents such as thiopental, propofol and etomi-date can be used. Fentanyl has been a popular narcotic agent used in the dose of 5 to 10 µg/Kg. Morphine in the dose of 0.3 to 0.5 mg/Kg can also be used. As the doses of narcotics are reduced (to accomplish early extubation), concomitant use of thiopental or propofol will be necessary during induction of anaesthesia. Pancuronium has been the commonest muscle relaxant, but other agents such as vecuronium or rocuronium can also be used depending upon the baseline HR. The anaesthesia can be supplemented with an inhalational agent such as isoflurane, halothane or sevoflurane. Thoracic epidural analgesia can be combined with general anaesthesia and will be discussed separately in the subsequent pages.

Current Status of OPCAB

Since its inception, the OPCAB technique is continuously evolving and being evaluated. Whenever the OPCAB is evaluated, the first question that should be asked is whether OPCAB provides cardiac outcome equivalent to that of conventional CABG with CPB. This is so, because OPCAB is technically demanding and may compromise the quality of anastomosis or lead to incomplete revascularization. Having met this, the other possible advantages of OPCAB in terms of neurological outcome, renal complications, atrial fibrillation, blood transfusion, and others should be explored. In a pro-con debate, Moinuddeen and colleagues[123] favoured the conventional CABG, because OPCAB does not improve the neurological outcome, it causes haemodynamic disturbances, may result in incomplete revascularization, the graft patency is questionable, and there is no reduction in cost. The graft patency following OPCAB was questioned by Khan and coworkers.[124] In a series of 104 patients randomized to OPCAB and conventional CABG, the authors showed that although, the troponin-T levels were lower in the

OPCAB group in the first 72 hours, the graft patency rate at 3 months was significantly lower for all graft territories in them. In an editorial, Feneck suggested that the increased graft thrombosis may be related to prothrombotic state following OPCAB, reduced dose of heparin or inexperience of the surgical team.[125] He further suggested that matching the operation to the patient is important, and the anaesthesiologists and the surgeons should be proficient in both techniques. Several other papers during the same period did not demonstrate any significant differences in the graft patency rates at varying time points.[126-128]

There are many clinical studies that have demonstrated the superiority of OPCAB over conventional CABG with CPB.[129-133] Its safety has been demonstrated in elderly patients also.[134] One meta-analysis that included only non-randomized trials showed significant benefit of OPCAB in terms of death, myocardial infarction, stroke and atrial fibrillation[135], while another meta-analysis was inconclusive.[136] The largest meta-analysis on the subject was published by Cheng and coworkers.[137] A total of 3369 patients from 37 randomized trials were included. There were no differences in all-cause mortality, stroke, acute MI, and renal dysfunction. However, there were significant reductions with OPCAB in AF, patients transfused, respiratory infection, need for inotropes, duration of ventilation, ICU and hospital length of stay, and neurocognitive dysfunction at 2 to 6 months. The authors concluded that the postoperative morbidity is significantly decreased at no measurable increased risk to the patient.

The most recent randomized trial on the subject is the ‘ROOBY’ (randomized on-pump off-pump bypass) trial.[138] The results of this trial that was spanned over a period of 6 years and conducted at 18 US medical centres comprising of 2203 patients showed that there was no difference in the 30-day mortality and major morbidity, but the one year deaths from all causes or cardiac causes was significantly higher in the OPCAB group (9.9 Vs 7.4 percent and 8.8 Vs 5.9 percent respectively). The authors attributed these differences to incomplete revascularisation and lower graft patency rates in the OPCAB group. There were no differences in the neurological outcome. In this study, however, high-risk patients were excluded, and surgical expertise may have been limited, as surgeons with prior exposure to only 20 OPCABs were allowed to operate. Furthermore, the study span was too long and only US centres participated. Another randomised trial performed on 4752 patients

at 79 centres in 19 countries has revealed that there were no significant differences between conventional CABG and OPCAB with respect to 30-day mortality, myocardial infarction, stroke or renal failure.[139] The use of OPCAB resulted in reduced rates of transfusion, reoperation for perioperative bleeding, respiratory complications, and acute kidney injury, but increased the risk of early revascularisation.[139] It seems that OPCAB will still continue to be practiced, at least in high-risk patients.

It may not be worthwhile performing future trials, as none can be large enough to conclusively prove the superiority of one technique over the other. It is more prudent to regularly update the existing meta-analysis. However, studies should be performed in high-risk patients with concomitant systemic diseases in whom avoidance of CPB is likely to be more beneficial. Also, the conversion rate from OPCAB to conventional CABG with CPB, and the outcome of such converted patients needs to be explored further. The current data is limited and confusing as few studies have reported conversion rates,[137] and some others have included converted patients to the conventional CABG group. In addition, there is underreporting of conversion rates.[140]

The neurological outcome has not changed with OPCAB, this is contrary to the expectations. However, this can be explained by the fact that although, CPB is not used, aorta is handled during proximal anastomosis, which is an important cause of aortic atheromas embolising into brain. The accompanying haemodynamic compromise may explain the occurrence of neurocognitive dysfunction in OPCABs. One study has shown that jugular oxygen saturation revealed poor global cerebral oxygenation (< 50 percent) in large number of patients undergoing OPCAB in comparison to those undergoing conventional CABG (48 Vs 27 percent).[141] They concluded that patients undergoing OPCAB are exposed to significantly fewer cerebral emboli, but the risk of cerebral hypoperfusion is much greater than CPB.

The OPCAB surgery looks promising and it seems that with increasing number of options for the treatment of coronary artery disease, the need to identify subgroups of patients who benefit from specific treatment option is necessary. The cardiac anaesthesiologist should strive to optimize his contribution towards the betterment of patient outcome. There is a need to clearly define the haemodynamic goals during distal anastomosis, and use of inhalational anaesthetic agents for providing cardioprotection needs to be

explored further. The neurological outcome can be improved by maintaining adequate cerebral perfusion throughout, but especially during distal anastomosis. The cerebral congestion should be avoided and monitoring jugular bulb saturation may be beneficial.

Thoracic Epidural Analgesia

The other form of anaesthetic technique that can be employed is the use of thoracic epidural analgesia with general anaesthesia. In the current era of early tracheal extubation, providing optimal pain relief after CABG can be challenging. There are several ways of providing postoperative analgesia (Table 6.5), however intravenous opioids have been used widely. Over the past decade, application of epidural techniques has increased.[142] The potential benefits include good analgesia, attenuation of stress response, optimal redistribution of coronary blood flow, haemodynamic stability, improved pulmonary function and early extubation. These advantages are likely to lead to a better clinical outcome. However, one of the major concerns of this technique is the risk of epidural haematoma in the light of heparinisation that the patient will receive during the course of surgery. Some precautions are necessary before its administration. It should be ensured that the coagulation status of the patient is normal. The coagulation status is generally considered normal, if the platelet count is more than 1,50,000/mm^3, international normalised ratio is less than 2, there is no history of bleeding diathesis, and antiplatelet drugs are discontinued for more than 5 days preoperatively. In addition, the epidural catheter is inserted the day before operation and if placed on the day of surgery, the surgery is postponed if a 'bloody tap' is encountered.[143]

Table 6.5: Methods of postoperative pain relief

• Intravenous opioids
• Patient controlled analgesia
• Intercostal nerve blockade
• Thoracic epidural analgesia
• Intrathecal techniques
• Intrapleural local anaesthesia
• Alpha-adrenergic agonists

More commonly, the catheter is placed on the day of surgery in the OT

before the induction of anaesthesia. A T_3 or T_4 intervertebral space is chosen for catheter placement and analgesia is provided through the thoracic epidural catheter with bupivacaine 0.25 to 0.5 percent, (20 to 25 mg) as a loading dose followed by a continuous infusion. Opioids such as fentanyl, sufentanil or preservative-free morphine can also be combined.

Many early reports demonstrated that administration of thoracic epidural opioids or local anaesthetics to patients before and after CPB provide reliable postoperative analgesia after cardiac surgery. In one report of 714 patients undergoing CABG, the authors placed the catheter on the day of surgery and proceeded with both the epidural placement and the surgical procedure even after a bloody tap (11 patients) after confirming that it was not an arterial bleed.[144] Using the approach, 75 percent of their patients were extubated in the OT and there were no spinal haematomas or neurological complications. Chakravarthy and Colleagues published their experience of 13 years (2113 patients) showing the safety of the technique.[145] These and other reports (mostly small) were poorly controlled as they were not prospective randomized investigations. However they demonstrated the utility of the technique in providing good analgesia, attenuation of stress response, and haemodynamic stability. A recent randomized trial on 654 patients failed to demonstrate a clinically relevant benefit of thoracic epidural on the frequency of major complications after cardiac surgery compared with fast-track cardiac anaesthesia without epidural anaesthesia.[146] The authors believed that in view of the potential complication of epidural haematoma, it is questionable whether it should be used routinely in cardiac surgery. Another randomized trial in 226 patients undergoing OPCAB has shown that addition of thoracic epidural to general anaesthesia significantly reduces the incidence of postoperative arrhythmias and improves pain control and overall quality of recovery, allowing earlier extubation and hospital discharge.[147] Some, studies have focused on the ability of these techniques to affect the clinical outcome in terms of morbidity and mortality. Scott and colleagues in 2001 in a large prospective randomized study showed that the use of epidural techniques may facilitate early extubation, decrease the risk of lower respiratory tract infection, and decrease the risk of supraventricular arrhythmias following cardiac surgery.[148] Priestley and associates revealed that the epidural techniques enhanced postoperative analgesia, yet had no effect on pulmonary (spirometry, saturations, radiography) nor cardiac (ischemia, enzymes, AF)

function.[149] Patients receiving epidurals were extubated sooner, but the length of stay data were not affected. Similar results showing earlier tracheal extubation were published by Royse and Hansdottir and their colleagues.[150,151]

High thoracic epidural anaesthesia has also been used as a sole anaesthetic technique in patients undergoing MIDCAB and has been designated conscious off-pump coronary artery bypass (COPCAB). Initial reports described its use in patients receiving one or two graft.[152,153] Later on it was also used for placement of multiple grafts[154,155] These techniques are labour intensive and also carry a conversion rate (to general anaesthesia), which may be as high as 20 percent.[156]

The thoracic epidural techniques are not without risks. The epidural local anaesthetic can lead to hypotension and opioids can lead to pruritus, nausea and vomiting, urinary retention, and respiratory depression. The most dreaded complication is the occurrence of epidural haematoma, the risk of which is increased during cardiac surgery due to systemic heparinisation. The first report of epidural haematoma associated with thoracic epidural catheter inserted in a patient before cardiac surgery was published in 2004.[157] The consequences of epidural haematoma can be catastrophic. Indeed subsequent reports of epidural haematoma leading to such consequences have appeared in the literature.[135,158] According to one study, the estimated risk of epidural haematoma is 1 : 1500 (minimal) to 1: 150,000 (maximal).[143] A more recent paper has estimated it to be 1:12,000 (95 percent confidence interval of 1 : 2100 to 1 : 68, 000).[159] It is perhaps due to this reason that the anaesthesiologists are reluctant to use this technique on a routine basis. Surveys amongst anaesthesiologists have revealed that most anaesthesiologists do not prefer to use epidural anaesthesia or analgesia for cardiac surgery.[109,160]

This may be related to the fact the patients understand and accept surgical complications more readily than anaesthetic ones. The technique of thoracic epidural anaesthesia remains controversial. Some argue that until there is clear evidence linking the use of thoracic epidural catheters in patients undergoing cardiac surgery to improved postoperative outcome (cardiac, pulmonary, renal, etc.), the potential benefits and potential risks should be seriously considered in each individual patient.[161] Others feel that although, thoracic epidural catheter insertion for patients undergoing CABG should not

be viewed as irrational, routine selection of this approach still seems inadvisable.[162] A recent meta-analysis has concluded that thoracic epidural reduces the risk of postoperative supraventricular arrhythmias and respiratory complications. The complications such as epidural haemotoma could not be assessed.[163] The authors concluded that epidural anaesthesia should be used with caution until risk-benefit profile is further elucidated.

Patients presenting for cardiac surgery continue to get older and sicker with more comorbidities such as neurological dysfunction, myocardial dysfunction, renal dysfunction etc. Furthermore, more and more patients are likely to be receiving antiplatelet agents (aspirin, clopidogrel). Therefore, it seems that an individualized approach should be applied while practicing thoracic epidural anaesthesia. In addition, the technical expertise should also be a consideration.

Magnesium

It has been shown that administration of magnesium (magnesium sulfate) before an ischaemic insult can reduce the infarct size.[164] In practice, it has been shown to cause reduction in new postoperative atrial and ventricular arrhythmias.[165] The optimal dose of magnesium is difficult to define due to variability of the doses administered. However, timing of administration is important. Maslow et al have shown that a median dose of 5 gm administered before manipulation of the native coronary artery significantly decreased the postoperative atrial tachyarrhythmias.[165] It is also suggested that the magnesium therapy should be continued for four days as magnesium deficiency persists for four days after surgery, when the frequency of atrial arrhythmias is the highest.

Postoperative Pain Relief

Since the anaesthetic technique is tailored to achieve early extubation (high-doses of opioids are not administered), postoperative pain relief becomes an important consideration to make this period comfortable for the patient. Table 6.5 shows the methods of postoperative pain relief. Posterior intercostal nerve blockade (using 0.5 percent bupivacaine) can be performed by the surgeon under direct vision at the conclusion of operation. This technique carries a very low risk and offers very good postoperative pain relief. Use of thoracic epidural analgesia (bupivacaine 0.125 percent with or without opioid) has

been described, but as discused earlier, there is a concern for epidural haematoma in the face of systemic anticoagulation. The other methods of pain relief that can be used are intravenous opioids, patient controlled analgesia, intrathecal opioids[166], and intrapleural local anaesthesia.[167] Intrathecal morphine administered before anaesthetic induction provides an extended analgesic effect (up to 24 hours) leading to decreased postoperative systemic opioid consumption. These aggressive measures of controlling postoperative pain allow patients to be extubated immediately or shortly after the surgery. Selective alpha-2 adrenoceptor agonist dexmedetomidine may be a very useful agent in the postoperative period as it is associated with minimal respiratory depression. In addition, due to its analgesic properties, it significantly decreases the requirement of additional opioids in patients on mechanical ventilation.[168,169] It may be associated with hypotension.

Port-access Cardiopulmonary Bypass

The OPCAB surgery is now being performed at many centres. This approach demands surgical expertise to complete anastomoses on a ‘beating heart’. The main advantage of the technique is that it avoids the problems related to extracorporeal circulation. In contrast, the port-access surgery permits minimally invasive cardiac surgery while providing the support of extracorporeal circulation for myocardial preservation during procedures on the heart. However, there are no prospective data from randomised studies to prove the efficacy of this approach.

The anaesthesiologist needs additional expertise for the conduct of port-access CPB. He is responsible for inserting the endo-pulmonary vent and endo-coronary sinus catheter through the introducer sheath placed in the internal jugular vein. These catheters form a part of the series of catheters that are introduced through various puncture sites including the femoral artery and vein.

An endo-aortic catheter is placed through the femoral artery for systemic perfusion. An inflatable balloon at the end of this catheter acts as an aortic cross clamp. The antegrade cardioplegia is administered through one of the lumens and the same can also function as an aortic root vent. The venous return is provided by a catheter that is advanced to the level of inferior vena-cava-RA junction through the femoral veins. The endopulmonary vent can

further augment the venous return. The retrograde cardioplegia canbe delivered through the endocoronary sinus catheter placed by the anaesthesiologist via internal jugular vein. TOE and colour-flow Doppler along with fluoroscopy is necessary for accurate placement of the catheter. Nowadays thoracoscopic video-assisted surgery, often with robotic assistance is performed. This requires prolonged one-lung ventilation to optimise exposure. Limited exposure of the heart during surgery poses challenges and management of arrhythmias, haemostasis, myocardial protection, and deairing at the end of surgery are important considerations.[170] Endoscopic robotic harvesting of internal mammary arteries is routinely performed at some centres, but endoscopic technique for harvesting the right gastroepiploic artery is being developed.[171] These surgical techniques not only require expensive equipment, but are also associated with steep learning curve. They have not shown the benefits that were expected of them. Consequently, its present role in cardiac surgery remains undefined.

In summary, improvements in both traditional and minimally invasive CABG have decreased the length of stay, morbidity and mortality. In particular, the OPCAB has established itself as an alternative technique, and it will be increasingly performed in sicker patients. The role of inhalational anaesthetic agents for myocardial protection is being explored. New approaches to CABG are continuing to evolve that demand the anaesthetic skills of the highest order. The anaesthesiologists will have to fulfill this responsibility and contribute in the welfare of the patient.

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Chapter 7: Anaesthesia for the Management of Congenital Heart Defects

Cardiac surgery was initially attempted on patients suffering from congenital heart disease (CHD). For obvious reasons, the surgery was performed on grown up children or adults. With the remarkable advances in open-heart surgery during past 30 years, the correction of congenital heart defects including the complex defects is now performed during infancy or early childhood. The past decade has witnessed significant progress in paediatric cardiac surgery and anaesthesia leading to significantly improved survival of patients with CHD. Of note, are the monitoring of the cerebral oxygen saturation by near infrared spectroscopy during cardiopulmonary bypass (CPB), outcome advantage of Sano shunt (connection by vascular graft from the right ventricle to the pulmonary artery) over the Blalock-Taussig shunt in the Norwood procedure, and the developments in the ventricular assist devices in the paediatric cardiac surgical population.[1] The outcome of neonatal cardiac surgery has dramatically improved and low body weight is considered an important risk factor. However, it has been shown that low body weight itself (< 2500 gm) is not associated with patient morbidity or mortality, but emergency surgery and perioperative low cardiac output (CO) strongly influence early mortality.[2] The anaesthesiologists should be familiar with both the pathophysiology of the CHD as well as that of the infant. For detailed information on the subject, the reader is referred to the standard books on cardiac[3] and paediatric cardiac[4] anaesthesia. The purpose of this chapter is to present an overview of the pathophysiology of important congenital defects along with the principles of anaesthetic management.

The infant or child suffering from CHD has an immature cardiopulmonary system. In addition, intracardiac shunts, obstruction or both leading to cyanosis or congestive heart failure (CHF) is commonly present. Pulmonary vascular disease and right ventricular (RV) failure can also be frequently present. Coronary artery disease (barring abnormalities in the coronary arterial origin and distribution) is never associated with CHD, although, myocardial ischaemia may still be a problem during certain surgical repairs such as transposition of great arteries (TGA). In lesions with right-to-left shunting, severe arterial hypoxaemia is present. This leads to polycythaemia with increased blood viscosity and coagulopathies. These are some of the important differences between acquired heart disease and CHD.

In a normal child, the foetal parallel circulation (Fig. 7.1) is transformed into adult type series circulation (Fig. 7.2) after birth. This changeover is completed several days after birth. After birth, as a result of expansion of the lungs with oxygen, pulmonary vascular resistance (PVR) decreases rapidly for 24 to 48 hours. By this time the pulmonary artery (PA) pressure becomes lower than the systemic pressure and flow across the ductus becomes predominantly left-to-right. The ductus normally closes by second or third day of life. These changes also functionally close the foramen ovale due to an increase in the left atrial (LA) pressure to more than the right atrial (RA) pressure. The pulmonary circulation undergoes extensive remodelling in the first few years of life that further decreases the PVR. As the PVR decreases and the systemic vascular resistance (SVR) increases, the right and left ventricular masses that are virtually equal at birth, undergo changes resulting in a much more muscular left ventricle (LV) as compared to the RV.

These normal developmental changes are altered in the presence of CHD. For instance, if hypoxia and acidosis occur due to CHD during neonatal and infant period, the normal decrease in PVR may slow or reverse. Additionally, ductus may remain patent resulting in the persistence of transitional circulation. In defects such as ventricular septal defect (VSD), the decrease in PVR can result in excessive pulmonary blood flow due to left-to-right shunting. In some severe cardiac defects such as tricuspid atresia or pulmonary atresia, the transitional circulation through patent foramen ovale (PFO) and/or patent ductus arteriosus (PDA) must persist for the survival of the child. If not, emergency balloon septostomy and prostaglandin E_1 administration for delaying or reversing the PDA closure is necessary.

In addition to changes outlined above, the heart of an infant can be

immature, that is, significantly less compliant than the adult heart so that small increases in circulating volume can lead to ventricular failure.

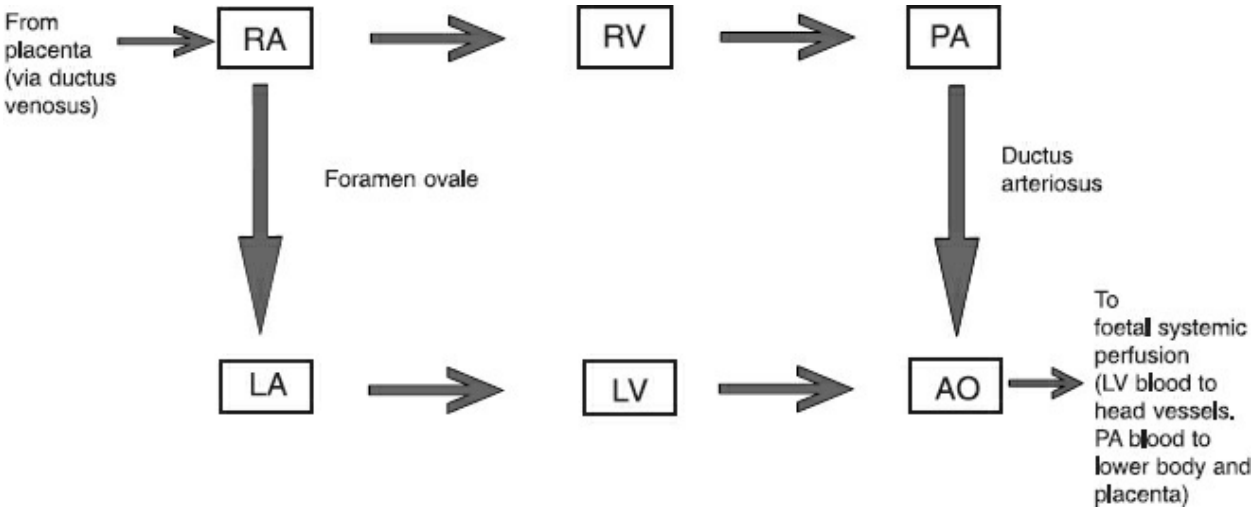

Figure 7.1: Diagrammatic representation of the foetal parallel circulation (RA: right atrium, RV: right ventricle, PA: pulmonary artery. LA: left atrium, LV: left ventricle, AO: aorta).

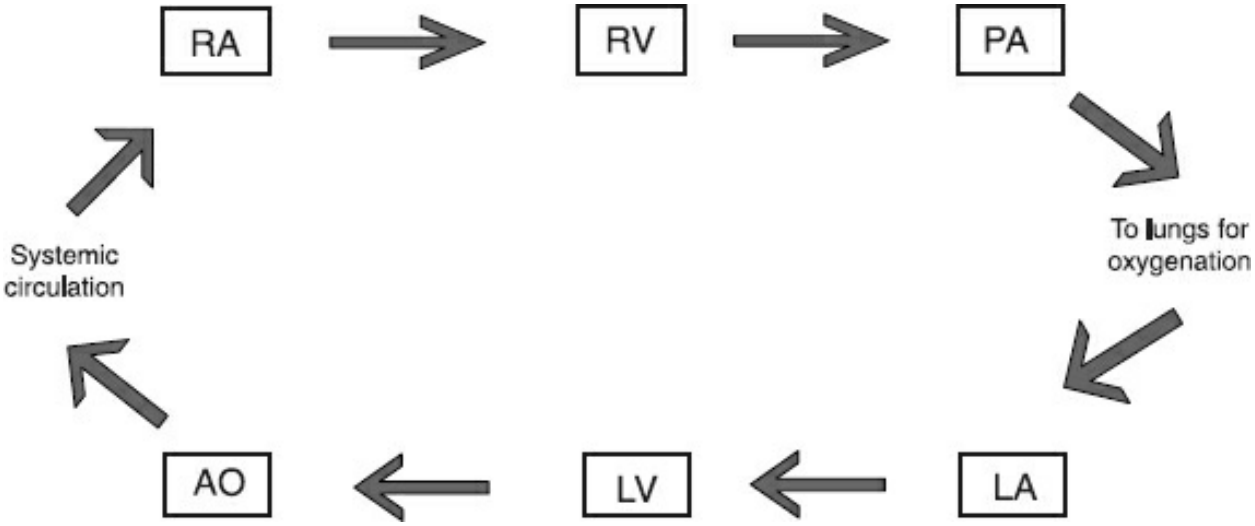

Figure 7.2: Diagrammatic representation of the foetal series circulation (RA: right atrium, RV: right ventricle, PA: pulmonary artery, LA: left atrium, LV: left ventricle, AO: aorta).

Classification of Congenital Heart Defects

There are many ways of classifying congenital heart defects. From the anaesthesiologist's point of view, however, patients with CHD can be classified into two groups: 1. children who have cyanosis and a right-to-left

or bidirectional shunt but with a predominant right-to-left shunt, and 2. children who have acyanotic congenital heart defects. The second group can be further divided into those who have dominant left-to-right shunt and those without a shunt. The common lesions are listed in table 7.1.

Pathophysiology

Shunting

The normal circulation is divided into two parts: 1. systemic circulation, and 2. pulmonary circulation. These two circulations are separate and there is no communication between the two. In some CHDs, a direct communication of various sizes exist. These central shunts are labelled as simple shunts when they occur alone or complex shunts when associated with obstructive lesions. Figures 7.3 and 7.4 show the diagrammatic representation of the simple and complex shunts. When the shunt is in the right-to-left direction (usually complex shunt), it leads to mixing of venous blood into systemic blood causing hypoxaemia. This is compensated by increased CO and haemoglobin concentration to maintain oxygen transport which lead to volume and pressure load on the heart. When the shunt is in the left-to-right direction (usually simple shunt), it can lead to an increase in pulmonary blood flow causing important changes in the pulmonary circulation that cause increase in the PVR. It is important to remember that the direction and magnitude of shunts may change during anaesthesia as well as operative manipulations of the heart and great vessels. For instance, an improper anaesthetic induction leading to hypercarbia and acidosis can increase the PVR substantially leading to a temporary decrease or reversal of shunting across an atrial septal defect (ASD). Similarly, compressing subclavian artery by the surgeon during performance of a Blalock Taussig (BT) shunt may decrease the right-to-left shunting across the VSD in a patient with tetralogy of Fallot (TOF). Although, haemodynamics of cardiac shunts is complex and depends on many factors, some basic principles and concepts that control shunting can be useful.

Table 7.1: Classification of congenital heart defects

Cyanotic

	Tetralogy of Fallot
	Pulmonary stenosis with atresia with ASD or VSD
	Transposition of great arteries
	Common ventricle
	TAPVC
	Tricuspid atresia
	Ebstein anomaly
Acyanotic	
	Without shunt
	Coarctation of aorta
	Aortic stenosis
	Subaortic membrane
	With left to right shunt
	ASD
	VSD
	Patent ductus arteriosus
	Truncus arteriosus

ASD: atrial septal defect, VSD: ventricular septal defect, TAPVC: total anomalous pulmonary venous connection.

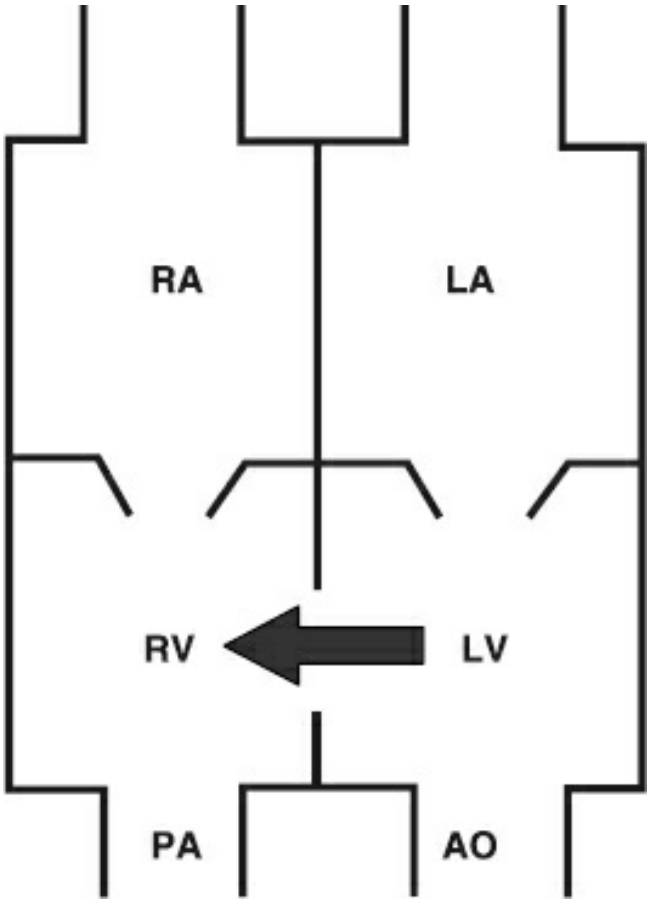

Figure 7.3: Diagrammatic representation of simple shunt in a patient with ventricular septal defect (RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle, PA: pulmonary artery, AO: aorta).

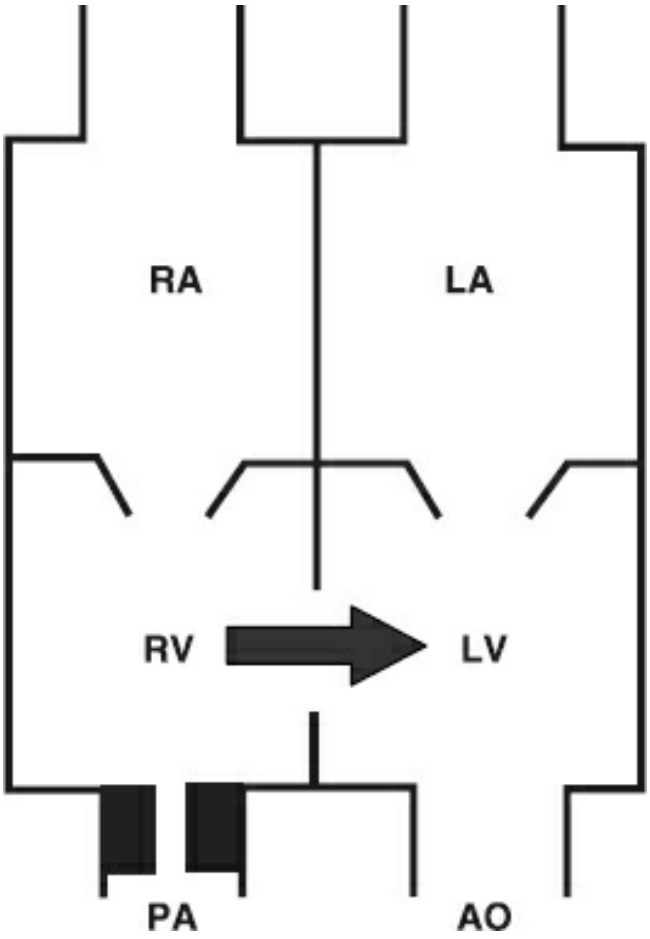

Figure 7.4: Diagrammatic representation of complex shunt in a patient with ventricular septal defect with pulmonary stenosis. Due to pulmonary stenosis, the right ventricular (RV) pressure may be higher than the left ventricular (LV) pressure resulting in right-to-left shunt (RA: right atrium, LA: left atrium, PA: pulmonary artery, AO: aorta).

In those shunts that are not associated with obstructive lesions (simple shunts), PVR on the right side and SVR on the left side offer the outflow resistances. This is especially so when the defect (shunt orifice) is large. In patients with small shunt orifice, the shunt is relatively fixed. Therefore, in lesions with larger shunt orifices, the direction and magnitude of the shunt is determined largely by the balance of outflow resistances (PVR and SVR). When the communication is very large, complete mixing occurs resembling a common chamber. In the absence of any anatomical outflow obstruction, the flow into the pulmonary and systemic circulation is determined by the PVR and SVR respectively. Since the normal PVR is much less than the SVR, pulmonary blood flow can be excessive in a simple shunt (e.g. VSD), even in the neonatal period. Thus, by manipulating the relative vascular resistance of systemic and pulmonary circulation, shunting can be altered by the

anaesthesiologist to a variable extent depending upon the size of the communication (more if shunt orifice is large).

In the shunts where an outflow obstruction is present on one side of the circulation (complex shunt), the fixed resistance is added to the outflow resistance of the vascular bed on that side. This generally leads to an increase in shunting to the opposite side. If the obstruction is dynamic (such as infundibular obstruction in TOF), in addition to the fixed right-to-left shunting across the VSD, a variable component of shunt caused by infundibular spasm can exist. Thus, the infundibular spasm can lead to a cyanotic spell and relief of spasm leads to recovery from the spell. Likewise, large changes in SVR can also change shunting by altering the balance.

The understanding of the concepts about shunting helps the anaesthesiologist to make attempts to control the PVR and SVR in such a way that the haemodynamic status is maintained or even improved during surgery.

Pulmonary blood flow

The pulmonary blood flow may be decreased or increased in shunt lesions. The pulmonary blood flow is less than systemic blood flow when there is right-to-left shunting (e.g. TOF). This results in systemic arterial desaturation due to mixing of mixed venous blood into the systemic blood flow. The decreased pulmonary flow during foetal and infant development can lead to significant abnormalities in the pulmonary arterial tree, fn defects such as TOF, this may result in high PVR that does not decrease normally in the first few years of life.[5] When the pulmonary blood flow is reduced considerably in relation to the systemic blood flow, several compensatory mechanisms come into play in order to maintain the oxygen transport. These include polycythaemia, increased blood volume, alveolar hyperventilation and development of aorto-pulmonary collaterals. Polycythaemia increases the blood viscosity leading to peripheral sludging, acidosis, and organ thrombosis or infarction. Cerebral and renal thrombosis are particularly common in children with haemoglobin concentrations above 20 g/dL. These patients also have associated coagulopathies.

When the pulmonary blood flow is greater than the systemic flow (e.g. VSD), the pulmonary reserve is compromised. The excessive blood that is present in the lungs at any given time results in an increase in the airway

resistance and decrease in the pulmonary compliance. In addition, the normal decline in PVR is retarded that causes structural alterations in the pulmonary vasculature. The PVR may become irreversibly elevated if the condition is left untreated. In lesions such as ASD where the shunt is less, these changes occur over a longer period of time. On the contrary, in conditions such as a large VSD or atrioventricular (AV) canal, the pulmonary blood flow may be very high resulting in high PVR in the first year of life.

The cardiac dysfunction that is present in these patients is due to volume and pressure overload. The associated hypoxaemia contributes to CHF in patients with CHD. Early surgical repair, however, is known to restore normal cardiac function in most patients.

General Principles of Anaesthesia in Congenital Heart Disease

There are no particular anaesthetic techniques for specific lesions. The choice of anaesthetic technique and agents is made with the objective of achieving the control of haemodynamic variables within the limits imposed by the lesion and the state of compensation of the child at the time of surgery.

Preoperative assessment

The aim of preoperative assessment is to obtain as much information as possible about the type of CHD and its effects on the circulation as well as other systems of the body. In addition, associated congenital anomalies such as macro-glossia, micrognathia or cervical spine abnormalities leading to intubation difficulties should be noted. A suitable anaesthetic plan can then be worked out. Some of the children who are not provided with surgical treatment or those who undergo palliative surgery early in life may present for surgery much later in life. The older children may have a severely deranged cardiovascular and/or respiratory system. For instance, a patient with long standing VSD, may have developed severe pulmonary artery hypertension (PAH) leading to RV dysfunction.

In addition to the history, physical examination and routine investigations, echocardiographic and catheterisation reports must be assessed thoroughly. Normal catheterisation findings are shown in table 7.2. These help to

understand the exact nature of the congenital defect and its effect on the circulatory system.

Cyanotic children with high haematocrit levels tend to have haemostatic abnormalities. Several coagulation defects including thrombo-cytopaenia, factor deficiencies, fibrinolysis and disseminated intravascular coagulation have been reported in these patients.[7] Polycythaemia and the ensuing hyperviscosity have an important role to play in the pathogenesis of coagulation defects. A detailed coagulation profile should be available for all the patients and if necessary, a haematologist should be consulted to decide about the treatment of coagulation abnormalities. It is noteworthy that while performing the laboratory coagulation tests, the amount of anticoagulant added to the venous blood collected from the patient be appropriately reduced. This is necessary as polycythaemia reduces the amount of plasma in a given volume of whole blood. Blood samples normally are collected with the usual ratio of 1 part of anticoagulant to 9 parts of blood. The volume of blood added to 0.25 mL of 3.8 percent trisodium citrate for coagulation tests can be calculated according to the formula: Volume mL = 2.25 × (100 - normal haematocrit /100 - patient's haematocrit).[8]

Table 7.2: Normal pressures and saturation in cardiac chambers.[6]

	Pressure (mm Hg)	***Saturation (%)***
Vena cava	–	75
RA	(3)	75
RV	30/3	75
PA	30/10	75
Pulmonary capillary	(8)	–
Pulmonary vein	–	95
LA	(8)	95
LV	100/8	95
Aorta	100/60	95

RA: right atrium, RV: right ventricle, PA: pulmonary artery, LA: left atrium, LV: left ventricle, ( ):

mean pressure.

Preoperative haemodilution, also known as phlebotomy, by removal of the patient's blood followed by an infusion of fresh frozen plasma may be beneficial. This should be considered in children with haemoglobin concentrations above 20 g/dL. The red blood cell volume reduction performed in this way can be useful in children with cyanotic heart disease with defects in platelet function to lessen the risk of serious bleeding during the perioperative period. In children more than 5 years old, phlebotomy can be performed by replacing 15 to 20 mL/Kg body weight of the patient's blood with plasma in 50 mL increments over 1 to 2 hours.[9] In children less than 5 years old, proportionately smaller volumes are withdrawn. In adults, an initial 500 mL of blood over a 30 to 45 min. period is removed followed by replacement with an equivalent volume of isotonic saline solution or salt free dextran in patients with heart failure.[10] This is followed every 24 hours by an additional 500 mL phlebotomy until a haematocrit level of less than 65 percent is achieved. It is recommended only in patients with symptomatic hyperviscosity (headache, fatigue, faintness, dizziness, visual disturbances, paraesthesia, irritability, myalgia, reduced mentation and anorexia) when haematocrit levels are more than 65 percent, provided that dehydration is not the cause.

Pulmonary infection is common in patients with increased pulmonary blood flow and should be adequately treated. In addition, presence of upper respiratory infection (URI) should also be noted. In a study performed on 713 children scheduled to undergo cardiac surgery, it was shown that 96 children having symptoms of URI had a significantly higher incidence of respiratory and multiple postoperative complications as compared with asymptomatic children.[11] In addition, the children with URIs stayed longer in the intensive care unit (ICU) and the presence of URI was an independent risk factor for multiple postoperative complications and postoperative infection in children undergoing open-heart surgery.[11] Therefore, URI should also be treated before operation. Chest radiograph provides important information about pulmonary vascular congestion as well as the severity of PAH. In addition, airway compression and alveolar lung disease can be detected.

Echocardiography and Doppler assessment generally provides accurate assessment about shunt size, gradients and chamber sizes. However, cardiac catheterisation remains an important method for the assessment of

physiological function, coronary anatomy and aorto-pulmonary collaterals.

Premedication

The premedication is an important aspect of good preoperative preparation. The arrival of a well sedated child in the operation theatre (OT) makes the induction of anaesthesia considerably smoother. It also reduces the dose of induction agents, thereby reducing the risk of hypotension during induction. This is important as it may not be possible to secure adequate size intravenous (IV) line for volume infusion before induction of anaesthesia, especially in neonates and small infants. In sick children and small infants, premedication may be omitted completely. In premature infants or infants with a history of episodes of bradycardia, atropine (0.02 mg/Kg intramuscularly) or glycopyrrolate (0.01 mg/Kg intramuscularly) can be used.

In children with right-to-left shunt (e.g. TOF), a slightly heavier premedication is preferable, as crying and struggling during induction may precipitate a cyanotic spell. After premedication, the child should be closely observed and oxygenated via a mask if necessary. Different drugs have been used via varying routes such as oral, nasal, rectal or intramuscular (IM). Unfortunately, none of the different premedication protocols are completely satisfactory and a small percentage of children may arrive in the OT in a relatively awake state. Morphine in the dose of 0.05 to 0.2 mg/Kg can be administered intramuscularly in such a patient. However, as suggested, doses should be reduced or omitted completely in a sick child or a very small infant. Oral diazepam 0.2 to 0.4 mg/Kg is an attractive option. Oral transmucosal fentanyl citrate in the form of a lozenge (15 to 20 μg/Kg) has also been used.[12] Although, it has been shown to induce preoperative sedation and facilitation of the separation of children from parents, it is associated with a decrease in the respiratory rate and arterial oxygen saturation that may be of clinical importance.[12] Midazolam, ketamine, or their combination has been used via intranasal route for premedication. It has been shown that intranasal ketamine provides good sedation and separation from parents and allows easy placement of IV cannula.[13]

Induction of Anaesthesia

The frequency of anaesthesia-related cardiac arrests is much higher in patients with CHD in comparison to children without CHD.[14,15] This may be

related to the fact that patients with CHD are sicker. The cardiac arrest may occur in cardiac as well as non-cardiac OTs and even in cardiac catheterization laboratory leading to a higher mortality after arrest.[16] Although all the arrests are not anaesthesia related, careful preparation and anticipation is important to ensure timely and appropriate resuscitation.

Before the child arrives in the OT, complete preparation of the anaesthetic equipment, monitoring equipment and drugs is essential. Emergency medicines, such as calcium, atropine, etc. must be readily available in dilute form. Appropriate sized endotracheal tubes and IV fluids should also be available. It is important that comfortable temperature is maintained in the OT when the child arrives. After induction of anaesthesia, the OT may be adequately cooled for open-heart procedures employing hypothermic CPB.

The choice of induction technique is influenced by the response to premedication and the overall anaesthetic plan. In general, the choice of induction agents and techniques is wider in older children having minimal compromise of the cardiac reserve. In contrast, in smaller and sicker children the choice is narrowed.

If the child arrives asleep, rectal, IM, IV or inhalational induction technique can be used. However, rectally administered agents (barbiturates) have unpredictable absorption, and IM technique may be painful and hence are not preferred. In children who arrive in awake state, inhalational induction may be preferred. Occasionally, children may allow insertion of a small bore IV line and in them, IV induction can be carried out. The child who has fear of mask as well as needle and arrives awake in the OT is a real problem. An experienced anaesthesiologist generally prefers to quickly insert a very small bore IV needle with attached syringe containing induction agent for quick induction. Cooperative small children who have difficult IV access or hate needles can be induced with inhalational anaesthetic. This is true, even for cyanotic children. In clinical practice, the induction is commonly performed by IV or inhalational agents. Occasionally, it may be difficult or impossible to establish venous access, especially in children exposed to repeated surgical procedures or those with underlying co-morbid features. In them, the options include, IM, intraosseous and intratracheal administration of medications. Intentional and elective use of intra-arterial administration of muscle relaxant, induction agents, and fluid has also been reported.[17] Such an approach is questionable and should be reserved only for an exceptional situation.

Inhalational agents

Theoretically, inhalational induction has a slower onset of action in patients with right-to-left shunt and limited pulmonary blood flow. The induction is slowed in proportion to the right-to-left shunt.[18] In pure left-to-right shunts, there is little effect. This effect is most marked for insoluble gases such as nitrous oxide, and there is little effect on the speed of induction with more soluble gases such as halothane. In most children with reasonable functional cardiac reserve, inhalational induction can be carried out. Halothane (with oxygen or oxygen and nitrous oxide) was frequently used earlier due to its advantages of easy acceptability, smooth awake induction, relaxation of infundibular spasm, minimum effect on SVR (in concentrations used) and bron-chodilatation. Inhalational induction is also found to be safe in cyanotic children (e.g. TOF) and does not lead to significant decrease in saturation. In fact, arterial oxygen saturation generally gets better with induction of anaesthesia. Inhalational induction also circumvents the need for preinduction IV cannulation.

In infants and children with severe heart disease, the immature cardiovascular system may have increased sensitivity to inhalational agents. The margin of safety is narrowed in younger patients with these agents. Halothane and isoflurane may produce hypotension and bradycardia in infants.[19,20] The use of atropine before induction can partially compensate for the adverse effects.

The clinical experience suggests that potent inhalational agents are not a good choice for young infants with CHD and minimal cardiac reserve. However in older children with reasonable cardiac reserve, inhalational agents, can be used successfully. Isoflurane is not preferred as it is not so well accepted and can lead to airway problems on induction[20] that may be dangerous in cyanotic children who have decreased oxygen reserve.

Sevoflurane is rapidly replacing halothane as the inhalational induction agent of choice in children.[21] This is due to the fact that of all the currently used anaesthetics, the physical, pharmacodynamic, and pharmacokinetic properties of sevoflurane are closest to that of the ideal anaesthetic.[22] In addition, when compared with halothane, it has been shown to cause lesser number of episodes of hypotension leading to decreased use of vasopressors.[23] Apart from providing a pleasant and rapid induction, it is not arrhythmogenic and the heart rate (HR) remains unchanged. Halothane can

sensitize the myocardium to catecholamines and its arrhythmogenic potential may be deleterious. However, it may be preferred in patients with prolonged QT syndrome, as unlike most other inhalational agents, it does not prolong the QT interval.

Nitrous oxide

The use of nitrous oxide in children with CHD and shunts is controversial. Expansion of air emboli by nitrous oxide is the main concern. Systemic air embolism in patients with right-to-left shunt is a matter of concern, but even in patients with left-to-right shunt, there is always a potential for reversal of shunt during anaesthetic management. In any case, once the left heart has been opened to atmosphere, systemic air microbubbles can be demonstrated in the aortic outflow after CPB in many patients. In addition, nitrous oxide can cause mild but significant decrease in CO, blood pressure (BP) and HR.[24,25]

Use of nitrous oxide compels the reduction in inspired oxygen concentration. However, its use during induction of cyanotic children with halothane does not decrease arterial oxygen saturation but sometimes results in an increase in saturation.[26] This is so because in cyanotic children, arterial oxygen tension (PaO_2) is primarily dependent on pulmonary blood flow and intracardiac mixing of pulmonary and systemic venous return, and increases in fractional inspired oxygen concentration (FiO_2) have little effect on the PaO_2.

Thus expansion of air emboli and cardiac depression produced by nitrous oxide are the main concerns against its use in patients with CHD. It does not appear to have effects on PVR (in infants) and arterial saturation. Perhaps, due to these reasons, nitrous oxide is still used by some centres for induction as well as maintenance of anaesthesia in children with CHD, but is discontinued after the institution of CPB.

Intramuscular and intravenous anaesthetic agents

These agents provide a useful alternative to inhalational agents in uncooperative children. They also provide a better margin of safety in sick patients. In patients with right-to-left shunting, the pulmonary circulation is bypassed and the drugs reach the brain faster. Due to this lack of mixing in the pulmonary circulation as well as the lack of uptake of the drug, the

normal intravenous dose might result in high arterial and brain concentrations. All the IV agents should, therefore, be administered slowly and with caution in patients with right-to-left shunts. IV injection permits the introduction of air bubbles into the vasculature. Bubbles in the venous blood may be shunted to the arterial circulation (even in those who have left-to-right shunt). Thus, systemic air embolism is possible in any child with shunting. Appropriate precautions against the introduction of air from needles and cannulae is the best way to safeguard against this complication.

Ketamine

In small children who are uncooperative, and those who have difficult venous access, intramuscular ketamine (5 to 10 mg/Kg) can be used for induction. As ketamine can affect the airway management (due to secretions), smaller intramuscular doses of ketamine (1 to 3 mg/Kg) can be used for supplemental sedation in the OT in uncooperative children. In this dosage the airway problems are less. In adults, increase in the PVR with ketamine has been reported, but IV induction with ketamine (2 mg/Kg) results in rrunimal increase in PVR.[27] In children with pulmonary hypertension, it does not increase PVR in presence of sevoflurane in spontaneously breathing children.[28] However, adequate airway management and ventilation should be ensured, as hypoxia and hypercarbia can have deleterious effects on the PVR. In clinical practice, ketamine has been used successfully even in patients with cyanosis and limited pulmonary blood flow.[29] It has been shown that ketamine induction actually increases the oxygen saturation.[30] It appears that the state of anaesthesia is responsible for this beneficial effect.[31] It has been compared with sevoflurane for anaesthetic induction in children with CHD and found to maintain haemodynamic stability with minimal side effects.[32] Thus it can be considered as a good alternative for induction of anaesthesia in children with CHD.

The greatest disadvantage of ketamine is the associated emergence delirium in children over 4 years old. Many anaesthesiologists do not use ketamine for this reason.

Etomidate

Etomidate has been used for induction of anaesthesia in the dose of 0.3 mg/Kg in combination with fentanyl 1 μg/Kg, and when compared with ketamine, it has been shown to decrease the plasma Cortisol levels following

induction. This effect persists for 24 hours postoperatively suggesting that it suppresses the stress response caused by CPB and can be used safely.[33]

Opioids

High-dose opioid anaesthesia provides excellent haemodynamic stability in patients with CHD. In the author's unit, morphine (1 mg/Kg) is frequently used in children with good haemodynamic stability. Fentanyl (25 to 75 µg/Kg), alfentanil (20 µg/Kg) and sufentanil (5 to 20 µg/Kg) all provide reasonably good haemodynamic stability during induction even in sick infants with all forms of CHD.[34-38] Morphine should be administered slowly as hypotension can result due to histamine release. Fentanyl, alfentanil and sufentanil are more potent narcotics and are also useful for suppression of hypertensive pulmonary responses to intense stimulation such as sternotomy or endotracheal suction. This may be desirable in patients with PAH or diminished pulmonary blood flow. Fentanyl in doses of 10 to 25 µg/Kg can be used for this purpose. It is important to use pancuronium as the muscle relaxant along with high-dose opioid technique in order to counter the bradycardia produced by opioids.[39] With growing interest in the practice of early extubation even in children, many centres have substantially decreased the doses of opioids. For instance, fentanyl is commonly used in the dose of 5 to 10 µg/Kg for induction of anaesthesia. However, a study has shown that fentanyl in the dose of 25 to 50 µg/Kg is necessary to obtund the haemodynamic and stress responses to the prebypass phase of surgery.[40]

Other intravenous agents

Thiopental: (3 to 5 mg/Kg) can be employed in relatively older children and its use is not associated with deterioration in oxygen saturation in cyanotic children. It is utilised less frequently in neonates and small infants. Small doses (1 to 2 mg/Kg) of thiopental can be used in combination with high-dose opioid induction to suppress stress response or ensure amnesia.

Propofol: is a more recent induction agent. It is associated with smooth induction and rapid recovery from anaesthesia. Although, its safety and efficacy in paediatric patients has been demonstrated,[41-43] the manufacturers do not recommend its usage in children. Propofol has been utilised to decrease the dose of opioids so that the duration of postoperative ventilation and ICU stay can be nunimised. In one report of a large series of patients, the dose of fentanyl was decreased to less than 20 µg/Kg and propofol was

infused in the dose of 70 µg/Kg/min. after CPB.[44] The ICU stay was shortened with this regime. It has been shown that propofol kinetics are altered in very small babies and in children recovering from cardiac surgery, and the increased peripheral distribution volume and reduced metabolic clearance following surgery causes prolonged elimination.[45] Propofol has been successfully used in children of all age groups following cardiac surgery for sedation during mechanical ventilation,[46] and its use may further increase as it has been shown to have antioxidant and anti-inflammatory action along with its ability to shorten the extubation time.[47]

Benzodiazepines: may be used as premedication or as an adjunct to general anaesthesia. When used with opioids and potent volatile anaesthetics, benzodiazepines produce significant hypotension. They can be used to ensure amnesia and also to suppress stress response in combination with opioids. Midazolam (0.01 to 0.02 mg/Kg) can be used along with opioid induction to provide sedation and amnesia.

Dexmedetomidine: is an alpha-2 agonist that can be used as an adjunct to opioid anaesthesia. It can be administered as an infusion in the dose of 0.7 µg/Kg/hour in combination with fentanyl (5 to 10 µg/Kg). It has been shown to obtund the haemodynamic response to surgery and decrease the requirement of isoflurane supplementation in children with CHD.[48] In addition, it has been used with propofol in cardiac catheterization laboratory in children requiring device closure of the ASD with shorter recovery times.[49] Caution should be exercised in its use in patients with predisposing conduction abnormalities and patients who are pacemaker dependent as it can interfere with pacemaker functioning.[50]

Muscle relaxants

Pancuronium has been well studied and widely used in children with CHD. Its ability to produce tachycardia and hypertension through its sympamomimetic effect[51] is especially desirable to support CO in infants with CHF when stroke volume is relatively fixed. Atracurium and vecuronium cause bradycardia in combination with high-dose opioids and are not preferred in sick patients. They may be used in fit patients undergoing short surgical procedures (e.g. PDA ligation).

Combined regional and general anaesthesia

The use of regional anaesthesia in combination with general anaesthesia is receiving increasing attention. This is done with the objective of improving the clinical outcomes and decreasing the costs as a result of the reduced need for postoperative mechanical ventilation. Substantial reductions in the dose of opioids are made in this technique. Alternatively, an inhalational anaesthetic based technique can be used. Intrathecal morphine (caudal or lumbar) with or without a local anaesthetic is used.[52,53] The technique has been shown to provide good haemodynamic stability and facilitation of early extubation. Morphine is used in the dose of 50 to 60 μg/Kg and the intrathecal injection is administered after anaesthetic induction. Epidural anaesthesia using local anaesthetic such as lidocaine with or without an opioid has also been described.[54,55] These reports have demonstrated the safety and efficacy of the technique. The adverse effects of such techniques include emesis, pruritus, urinary retention, postoperative transient paraesthesia and respiratory depression.[54] Usual precautions such as choosing the patients without coagulation alterations and strict measures to avoid post-puncture bleeding should be followed.

Manipulation of pulmonary and systemic vascular resistance

The outflow resistances are mainly determined by the PVR and SVR unless aortic or pulmonary stenosis is present. The intracardiac shunting is controlled by the relation between the two, especially in large simple shunts. The anaesthesiologist can alter the PVR and SVR in several ways so that optimal shunting conditions are obtained to suit a particular lesion.

Pulmonary vascular resistance

Increases in the PVR during operation can induce or worsen right-to-left shunting. This results in arterial desaturation as well as increased stress on the RV. Acute RV failure from increases in the PVR is frequently observed in children with CHD. In contrast decreases in the PVR in patients with large left-to-right shunts (large VSD, aorto-pulmonary window, single ventricle, large PDA, etc.) can result in excessive pulmonary flows leading to decreases in systemic flows. This results in systemic hypotension and acidosis.

However in clinical practice, increase in the PVR leading to pulmonary hypertensive crisis and RV failure/dysfunction is more common. The basic

objective is to control the PVR and the PA pressure. Over the years, there have been multiple classes of drugs developed for the treatment of PAH. Nitroglycerin and sodium nitroprusside are the oldest pulmonary vasodilators used is the OT. Later on phosphodiesterase (PDE) inhibitors were introduced. Milrinone, a PDE-3 inhibitor is one of the most commonly used agents in this class in the OT, and sildenafil, a specific PDE-5 inhibitor has been shown to be highly effective in the management of PAH.

Prostaglandins are potent endogenous vasodilators that mediate the action via increase in the cyclic AMP in the vascular smooth muscle. They have an additional therapeutic effect in the form of remodeling of the pulmonary vascular bed with subsequent reduction of endothelial cell injury and hypercoagulability.[56] Among the newer lot, levosimendan, an inotrope, which is a calcium ‘sensitizer’ has been shown to decrease the pulmonary capillary wedge pressure, SVR and PA pressure in patients with moderate to severe CHE[57] Adenosine infusion at a dose of 50 μg/Kg/min. can produce significant decrease in PVR and an increase in CO without adversely affecting the systemic haemodynamics.[58] Bosentan, an orally active endothelin antagonist has significantly changed the therapeutic approach to PAH.[59] Brain (or beta) natriuretic peptide (BNP) secreted by the ventricles of the heart cause an increased intracellular concentration of guanosine 3'5'-cyclic monophosphate (cGMP), and smooth muscle relaxation. It is currently the most selective and efficient intravenous pulmonary vasodilator without any significant systemic effects and is being increasingly used during cardiac surgery.[60]

All the intravenous agents suffer from the disadvantage of systemic vasodilatation leading to hypotension, necessitating the simultaneous use of vasopressors with their inherent drawbacks. Therefore, an agent having selective vasodilatory action on the pulmonary vasculature is desirable. In this respect, inhaled nitric oxide has long been the ‘gold standard’ of inhaled pulmonary vasodilators. Nitric oxide activates the enzyme guanylate cyclase. Activated guanylate cyclase produces cGMP, which causes vasodilatation.

The systemic exposure is limited by rapid in-activation in the blood cells; the half life of nitric oxide is only a few seconds. Nitric oxide is administered in the dose of 5 to 40 parts per million via the inspiratory limb of the breathing circuit. The efficiency and safety of nitric oxide in the cardiac OT, even in children with a preoperative PVR of more them 7 woods units/m^2 is

well documented.[61-63] Nevertheless, nitric oxide suffers from the disadvantage of rebound PAH and RV failure on discontinuation, risk of methaemoglobinaemia, and toxicity of nitrogen dioxide.

Inhalation of all other vasodilators, such as sodium nitroprusside, nitroglycerin, PDE inhibitors, as well as prostaglandins has been tried.[64] Amongst these, milrinone and prostaglandins deserve mention. In a report of 18 heart transplant recipients, inhaled milrinone has been shown to decrease the mean PA pressure, transpulmonary gradient, and PVR.[65] No systemic side effects were seen with a dose of 2 mg inhaled through a nebulizer. It seems that inhaled milrinone presents a novel method of therapy for PAH. It is cheaper and less cumbersome to administer as compared with nitric oxide and it can be administered prior to the institution of CPB in patients with severe PAH, where it could prevent the post-bypass reperfusion injury associated with severe PAH.[66]

Inhaled prostaglandin I_2 (PGI_2) offers similar advantages. It has emerged as a real alternative to inhaled nitric oxide and has been shown to be equivalent to inhaled nitric oxide in the treatment of PAH.[67] Inhaled PGI_2 suffers from the theoretical disadvantage of bleeding (due to platelet inhibition) and rebound PAH with abrupt discontinuation. A possible alternative is iloprost, which is a stable derivative of PGI_2. It has similar vasodilator properties and a longer half-life of 30 min. It has been seen to be effective as a rescue therapy for pulmonary hypertensive crisis in children undergoing congenital heart surgery.[68] Prostaglandin Ea is another potential alternative via the inhaled route, but there is lack of published data with the prostaglandin.

It is clear that several newer options are now available for the management of perioperative PAH and RV failure. However, the anaesthesiologist must not ignore the basic principles of anaesthesia and must avoid, hypoxia, hypercarbia, acidosis and hypothermia, which can lead to pulmonary vasoconstriction. Table 7.3 shows the vertilatory parameters that the anaesthesiologist can control for the patient’s benefit. Careful airway manipulation and pain management are of paramount importance. These must be the first steps of the overall treatment strategy. The next step should be the use of appropriate inotropes such as dobutamine, epmephrine and PDE3 inhibitors. More often than not, a multimodal approach is more rewarding than using a single therapeutic agent.

Table 7.3: Ventilatory control of pulmonary vascular resistance

Increased PVR	
	Hypoxia
	Hypercarbia
	Acidosis
	Hyperinflation
	Atelectasis
	Sympathetic stimulation
Decreased PVR	
	Oxygen
	Hypocarbia
	Alkalosis
	Normal FRC

PVR: pulmonary vascular resistance; FRC: functional residual capacity.

Systemic vascular resistance

In some situations, altering the SVR can be used to manipulate the shunt for the benefit of the patient. In the presence of a complex right-to-left shunt with pulmonary outflow obstruction (TOF), an increase in the SVR will decrease the shunting and increase the arterial oxygenation. In hypercyanotic spells, using a pressor agent is useful, as it reaches directly into the systemic circulation (due to right to left shunt) and by raising the SVR decreases the right-to-left shunting. Phenylephrine or norepinephrine can be used for this purpose. Based on the same principle, in patients with BT shunt who develop desaturation, manual external compression of the abdominal aorta or axillary artery on the side of the shunt can be used to improve oxygenation.

Monitoring

Electrocardiogram (ECG), non-invasive blood pressure (BP), temperature, pulse oximeter and end-tidal carbon dioxide form the standard monitoring as in any other surgery. The surgical repair of a defect such as PDA with left-to-right shunt in a slightly older child may be performed with this much

monitoring. However, in most other procedures (close as well as open) more invasive monitoring will be necessary.

Direct arterial pressure monitoring

Intra-arterial catheters provide continuous beat to beat pressure measurements. In certain surgical procedures such as PA banding or ligation of a large PDA, wide fluctuations in the BP may occur. Therefore, continuous monitoring of BP is extremely important at the time of PA banding or PDA ligation. In addition, arterial blood gas measurements can also be easily performed. Invasive arterial pressure monitoring is of course a necessity in all open-heart surgical procedures.

Insertion of arterial catheters in neonates and small infants can be difficult and even an experienced anaesthesiologist may sometimes take long time to accomplish cannulation. Generally radial arterial catheters are preferred. A 24 G catheter is used in a neonate and left side is generally preferred. History of previous shunt or the surgical procedure that is likely to temporarily interrupt the flow to the subclavian artery (BT shunt) should be considered in choosing the side of radial artery (i.e. do not cannulate the radial artery on the side of the shunt). Both radial and femoral arterial cannulation should be considered in patients with coarctation of aorta. Peripheral arterial catheters may not accurately reflect the central aortic pressure, especially after CPB. For this reason, at many centres femoral artery is cannulated, using a 22/20 guage cannula with Seldinger technique.

Central venous pressure monitoring

Cannulation of the internal jugular vein (IJV) is preferred for central venous pressure (CVP) monitoring and a high success rate is reported.[69,70] However, it can be difficult in infants and neonates and considerable experience is necessary. Ultrasound guided central venous cannulation is being increasingly practised, however, even this requires experience. Central venous cannula also provides an access for infusion of inotropes and dilators that may be necessary even in closed heart procedures.

Intra-cardiac pressure measurements

Intra-cardiac pressure measurements are routinely performed for many surgical corrections before and after the repair has been performed. These

pressure measurements are taken by the surgeon who inserts a needle connected to a transducer at various sites. At times, insertion of a catheter by the surgeon into the LA, PA or RV maybe necessary for postoperative monitoring. The catheter is introduced through the chest wall by the surgeon. Rarely, when the anaesthesiologist fails to cannulate the IJV, a line may be provided by the surgeon during weaning of a patient from the CPB. Although, transthoracic catheters provide useful data, there is a small but real risk of complications associated with their use. Air embolism is always a risk and bleeding with cardiac tamponade may occur.

Pulse oximeter

It forms an important monitoring tool for detection of hypoxaemia. Although, the accuracy of pulse oximetry at the desaturated levels seen in severe cyanotic congenital heart diseases is questionable,[71] most anaesthesiologists consider it to be a valuable monitoring tool in these children. In addition, in procedures such as PA banding, pulse oximetry provides immediate knowledge of the arterial saturation that is used for assessing the tightness of the PA band.

Echocardiography and Doppler measurements

Small size transoesophageal echocardiography (TOE) probes are now available that can be used in younger children. If not, epicardial probes can be used that provide valuable information about the adequacy of surgical repairs, especially those performed on complex lesions. Measurements of flows and pressure gradients obtained on the operating table are a useful guide and if necessary the repair can be revised by the surgeon.

Temperature monitoring

Monitoring the brain, core and lower body temperature is performed with the help of nasopharyngeal, oesophageal, and rectal temperature probes. Since brain temperature can differ from core or rectal temperature, it should be monitored in patients undergoing deep hypothermic circulatory arrest (DHCA). Large discrepancies between various temperature sites indicate inadequate arterial perfusion or venous drainage of head or lower body.

Cerebral oxygen saturation

Continuous monitoring of cerebral saturation by near infrared spectroscopy is being increasingly used during CPB. It has been shown that the cerebral oxygen saturation decreases at the institution of CPB with a further reduction during the cooling phase and recovering during rewarming and weaning and CPB discontinuation.[72]

A recent trial has evaluated the relationship of intraoperative near infrared spectroscopy values of cerebral oxygen saturation to longterm neurodevelopmental outcomes in infants undergoing biventricular repair.[73] The results of the study revealed that persistent cerebral desaturation below 45 percent, significantly correlated with psychomotor delays and brain magnetic resonance imaging abnormalities at 1 year of age.[73] Any abrupt decrease in the saturation can be corrected by correcting the aortic cannula malposition, if any, thus preventing potential neurological injury.[74] The cerebral oxygen saturation is an important monitoring tool during the perioperative period and it is likely that it will become a perioperative monitoring standard.[75]

Cardiopulmonary Bypass

Intracardiac repair of CHD requires CPB and sometimes circulatory arrest. CPB can complicate the postoperative course by leading to multiorgan dysfunction. The negative effects mediated by inflammation, oxidative stress, haemodilution, abnormal coagulation and ischaemia/reperfusion injury can lead to low CO syndrome, capillary leak and respiratory failure. One of the reasons for increased morbidity associated with CPB in infants and neonates is the relatively larger prosthetic area that the blood is exposed to. The blood volume of an infant is very small and even the small cardiotomy reservoirs and oxygenators used in infants provide a large prosthetic surface area. This leads to damage to the blood elements and proteins. In addition, the priming volume is relatively large so that excessive haemodilution is produced, if clear prime is used. The improvements in the technology of CPB have greatly reduced the hazards of CPB in infants and neonates. The priming volume with the use of infant sized oxygenators and extracorporeal circuit has been reduced to as low as 700 mL. However, since the blood volume of a neonate is only 200 to 250 mL, even this priming volume leads to significant

haemodilution. Therefore, it is a common practice to add bank blood to the priming volume so that haematocrits of around 20 percent can be maintained on CPB. Addition of sodium bicarbonate will be necessary to maintain normal pH of the prime. In a comparison of haematocrit level of 20 percent with 30 percent in infants undergoing surgery with CPB, it has been shown that lower haematocrit level resulted in greater adverse perioperative and developmental outcomes.[76]

The management of CPB is complicated by the presence of shunts and immature cardiovascular system. Although relatively large flows (150 to 175 mL/Kg/min.) are employed in neonates, adequate systemic perfusion may not be guaranteed. In the presence of large left-to-right shunts (e.g. PDA), the blood pumped into the aorta returns to the heart (and then to the oxygenator) via PDA resulting in relative hypoperfusion of the systemic circulation. Therefore, all existing left-to-right shunts (Blalock-Taussing or Waterson, PDA) must be ligated before establishing the CPB. In the author's experience, in some patients, the PDA that was missed during the preoperative workup was diagnosed and ligated during operation on the basis of inability to maintain adequate systemic pressure despite full flows. Consequently, it should be considered a good policy to rule out PDA in all patients before establishing CPB. One study performed on children undergoing ASD closure has shown that lower weight-indexed CPB flow rate is an independent risk factor for early postoperative hyperlactatemia.[77] In some children with cyanotic heart disease, extensive aorto-pulmonary collaterals may be present which cannot be easily controlled. It is needless to emphasize, therefore, that adequate pump flow is not an index of adequate perfusion and the anaesthesiologist must carefully monitor other indices such as urine output, rate of cooling of different parts of the body (by multiple temperature probes) and maintenance of normal acid-base status.

In some patients, persistent left superior vena-cava (SVC), usually draining to the coronary sinus may flood the operating area. It should be detected and cannulated to ensure adequate venous drainage for CPB. The placement of SVC and inferior vena-cava (IVC) cannulae must be accurate, as the sizes of the veins are small and improper positioning might result in venous obstruction leading to gradual distention of the abdomen or facial oedema. However, if DHCA is planned, a single venous cannula inserted in the right atrial appendage is used.

Anticoagulation

The management of anticoagulation during CPB is similar to that in adults, and activated coagulation time (ACT) values are maintained above 400 to 480 seconds. However, ACT values may be prolonged by factors other than heparin, such as haemodilution and hypothermia. Therefore, the ACT may not always accurately reflect the anticoagulant effect of heparin during CPB and heparin levels can decline to below 2 units/mL (despite ACT of 400 to 480 seconds), which may be inadequate to suppress thrombin generation/activity.[78] This problem is likely to be important, especially when CPB duration is prolonged. Therefore, it has been suggested that to minimise the deleterious effects of thrombin during CPB, especially in longer bypass runs, administration of higher doses of heparin than those being currently used should be considered.[78] In contrast, inadequate anticoagulation by heparin may be a problem, especially in small infants. Heparin potentiates the activity of antithrombin-III, which catalyses the inactivation of thrombin and other clotting factors. Infants less than 6 months of age have decreased antithrombin-III levels, and these may be further lower in children with CHD.[79] Therefore, heparin may not achieve adequate anticoagulation. Since, antithrombin-III supplementation has been shown to restore heparin responsiveness and reduced haemostatic activation in heparin resistant adults, this therapy may be tried in infants.[80]

Hypothermia and electrolyte balance

Moderate hypothermia (25 to 28°C) is generally employed. This helps to provide organ protection as well as reduction in pump flows so that CPB trauma is also reduced. During CPB, blood gases, acid-base status and electrolytes are periodically monitored. Restoring serum electrolyte levels to normal (especially potassium) is important before attempting separation from CPB. Although clinically significant arrhythmias caused by an abnormal calcium concentration are much less common, efforts should be made to maintain normal calcium levels.

Weaning from bypass

The haemodynamic performance of the heart should be estimated before weaning is attempted. This is done by observing the contractility of the heart,

arterial pressure and measuring intra-cardiac pressures. TOE can be useful at this stage to estimate the myocardial contraction, and to confirm the adequacy of the surgical repair. Rhythm problems and general state of myocardial performance are estimated and corrective steps in the form of direct current (DC) cardioversion, external pacing and infusion of inotropes etc. are taken. When rewarming is complete and myocardial function is judged to be adequate, weaning from CPB can be attempted and a small load is placed on the heart by occluding the venous return by the perfusionist. The venous and arterial pressures should be observed. The arterial pressure should improve with arterial waveform showing the pulsatile nature. The myocardial performance should be continuously monitored with each increment of volume load, and the CPB is terminated, if the performance is satisfactory as judged by the improvement in arterial pressure and myocardial contractility. If not, CPB is reestablished, and the problem is analysed for taking corrective measures.

The difficulty in weaning the CPB is usually not the result of primary pump failure, except in situations where extensive ventriculotomy is performed by the surgeon. Mixed or residual lesions are the common causes for unsuccessful weaning. In addition, improper oxygenation or increased PVR leading to RV dysfunction can be present. Manual ventilation to produce hypocarbia and alkalosis is useful in lowering the PVR. Intracardiac pressure measurements along with TOE may also be necessary to arrive at a correct diagnosis. Revisions of surgical repair are sometimes necessary in order to be able to separate the patient from CPB. In some patients extracorporeal membrane oxygenation (ECMO) can be offered, if potentially reversible pulmonary, cardiac or cardiopulmonary failure exists. Although, the mortality is high, an acceptable proportion of patients weaned from ECMO survive to leave the hospital.[81] The main complications of ECMO include pulmonary haemorrhage, cardiac tamponade, surgical bleeding, haemolysis and hyperbilirubinaemia.[82]

Deep hypothermic circulatory arrest

It is easy to understand the importance of quiet, bloodless and unobstructed surgical field for repair of complex intracardiac lesions in small hearts of infants. DHCA at temperatures of less than 20°C provides ideal operating conditions. It is, therefore, not surprising to know that DHCA is used

extensively for cardiac surgery in small infants and occasionally in older children and even adults. Some operations such as reconstruction of the aortic arch are not possible without the use of circulatory arrest.

Lowering of the metabolic rates by hypothermia down to 18° to 20°C permits the survival of tissues, especially brain during the circulatory arrest. Most people agree that at temperatures of less than 20°C, a circulatory arrest of 45 minutes is tolerated by the central nervous system. Many times, however, surgical procedure may not be completed within 45 minutes and there may be a need to prolong the arrest time further. Generally this is not permitted and the CPB is reinstituted at low flows to complete the remaining surgical procedure. Although DHCA provides significant protection from cerebral damage, there still is a substantial risk of brain injury from circulatory arrest.[83,84] There is no safe duration for circulatory arrest, and the incidence of neurological sequelae increases exponentially with the duration of arrest. Therefore, some units avoid circulatory arrest altogether. Instead, low flow bypass at deep hypothermia is utilised. In a patient undergoing aortic arch reconstruction, Norwood or Damus-Kaye-Stansel procedures, the innominate or the left common carotid artery can be used for arterial cannulation and continuous cerebral perfusion can be maintained throughout the period of repair.[85,86] Although these regional cerebral perfusion techniques throughout the procedure have been adopted widely[87], a single centre randomized trial failed to demonstrate any improvement in developmental outcome.[88] A large randomized trial comparing regional cerebral perfusion with DHCA is necessary to prove the superiority of one over the other.[89] In an animal experiment, it has been shown that treatment with high-dose methylprednisolone (30 mg/Kg) at 8 and 2 hours preoperatively attenuates the normal cerebral response to DHCA. It can, therefore, offer yet another strategy for cerebral protection with the use of DHCA.[90] CPB and DHCA remains one of the most important factors for long-term neuro-developmental disability suffered by children undergoing surgery for CHD. The causes of the neurodevelopmental problems are diverse and complex, but it is generally agreed that perioperative period is an important time of risk.

Technique

In the early days, surface cooling and rewarming was used without CPB for

DHCA. Now, most centres use CPB for the entire cooling period. At some centres, after anaesthetic induction, surface cooling down to 30 to 32°C is performed by placing crushed ice bags around the body (especially head). Further cooling is performed by establishing CPB. This delays the surgery, but may add a degree of safety when right-to-left shunting could increase during preparation for bypass, or for a re-do with the possibility of serious haemorrhage (e.g. conduit stuck to the back of sternum). Since no data are available to demonstrate superiority of one technique over the other, most centres use CPB for entire cooling to save time. As soon as anaesthesia is induced, cooling is initiated with cooling blanket and lowering the ambient temperature. Simultaneously, surgery is begun and CPB is established to proceed with the cooling.

Anaesthetic management

At some centres, barbiturates are administered just before the initiation of circulatory arrest for enhanced cerebral protection. However, no clinical studies are available to confirm the additive cerebral protective effect of barbiturates during DHCA. An alternative approach to enhance cerebral protection, especially with prolonged periods of DHCA is to prevent reperfusion injury. Calcium channel blockers and free radical scavengers can be used to reduce the reperfusion injury and perhaps, extending the safe period of circulatory arrest.[91,92] The anaesthetic management should aim at maintenance of adequate brain hypothermia, use of pH-stat acid-base management, adequate muscle relaxation, avoidance of hyperglycaemia and monitoring and suppression of brain activity with electroencephalogram (EEG) monitoring and anaesthetic agents (for details, refer to chapter 14).

Fast-tracking and early endotracheal extubation

In general, children undergoing open-heart surgery are electively ventilated until the haemodynamics is stabilised. This is especially so in those who have undergone repair of complex congenital lesions or those having increased PVR. However, fast-tracking and early endotracheal extubation have been described in children undergoing surgery for CHD. According to one recent report, a large proportion of patients can be extubated in the operating room.[93] The authors of this paper emphasized that patients without aortic

cross clamp and patients with simple procedures were extubated in the operating room. Procedure complexity, trisomy [presence of additional (third) chromosome] and age were significant independent predictors for deferring extubation.

Minimal invasive techniques

Significant advances have taken place in the last decade in the percutaneous transcatheter techniques. These have emerged as possible alternatives to the conventional surgery. The procedures are performed under general anaesthesia, and with continuous fluoroscopic and TOE guidance. The atrial and ventricular septal defects, and PDA are the common congenital defects that are closed by trans-catheter technique utilizing 'Amplatzer' device. The device closure of ASD is being performed even in large defects and is those with deficient inferior vena-cava rim.[94,95] In addition, a variety of congenital heart defects are repaired utilizing mimi-sternotomy incision, which has been shown to be safe with improved cosmetic results.[96] Further, video assisted thoracoscopic ligation of a PDA is also practised.[97] The anaesthetic considerations are similar to those of surgical interventions.

Anaesthesia for Closed Heart Surgery

Closure of PDA and systemic to pulmonary shunts are the commonest closed procedures performed. Due to ignorance and lack of medical facilities, children born with these defects do not present for surgery early in life and it is not uncommon to operate on relatively older children in the developing countries. Repair of coarctation of aorta and PA banding are other less commonly performed closed procedures. In the developed countries, early correction (before 1 year of age) for many CHDs has become possible with low mortality. Consequently, palliative procedures such as systemic to pulmonary shunts are performed less frequently. In developing countries, these procedures are still very commonly performed as facilities for open-heart surgery are not widely available.

In some respects, anaesthesia for these procedures is more demanding (as no CPB support is available), if the haemodynamic situation worsens. Arterial and central venous lines are quite important except in older children. As some compromise in ventilation and pulmonary blood flow usually occurs

during surgical manipulations leading to severe decreases in arterial oxygen saturation, pulse oximetry is an invaluable monitoring tool.[98] It is also helpful in assessing the effectiveness of surgical procedure.

Patent ductus arteriosus

The functional closure of the ductus is usually complete within a few hours after birth in the full-term infant. However, anatomical closure may take up to a few months after birth. When the ductus remains open, some of the left ventricular output is shunted through it to return via the pulmonary circulation to the left side again, thus increasing LV volume load. Left sided heart failure with LA dilatation and pulmonary oedema can, therefore occur. The severity depends upon the severity of the left-to-right shunt across the PDA.

In a premature infant, the surgical repair is not advisable unless the patient is in gross failure (failure to thrive) that does not respond to conventional medical therapy with digoxin, diuretics and oxygenation. Such an infant generally requires mechanical ventilation before surgery. The inspired oxygen concentration should be limited due to me inherent dangers of pulmonary oxygen toxicity and retrolental fibroplasia. Strict control of electrolyte and acid-base status is necessary. The ambient temperature in the OT should be 25° to 27°C before the baby arrives in the OT. Peripheral venous access can be difficult and sometimes impossible. A 22 G catheter may be placed in the IJV. Nitrous oxide along with low concentration of inhalational agents (halothane, sevoflurane, isoflurane) and pancuronium can be used for anaesthesia and muscle relaxation. Oesophageal stethoscope and pulse oximetry are important monitoring tools. Radial arterial line, preferably on the opposite side to the aortic arch (umbilical artery may also be used) may be inserted in very sick infants. Bleeding during ligation of the PDA is a real danger and therefore, blood must be available in the OT and should be transfused by a 5 to 10 mL syringe, as required. Postoperative elective ventilation is necessary till the child becomes warm and acid-base status is maintained.

In children up to 3 years of age, the increase in pulmonary blood flow may have caused some degree of pulmonary hypertension. Nevertheless, surgical results are excellent at this stage. As the child grows older without surgical correction, the severity of PAH increases and the child may develop a

predominant right-to-left shunt instead of the previously present left-to-right shunt. Such a stage generally occurs in older children and adults. Patients who have reached such a stage may occasionally present for surgery in the developing countries. Although, surgical closure is usually not advised at this stage," it is still attempted, perhaps with the intention of improving the quality of life or with the hope that the PAH may regress after PDA closure. The surgeon has to measure the PApressures after temporarily occluding the PDA and if it increases more than the systemic pressure, the PDA ligation should be abandoned. Adequate ventilation with 100 percent oxygen should be ensured during pressure measurements. The PDA closure in such a patient involves considerable surgical risk. In patients who have developed irreversible PAH with right-to-left shunt, the surgery is contra-indicated as the PDA is acting as a relief valve for the pulmonary circulation.

Routine monitoring with ECG, arterial pressure and pulse oximetry should be carried out in all patients. With PDA ligation, the aortic leak is closed. Therefore, systemic blood pressure may increase precipitously. The anaesthesiologist should lower the systemic pressure before the ductus is ligated by the surgeon. A systolic pressure of 80 to 90 mm Hg is generally sufficient and sevoflurane or a bolus of chlorpromazine may be used for this purpose. After the PDA is ligated, the diastolic BP becomes somewhat higher than before.

Perhaps, the most dangerous complication during ligation of the PDA is profound haemorrhage due to its rupture. Anaesthesiologist must be fully prepared to transfuse large volumes of blood rapidly. The anaesthetic induction should not be performed until the blood is available inside the OT.

The PDA can also be closed by the percutaneous trans-catheter techniques, such facilities are now available. The anaesthetic considerations are similar, but the procedure is performed in the cardiac catheterisation laboratory or a hybrid operating suite.

Systemic to pulmonary shunts

Surgical shunts (systemic to pulmonary) are performed in conditions in which the pulmonary blood flow is not sufficient and definitive surgery is contraindicated. The creation of a left-to-right shunt helps to improve the oxygenation and the general condition of the patient so that corrective surgery is delayed until a more favourable time. In the developing countries,

surgical shunts are often performed as primary procedures due to the constraints of facilities of open-heart surgery. The common defects for which shunts are performed are TOF, tricuspid atresia, pulmonary atresia, single ventricle, etc. The anaesthetic considerations for the defects with right-to-left shunts will apply.

Blalock-Taussig shunt

The subclavian artery is anastomosed to the pulmonary artery. The subclavian branch of the innominate artery (right side) is preferred as the angle of its origin is more favourable with less chance of kmkrng than when the subclavian branch of the aorta is used. A modified BT shunt employs a Gore-Tex shunt of 4 to 5 mm diameter between the subclavian artery and pulmonary artery (Fig. 7.5).

When the right subclavian artery is used for anastomosis, radial artery cannulation should be performed on the left side and vice versa.

Compression of the lung tissue by the surgeon as well as clamping of the pulmonary artery during anastomosis of the pulmonary end may lead to severe decreases in arterial oxygen saturation. Therefore, 100 percent oxygen may be started once the surgeon opens the chest. Prompt treatment of bradycardia and acid-base abnormalities is very essential during the procedure. Inotropic support may also be necessary and should be readily available.

The other shunts that may be performed are, Waterson shunt (ascending aorta to right pulmonary artery, direct) and central shunt (ascending aorta to main pulmonary artery, tube graft).

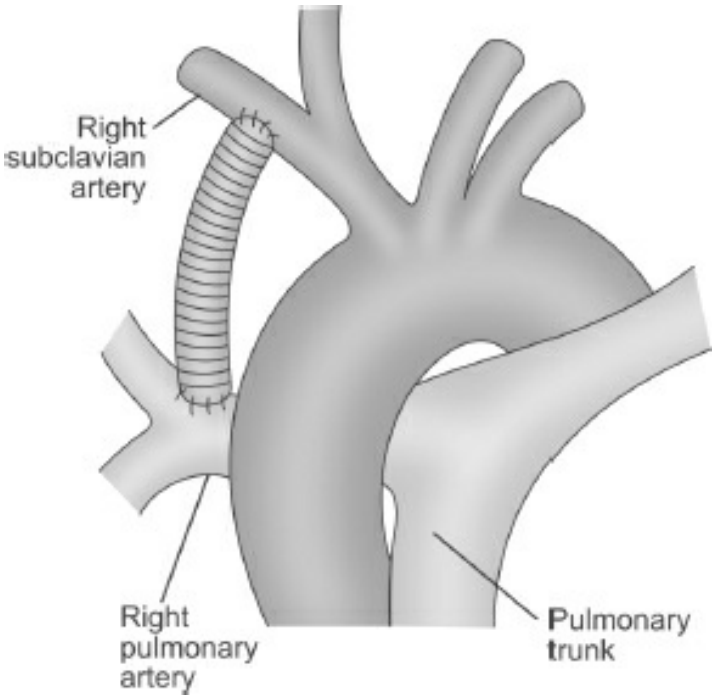

Figure 7.5: Modified Blalock-Taussig shunt: anastomosis of right subclavian artery and right pulmonary artery with a Gore-Tex shunt.

The commonest complication of shunt operation is hypoxaemia, which may occur during or immediately after the operation. Intra-pulmonary shunting in a retracted lung resulting in ventilation perfusion inequality, of course, needs to be considered. However, mechanical obstruction of the flow into PA due to retraction or shunt obstruction due to Icinking or thrombosis is not uncommon. Factors relating to acute blockage of modified BT shunt have not been well described. According to one study, the rate of acute shunt blockage (within first 24 hours) is 11.8 percent and the main risk factors are, preoperative high haemoglobin, weight less than 3 Kg, and duct patency on echocardiogram after surgery.[100] The authors suggest that further work is needed to determine if reduction in preoperative haemoglobin concentration and attempts to reduce postoperative ductal patency may alter the outcome. Patients can be heparinised (to ACT of an 150 to 200 seconds) in order to prevent thrombosis of shunts. Occasionally, the shunts may lead to excessive pulmonary blood flow leading to pulmonary oedema which may be at times unilateral. Manoeuvres to increase the PVR may be utilised to reduce the pulmonary blood flow. Shunt revision may also be necessary.

Some patients can be extubated shortly after successful shunt surgery. However, in sick patients who are in CHF, or severely hypoxaemic, and need

repeated acid-base correction, elective ventilation should be continued for several hours in the postoperative period.

Approximately 10 percent of neonates undergoing systemic to pulmonary artery shunt placement require shunt intervention before discharge. Such patients have higher incidence of infections, and in-hospital mortality. In addition, they require longer hospital stay, and have lower long-term survival. Low-birth weight, smaller shunt size, non-cardiac congenital abnormalities, and heterotaxy syndrome have been identified as potential risk factors for shunt intervention.[101]

Glenn shunt

In this operation, end-to-end anastomosis of the SVC to distal, transected right PA is performed. Thus, only systemic venous blood is shunted to the lungs and the flow has to rely on the low venous pressure to propel blood through the lungs. Therefore, this operation is not suitable for small infants who may have high PVR. Manoeuvres to lower the PVR should be utilised during postoperative period. If the anastomosis is of poor quality or kinks, cerebral oedema due to SVC obstruction may occur.

Bidirectional Glenn

In this operation, end-to-side anastomosis of the SVC to distal right PA that remains in continuity with left PA is performed. The procedure is generally performed as an intermediate stage procedure in the treatment of patients with left or right heart hypoplasia where two ventricle circulation cannot be easily achieved. The main pulmonary artery is left uninterrupted, if a pulsatile flow is desired. However, if the PA pressure is high (> 18 mm Hg, mean), it is either banded or interrupted. The physiological advantages of bidirectional Glenn are, an increase in pulmonary blood flow, without an increase in the ventricular volume load, less pulmonary artery distortion, and prevention of PAH.[102] Sometimes additional pulsatile pulmonary blood flow is obtained by BT shunt as a part of one and a half ventricle repair.[103] However, this may lead to development of increased systemic venous pressure and superior vena cava syndrome.[104] The azygous vein is usually ligated, but can be left open, if the PA pressure increases (beyond 18 mm mg) after ligation. The Glenn shunt is perfomed with the support of CPB. However, a novel technique of bidirectional Glenn shunt without CPB has been described.[105] In this

technique, a temporary shunt is established between the SVC and contralateral branch PA or RA for venous drainage during SVC clamping for bidirectional Glenn anastomosis.

Pulmonary artery banding

In some defects where pulmonary blood flow is excessive (univentricular heart, truncus arteriosus, large VSD) and primary surgical repair is not possible, PA banding is performed. Its use has expanded to allow it to be used for ventricular training prior to total corrective surgery in patients with transposition of great arteries. In this operation, a band is placed around the PA to reduce the pulmonary flow with the objective of controlling the pulmonary congestion and heart failure. It also protects the pulmonary circulation from developing PAH so that surgical correction can be performed at a later date with good outcome. A new implantable adjustable PA banding device (Flo-Watch PAB implant) has been described. The device allows noninvasive adjustment of the band post-implantation in an outpatient clinic.[106] Although such a device offers multiple advantages, it has not been widely used.

Due to high pulmonary flows, the infant may be severely ill with CHF. Anaesthesia is administered with usual precautions. Correction of acid-base status is important. If pulmonary pressures are decreased after induction, the pulmonary flow can further increase with reduction in systemic flow and hypotension. This can be corrected by the surgeon by partially occluding the PA with the finger.

PA banding is one operation where, monitoring of arterial oxygen saturation by pulse oximeter is obligatory. The surgeon tightens the PA band until the PA pressure distal to the band is one-half to one-third of the systemic pressure. If the band is too tight, severe hypoxaemia results due to a decrease in pulmonary blood flow. In addition, the RV may not overcome the higher resistance, and increased right-to-left shunting occurs. The decrease in saturation is rapidly detected by the oximeter and the band tension should be released appropriately.

If the band is too loose, the increased pulmonary blood flow will continue to occur and the objective of the operation will not be served. An appropriate balance between the arterial oxygen saturation and the PA pressure distal to the band has to be achieved for the success of the operation. Pulse oximeter,

by allowing rapid measurements of oxygen saturation plays a vital role during the operation. End-tidal carbon dioxide levels have also been utilised during the PA banding. A mean decrease of 3.8 mm Hg has been demonstrated with appropriate tightness of the band and it has been suggested that end-tidal carbon dioxide tension is a simple and convenient, yet highly reliable parameter for adjusting the tightness of PA band.[107] These infants are usually sick and require some duration of postoperative ventilation.

Coarctation of aorta

The coarctation may be opposite, proximal or distal to the ductus arteriosus. The pre-ductal coarctation does not promote the development of collateral vessels during foetal life as the perfusion distal to the coarctation is maintained via ductus arteriosus. Therefore, a child born with pre-ductal coarctation may develop CHF after birth due to increased afterload on the LV. In addition, patency of the ductus is important for survival, hence, measures to delay the closure of the ductus need to be taken (prostaglandin Ej). In contrast, with post-ductal coarctation, life in the foetal period would not be possible unless the collateral vessels develop. The infant born with post-ductal coarctation already has established collateral circulation and most often is asymptomatic.

Presence of any additional congenital heart defect with coarctation increases the risk even further. The child born with post-ductal coarctation is initially asymptomatic. However, hypertension in the upper part of the body develops and also the incidence of subacute bacterial endocarditis is increased. The life expectancy is decreased considerably and elective surgical correction of an otherwise asymtomatic and uncomplicated coarctation is performed between 2 and 5 years of age.

The various types of surgical procedures that canbe performed are, surgical correction by direct anastomosis, patch grafting and left subclavian flap angioplasty. The anaesthetic management is usually straightforward unless LV failure is present. In such a situation, an opioid based anaesthetic may be preferred. An arterial line should be inserted into the right radial artery as the left subclavian artery may have to be clamped during surgery. For monitoring the perfusion pressure of the distal aorta, a femoral arterial line may be placed if it is palpable.

Large amount of blood losses should be anticipated, especially if the

collaterals are well developed (older children). The surgeon may have to struggle to achieve haemostasis during thoracotomy. In addition, a sudden large loss of blood may occur during dissection around the aorta. Therefore, venous access with large bore lines for rapid transfusion as well as central venous catheter for CVP monitoring are desirable.

If the ductus is patent, it is tied off and the aorta is cross clamped. Perfusion of the distal aorta is generally sufficient in the presence of adequate collateral circulation. If femoral artery has not been cannulated, direct aortic pressure distal to the clamp is measured. The mean aortic pressure of 40 to 50 mm Hg distal to the clamp is considered adequate and the surgeon can proceed with the operation. Of particular concern is the inadequate perfusion of the anterior spinal artery as ischaemic damage of the spinal cord may sometimes occur.

Monitoring the somato-sensory evoked potentials can be utilised to diagnose the spinal cord ischaemia and various manoeuvres to improve distal circulation such as heparinised shunt, femoral-femoral bypass and reimplantation of intercostal arteries can be employed.[108]

When the aorta is cross clamped, moderate to severe hypertension in the upper part of the body develops. Inhalational agent and/or nitro-prusside infusion may be used to lower the BP to a moderate hypertensive level. Normotension or hypotension should not be produced as it will also affect the collateral circulation to the distal aorta. It is, therefore, desirable to continuously monitor both proximal (radial artery) and distal aortic (femoral cannula or needle in the distal aorta) pressures. It has been shown that simultaneous right upper and lower limb invasive pressure monitoring has an impact on the overall outcome in these patients.[109]

Arterial blood gas measurements must be checked, especially just before and after the release of the aortic cross clamp, and metabolic acidosis, when present, should be corrected by the adnunistration of sodium bicarbonate. Some brisk bleeding should generally be anticipated before the clamp is released by the surgeon and therefore, the anaesthesiologist must ensure that the patient is normovolaemic or hypervolaemic at this stage and inhalational agent/nitro-prusside should be discontinued sometime before the clamp is released. Rapid fluid replacement may still be required after releasing the clamp. Sometimes, clamp may have to be reapplied if the bleeding is severe to allow the surgeon to repair the defect. Once the haemodynamic stability is achieved, nitroprusside may have to be restarted and continued in the

postoperative period as some patients develop delayed postoperative hypertension.

Children without any cardiac failure pre-operatively are generally extubated at the end of the operation. Otherwise they can be electively ventilated in the postoperative period.

Specific Congenital Heart Defects Requiring Cardiopulmonary Bypass

Atrial septal defect

This is one of the most common congenital defects. Based on the anatomical location, the defect can be divided into 3 categories: 1. ostium secundum defect represents a deficiency in the septum primum, 2. ostium primum defect is a deficiency in endocardial cushion tissue and 3. sinus venosus defect which is at cavo-atrial junction. Ostium secundum is the most commonly encountered defect; ostium primum defect is usually accompanied by a cleft in the anterior leaflet of the mitral valve, and the sinus venosus defect is usually accompanied by anatomical drainage of a portion of the right pulmonary veins into either the RA or the SVC.

Pathophysiology

The direction of shunt across the defect depends on the respective pressures in the atria that are determined by the relative compliances of their ventricles in diastole. As the RV is thin walled and more compliant, the dominant shunt is usually from left-to-right. During the first few weeks of life, the shunting is minimal as the thickness of the walls of the two ventricles are nearly equal. As the age increases, the PVR decreases and the SVR increases leading to a relative decrease in the RV wall thickness so that left-to-right shunt increases. However, RA pressure may briefly exceed the LA pressure during cardiac cycle (e.g. at the onset of ventricular contraction) resulting into a small amount of right-to-left shunt. The net result is an increase in the pulmonary blood flow that may be tolerated until early adult life with normal or only slightly elevated PVR. A small defect may be tolerated without any difficulty with normal life expectancy. Patients having moderate shunts [ratio of pulmonary blood flow to systemic blood flow (QP/QS = 1.5)] may be

asymptomatic but with those having large left-to-right shunts (QP/QS > 3), symptoms of fatigue and dyspnoea, and cardiac failure may occur. Rarely, if the pulmonary vascular disease progresses, severe exertional dyspnoea develops with diminution of left-to-right shunt, shunt reversal, and cyanosis. Surgery is usually advised before the age of 5 or 6 because of the complications of uncorrected ASD in the later life. However, it is not uncommon to encounter patients with ASD later in life (adult) when they develop symptoms for the first time.

The indications for closing the ASD using percutaneous transcatheter techniques in the catheterisation laboratory have expanded over time with the closure of even large sized ASDs and those with deficient inferior vena-cava rim being attempted. Nevertheless, a substantial number of patients undergo surgical repair directly with sutures or with a patch. Sinus venosus defects require the use of a more extensive patch to direct the partial anomalous pulmonary venous return into the LA.

Figure 7.6 shows the TOE pictures of ostium secundum atrial septal defect with left-to-right shunt. Table 7.4 shows the catheterisation findings in a patient with secundum ASD. Note the characteristic step-up (rise) of oxygen saturation from 76 percent in the vena-cava to 92 percent in the RA signifying a left-to-right shunt at RA.

Anaesthetic management

These patients are generally amongst the healthiest encountered in open-heart surgery. The surgical repair is also considered one of the easiest. These facts, must not make both surgical and anaesthetic team members complacent, as major complications and even deaths after the procedure are not unknown.

Table 7.4: Catheterisation findings in a patient with secundum atrial septal defect.[6]

	Pressure (mm Hg)	***Saturation (%)***
Vena cava	–	76
RA	(4)	92
RV	20/4	92
PA	20/10	91

Pulmonary capillary	(8)	97
LA	(5)	97
LV	110/5	97
Aorta	100/60	97

RA: right atrium, RV: right ventricle, PA: pulmonary artery, LA: left atrium, LV: left ventricle, ( ): mean pressure.

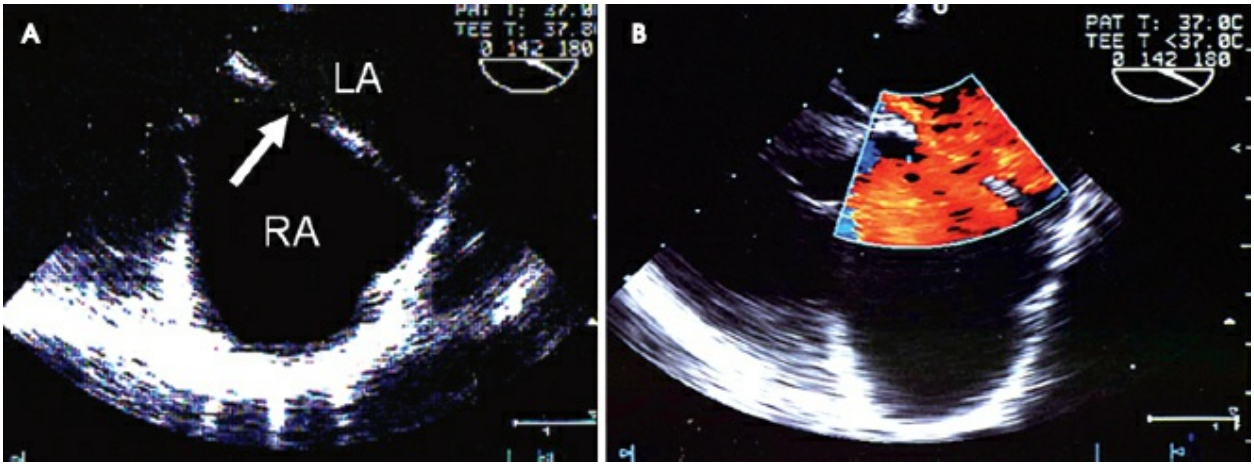

Figure 7.6: Mid-oesophageal bicaval view showing ostium secundum atrial septal defect (arrow in panel A). Note the colour flow across the defect (panel B, LA: left atrium, RA: rigth atrium).

Many options for anaesthetic management exist. Possibility of a paradoxical air embolism must be considered at all times, and manoeuvres such as hypercarbia and hypoxia that may reverse the shunting temporarily should be avoided. CPB with normothermia or moderate hypothermia can be used. Before insertion of the venous cannulae, the anaesthesiologist may be required to inflate the lungs with positive pressure in order to prevent the suctioning of air into the RA via the cannula. For short procedures (direct closure), fibrillation may be used after cross clamping the aorta, however, for longer procedures (sinus venosus defects), it is preferable to use cardioplegia. Failure to recognise partial anomalous pulmonary venous return will result in residual left-to-right shunt.

Most patients can be extubated in the OT or within 2 to 3 hours of operation. Lower doses of opioids (e.g. morphine 0.5 mg/Kg or fentanyl 5 μg/Kg), an inhalational based anaesthetic technique, or propofol infusion can be used to achieve early extubation. It has been shown that early extubation after secundum type ASD is safe and may offer certain advantages such as

lower requirement of opioids and a shorter stay in the ICU over prolonged intubation.[110] However, in patients with increased PVR (adult patient, Fig. 7.7), a longer duration of elective ventilation should be considered. Supraventricular arrhythmias can occur during the postoperative period with atrial flutter, atrial fibrillation, and nodal rhythm being the usual arrhythmias. In patients who have undergone repair of ostium primum defect, mitral regurgitation may occur.

Ventricular septal defect

A deficiency in the ventricular septum at one or more locations is present. The magnitude and direction of the shunt depends upon the size of the defect.

Pathophysiology

In a small defect, there is a small left-to-right shunt as the defect offers considerable resistance to flow. It also maintains the large systolic pressure difference between the two ventricles. Therefore, the tendency for an increase in PVR is not there.

In a defect of moderate size, the left-to-right shunt is increased and due to increased flow in the pulmonary circulation, the PVR is increased. The RV systolic pressure is increased, but is generally not equalised with that of the LV systolic pressure and a gradient of at least 15 mm Hg remains.[111]

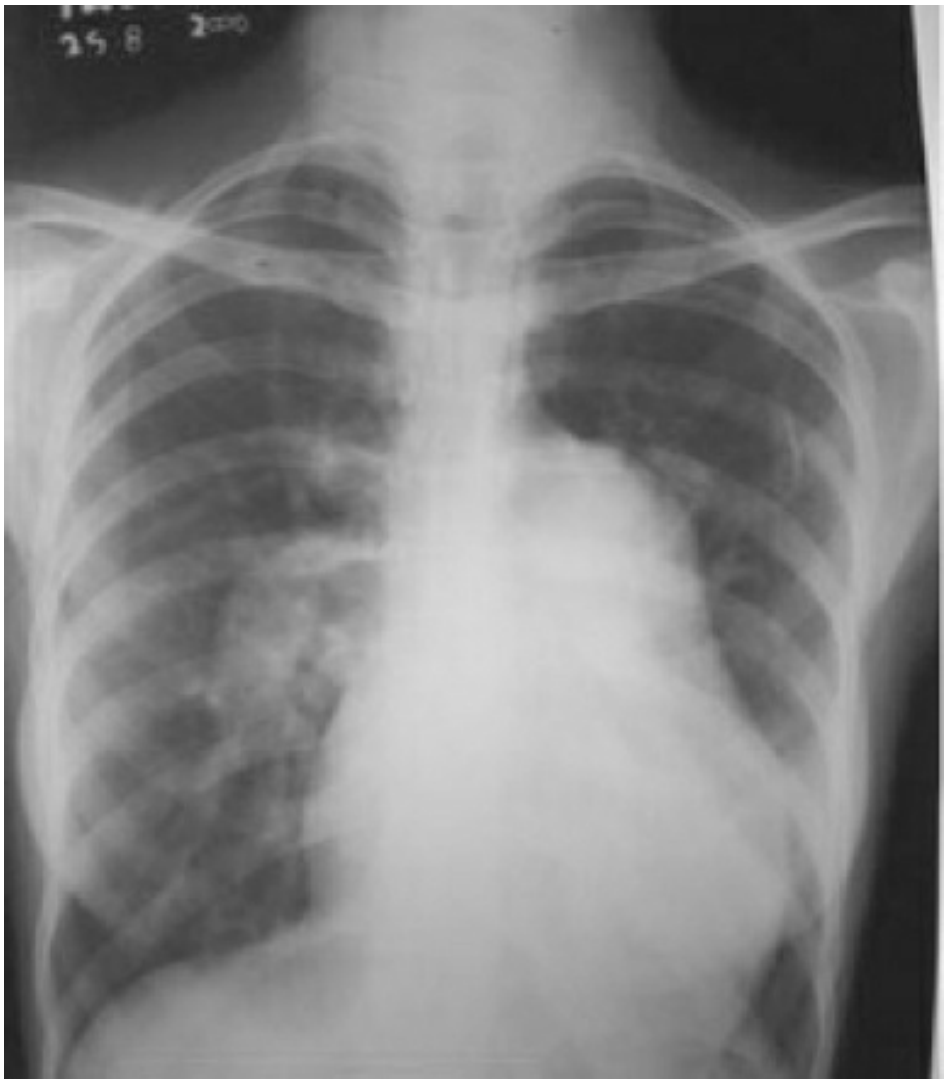

Figure 7.7: X-ray chest showing severe pulmonary hypertension in an adult who had a long standing atrial septal defect with a large left-to-right shunt.

In a large defect, the flow across the defect is not restricted so that the RV systolic pressure is equal to the LV systolic pressure and the pulmonary circulation is subjected to high flows at high pressure. PA pressure is, therefore, increased leading to an increase in the PVR. With the passage of more time, the PVR also increases leading to a decrease in the left-to-right shunt initially and when the PVR exceeds the SVR, the shunt may become predominantly right-to-left (Eisenmenger syndrome).

Small defects usually produce no detrimental effects on the circulation and there is a 50 to 80 percent chance that the defect will close spontaneously.[112,113] In the infant having a moderate to large defect, LV volume overload develops by 7 to 14 days after birth when the PVR

decreases. This leads to frequent respiratory tract infection, pulmonary congestion or pulmonary oedema. In a small infant with multiple VSDs with very high pulmonary blood flow, PA banding may be performed in order to protect the pulmonary vasculature from the high flow, and perform the VSD closure at a later, convenient date when the infant has grown enough to withstand the harmful effects of the CPB. With improvements in the extracorporeal technology as well as the surgical and anaesthetic expertise, primary repair of the defect is being performed more commonly.

The membranous defect is more common. It lies in the outflow tract of the LV, beneath the aortic valve. The bundle of His is in close proximity and may be damaged during the surgical repair of the defect. In muscular VSDs, the chances of heart block are remote as the conduction tissue is away from the defect.

Figure 7.8 shows the TOE pictures of VSD with left-to-right shunt. Table 7.5 shows the catheterisation data of a patient with VSD with PAH. Note the characteristic rise in the oxygen saturation from 58 percent in the RA to 85 percent in the RV signifying a left-to-right shunt at the level of RV. Also note the raised RV and PA pressures suggesting PAH.

Table 7.5: Catheterisation data of a patient with ventricular septal defect and pulmonary artery hypertension.[6]

	Pressure (mm Hg)	***Saturation (%)***
RA	(8)	58
RV	65/9	85
PA	60/20	88
LA	(16)	96
LV	75/10	96
Aorta	90/42	96

RA: right atrium, RV: right ventricle, PA: pulmonary artery, LA: left atrium, LV: left ventricle, ( ): mean pressure.

Anaesthetic management

The surgical repair is carried out by transatrial, transventricular and even

transpulmonary approach. CPB with moderate to profound hypothermia is used. In very small infants even circulatory arrest at 18°C may be used. Small infants who are malnourished and have CHF may be susceptible to myocardial depressant effects of anaesthetic agents and may require prolonged ventilation in the post-bypass period. An opioid-based anaesthetic technique with midazolam or inhalational agent is generally employed. As with any other defect, possibility of systemic air embolism must be borne in mind.

In the developing countries, many grown-up children with VSD are subjected to surgical correction. In these children, severe PAH is usually present. The closure of VSD increases the RV afterload that may not be well tolerated and inotropic support along with measures to decrease the PVR are frequently required. Intraoperative and postoperative pacemaker support is also necessary as small percentage of patients develop heart block following surgical correction of the defect. A transient heart block may occur due to oedema or tissue reaction by suture material placed near the conduction tissue. Presence of residual or previously unrecognised VSD must be suspected, if there is persistent CHF and a need for high inotropic support. TOE or epicardial echocardiography is useful for the diagnosis of residual shunts. Very rarely, patch dehiscence can occur leading to a sudden deterioration in the condition of the patient. Ventricular outflow tract obstruction due to the patch is also not unknown.

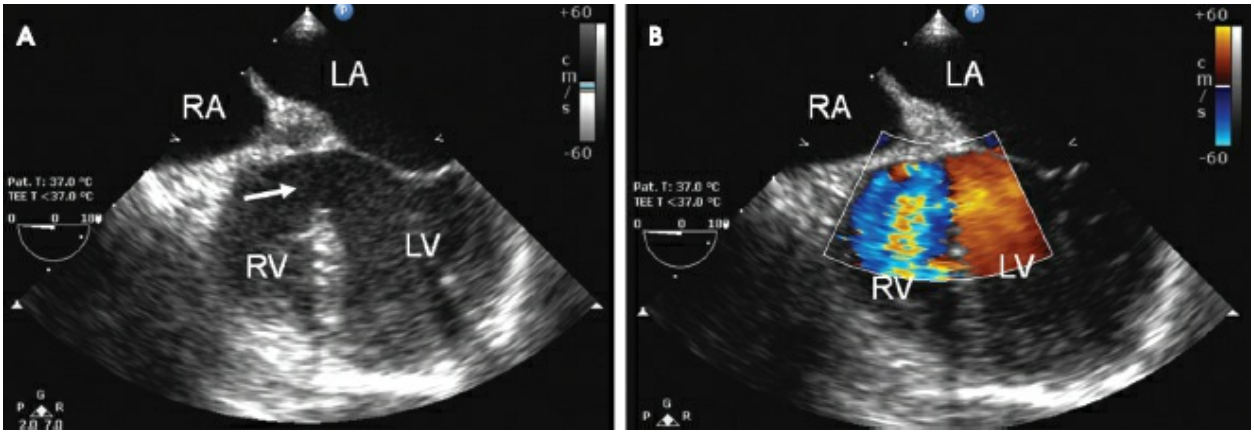

Figure 7.8: Panel A: Large subaortic ventricular septal defect (arrow). Panel B shows the colour flow across the defect. (LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle).

Atrioventricular canal defect

Abnormalities in the development of endocardial cushions produce these defects. The inferior portion of the atrial septum, the AV valves, and the superior posterior portions of the ventricular septum comprise the embryo-logic region of the endocardial cushion. In partial AV canal defect, the caudal portion of the atrial septum and the postero-basal part of the ventricular septum is absent. However, there is no interventricular connection because the AV valves are fused to the underlying ventricular septum. In complete AV canal defect, there is a combined deficiency of atrial and ventricular septum and all the four chambers may communicate and share a single common AV valve.[114] The leaflets of the valves are free floating or connected to the ventricular septum only by chordae. Abnormalities in the formation of mitral and tricuspid valves are always a part of complete AV canal defect and in partial AV canal defect, cleft in the mitral leaflet is often present. The main problem with the surgical repair relates to mitral regurgitation. With the availability of TOE or epicardial echocardiography, adequacy of mitral valve repair can be easily checked on the operation table. In some patients mitral valve replacement may be necessary at a later date.

Complete AV canal defect

In complete AV canal defect, all the four heart chambers communicate and both ventricles function at systemic pressures. Pulmonary blood flow is excessively high, if no pulmonary stenosis is present. As the PVR increases, the left-to-right shunt may decrease. In order to prevent severe pulmonary vascular disease, surgery should be performed early. The repair consists of division of the common AV valve and single patch closure of the ASD and VSD.[114] In addition, mitral and tricuspid valve repair may be necessary. Mild to moderate valvular incompetence is usually well tolerated after surgery. The anaesthetic management should take into consideration, the problems related to ASD, VSD as well as mitral regurgitation. Inotropic support and measures to decrease PVR may be necessary intraoperatively. In addition, prolonged postoperative ventilatory support may be necessary.

Tetralogy of Fallot

TOF consists of: 1. VSD; 2. RV outflow obstruction; 3. overriding of the aorta, and 4. hypertrophy of the RV. There may be additional VSDs in the muscular region of the septum and the RV outflow obstruction may be due to

one or more of the following reasons: infundibular stenosis, pulmonary valvular stenosis and hypoplastic main PA. The origin and distribution of coronary arteries may also be abnormal preventing the placement of RV outflow patch.

Pathophysiology

The basic disturbance is the reduced pulmonary blood flow due to RV outflow obstruction leading to a right-to-left shunt. The pulmonary blood flow is determined by a fixed anatomical RV outflow obstruction and a variable systemic resistance. In addition, a dynamic component of the RV outflow obstruction is also present and is responsible for the occurrence of cyanotic spell. Systemic vasodilatation along with increasing dynamic infundibular stenosis can lead to a profound right-to-left shunting and severe hypoxaemia. The exact mechanism of the hypercyanotic spell is not known but, is usually caused by an increased sympathetic tone. The hypercyanotic spell can occur anytime before the surgical correction and the anaesthesiologist must be familiar with the treatment of this problem. Hundred percent oxygen should be provided and the agitated child can be administered morphine sulfate to sedate him. The SVR can be elevated in an attempt to decrease the right-to-left shunt by an infusion of phenylephrine (starting rate of 5 to 10 μg/min.). Manual external compression of the abdominal aorta can also be used to increase the SVR.[115] IV propranolol (0.5 to 1 mg) or esmolol (100 to 200 μg/Kg/min.) is useful to slow the heart rate and relax the infundibular spasm thereby improving the pulmonary blood flow.[116] If the spell persists even after the above treatment, tracheal intubation and ventilation with 100 percent oxygen will be required.

The hypercyanotic spell is rare inside the OT, if the child has been premedicated adequately. With the induction of anaesthesia (inhalational or intravenous), saturation generally gets better. However, cyanotic spell may by precipitated before surgical incision. This may happen following intubation that leads to sympathetic stimulation. This usually responds to ventilation with 100 percent oxygen and deepening the level of anaesthesia with an inhalational agent, but may take long time to recover. It has been shown that during the spell, end-expiratory lung volumes decrease and ventilation inhomogeneities increase significantly and recover slowly even after return of oxygen saturation to pre-spell values.[117] The loss in lung volume can have a deleterious additive effect in the presence of a spell,

especially because of its slow recovery after treatment. If the oxygen saturation does not improve or improves slowly, an attempt should be made to initiate CPB as soon as possible.

Figure 7.9 shows the TOE picture of tetralogy of Fallot. Table 7.6 shows the catheterisation findings in a patient with TOF. Note the decrease in oxygen saturation from 98 percent in the LA to 91 percent in the LV suggesting a right-to-left shunt at the level of LV. Also note the high RV pressure and a low PA pressure because of the pulmonic stenosis.

The surgical procedure consists of a patch closure of the VSD through a right ventriculotomy. The ventriculotomy is extended through the outflow tract up to the PA. The obstructing muscle bundles are resected and the outflow is enlarged by placing a pericardial or synthetic patch.[118-119]

Table 7.6: Catheterisation findings in a patient with tetralogy of Fallot.[6]

	Pressure (mm Hg)	***Saturation (%)***
RA	(6)	77
RV	90/5	80
PA	16/8	79
LA	(6)	98
LV	85/4	91
Aorta	80/60	82

RA: right atrium, RV: right ventricle, PA: pulmonary artery, LA: left atrium, LV: left ventricle, ( ): mean pressure.

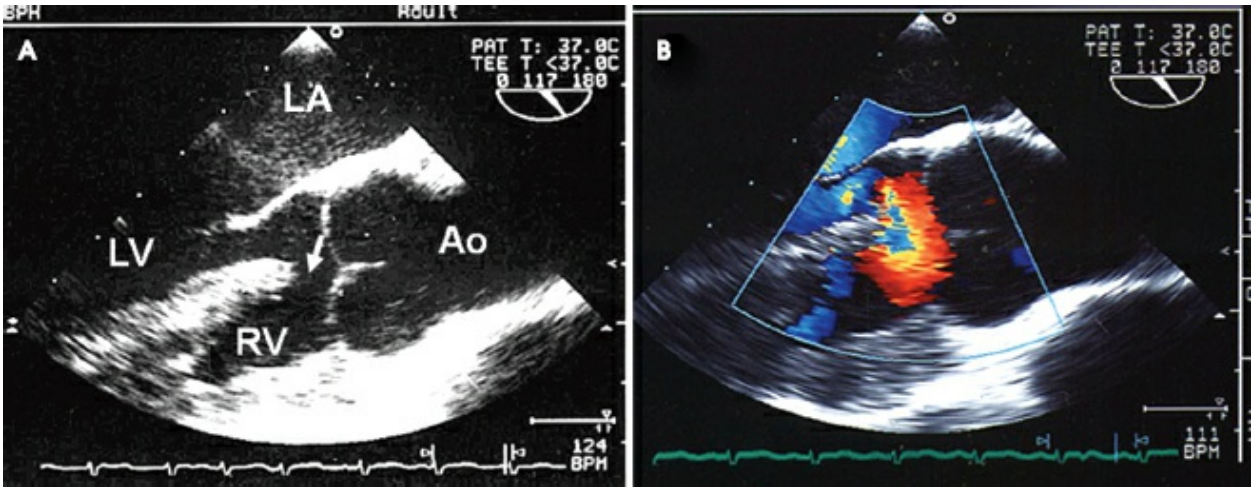

Figure 7.9: Mid-oesophageal aortic valve long-axis view. Panel A: Large subaortic ventricular serptal defect (arrow) with aortic over-ride in a patient with tetrology of Fallot. Panel B shows the flow acceleration from both ventricles into aorta. (LA: left atrium, LV: left ventricle, RV: right ventricle, Ao: aorta).

In patients who have an abnormal origin of the coronary artery and a major coronary artery crosses the RV outflow tract, ventriculotomy is not possible in this region. An external conduit is then placed between the RV body and the PA beyond the stenosis.

Anaesthetic management

The goals of anaesthetic management are, to maintain SVR, minimise PVR and provide mild myocardial depression and slower heart rate. This decreases the dynamic component of obstruction to the RV outflow and minimises the right-to-left shunt. Most anaesthetic agents interfere with systemic vasculature and myocardial contractility. Therefore, the choice of anaesthetic regimen has become an important concern in children with TOF. Opioid-based anaesthetic techniques with midazolam or inhalational agents have been successfully employed. Ketamine can also be used due to its property of maintaining the SVR. However, a major drawback is its potential effect on the pulmonary vascular bed. Nevertheless, it has been shown to be a safe agent in the dose up to 5 mg/Kg/hour when used in combination with fentanyl.[120] Following repair, the RV function may be suboptimal due to ventriculotomy and pulmonary regurgitation. This can be managed by inotropic support and decreasing the PVR. A residual VSD can further augment the RV stress leading to RV failure. The adequacy of repair is indicated by a decrease in the RV systolic pressure, the ratio of right-to-left

ventricular pressures being < 0.6 with an improvement in the arterial oxygen saturation. If the RV pressure remains systemic or supra-systemic, the repair must be reviewed carefully and revised appropriately.

In some patients, distal PAs may be hypoplastic and stenotic so that the stress on the RV cannot be relieved and the RV pressure remains systemic. A residual VSD or ASD may be created in such patients in order to off-load the RV at the cost of a decreased arterial oxygen saturation.

Right bundle branch block may occur in some patients following surgery, and occasionally, complete heart block may result. Junctional ectopic tachycardia is another common arrhythmia after surgery (15 to 20 percent), and prophylactic amiodarone may be used. Coagulation abnormalities are also common in patients with TOF and, therefore, they may bleed excessively in the perioperative period. Thus, adequate blood conservation techniques should be adopted. These are discussed in chapter 11.

Total anomalous pulmonary venous connection

In this type of defect, all the pulmonary venous blood enters a systemic venous structure due to an anatomical abnormality of the pulmonary veins. Pulmonary venous blood thus, mixes with the venous blood of peripheral circulation in the RA. The blood flows into the LA via an ASD which must be present for the survival of the patient. The blood then reaches the systemic circulation through the LV. The rest of the blood flows to the pulmonary circulation through the RV. Based on the location of the entrance of the pulmonary veins into the systemic veins or the RA, four different types of defects have been described.

Type I (supra-cardiac)

This is the most common type, in which the common pulmonary venous trunks drain into the left innominate vein through an anomalous vertical vein. Sometimes, the pulmonary veins drain straight into the superior vena cava.

Type II (cardiac)

The pulmonary veins drain separately into the posteroinferior portion of the RA. Alternatively, the veins join to form a common trunk, which connects to the coronary sinus that opens into the RA.

Type III (infra-cardiac)

The pulmonary veins return below the diaphragm into portal or hepatic vein or inferior vena cava.

Type IV

The anomalous connections are present at two or more of the above locations. A variable degree of pulmonary venous stenosis may also be present.

Table 7.7 shows the catheterisation findings in a patient with total anomalous pulmonary venous connection with pulmonary venous obstruction. Note the desaturation at the level of LA and pulmonary hypertension.

Table 7.7: Catheterisation findings in a patient with total anomalous pulmonary venous connection with pulmonary venous obstruction.[6]

	Pressure (mm Hg)	***Saturation (%)***
RA	(1)	72
PA	110/55	80
Pulmonary capillaries	(20)	–
Pulmonary vein	(20)	73
LA	–	65
LV	68/0	64
RV	120/3	71
Aorta	65/40	66

RA: right atrium, PA: pulmonary artery, LA: left atrium, LV: left ventricle, RV: right ventricle, ( ): mean pressure.

Pathophysiology

The defect provides common mixing of all systemic and pulmonary venous blood in the RA. In the absence of any pulmonary stenosis, most of the blood reaches the pulmonary circulation resulting in an excessive pulmonary blood flow. In patients having pulmonary venous obstruction, pulmonary

congestion occurs leading to an increase in the PVR. This may partially decrease the excessive pulmonary blood flow. Such patients may be very sick with severe pulmonary oedema, PAH and hypoxaemia. The pulmonary vascular bed of these patients is highly reactive resulting in RV dysfunction in the postoperative period.

Balloon atrial septostomy can be performed as a palliative procedure to improve haemodynamic condition and oxygen saturation in children who present with CHF.[121] The surgical repair consists of closure of ASD, and attachment or redirection of the pulmonary venous blood to the LA.[122]

Anaesthetic management

Infants with pulmonary venous obstruction, present with pulmonary oedema and hypoxia requiring early surgery. Avoidance of myocardial depressant agents, inotropic support for the RV function and manoeuvres to decrease the PVR should be followed.

Intraoperative and postoperative problems are usually related to the residual stenosis of the pulmonary venous pathway. In addition, the reactive pulmonary vascular bed may produce high PA pressures, pulmonary oedema and RV failure. Inotropic support should be continued in the postoperative period and prolonged period of elective ventilation is necessary.

Some complex congenital defects

Transposition of the great arteries

In this condition, the aorta arises from the RV and the PA originates from the LV (Fig. 7.10). In dextro-TGA (d-TGA), the RV is on the right side of the heart and gives rise to aorta so that the aorta is anterior or lateral and to the right of the pulmonary artery. The systemic venous blood returns to the RA and RV, and is ejected into the aorta. A VSD is usually present and a variable degree of subpulmonic stenosis is also present.

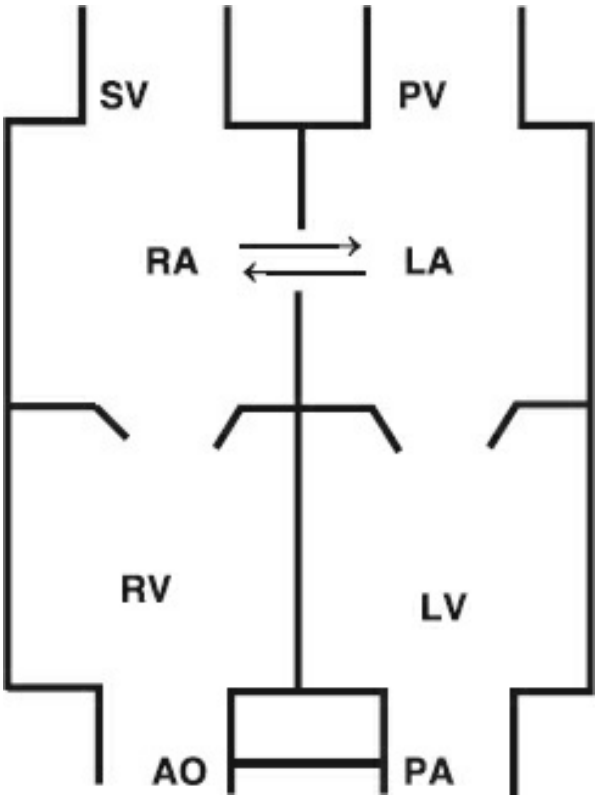

Figure 7.10: Diagrammatic representation of the anatomy in a patient with transposition of great arteries with intact ventricular septum. (SV: systemic veins, PV: pulmonary veins, RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle, AO: aorta, PA: pulmonary artery).

Pathophysiology

In d-TGA, there are parallel right and left circulations such that the oxygenated pulmonary venous blood returns to the LA and LV and then back to the PA. Similarly, the systemic venous blood returns to the RA and RV and again pumped into the aorta. Some mixing of the oxygenated pulmonary venous blood across the atrial or ventricular septum or through the ductus arteriosus is required for survival. Therefore, preoperative management of these neonates includes infusion of prostaglandin E] that helps to maintain the patency of the ductus arteriosus prior to definitive surgery. In addition, balloon atrial septostomy (echo guided or fluroscopy guided) can also be performed. A survey in the United Kingdom has revealed that there is a considerable variation in the early management of a patient with TGA.[123]

The following types of surgical repairs are performed:

Atrial switch (Mustard and Senning) operations

Physiological repair for TGA was performed first by Senning in 1959 and soon thereafter by Mustard. The Senning and Mustard procedures (atrial

switch) remained the standard treatment for TGA until the late 1980s when the arterial switch operation took over as the treatment of choice. However, atrial switch is invaluable as the treatment of choice for TGA in the developing countries, where the patients often present late and the morbidity and mortality attached to a two-stage arterial switch operation is prohibitively high.[124] In this procedure an atrial level partition is created with baffling and redirection of the pulmonary venous blood across the tricuspid valve to the RV and to the aorta.[125,126] The systemic venous blood is directed across the mitral valve into the LV and to the PA. Thus, the physiological correction is performed, but RV remains the systemic ventricle (pumping blood into the aorta) and LV remains the pulmonary ventricle (pumping blood into the PA). These procedures may be associated with obstruction to both systemic and pulmonary venous return resulting in the SVC syndrome and pulmonary venous hypertension.

Arterial switch

The arterial switch operation has become the procedure of choice for the TGA with or without VSD.[127] It is also considered the treatment of choice for double outlet right ventricle with a subpulmonary VSD. Since its first description by Jatene[128] in 1976, there have been remarkable improvements in surgical techniques leading to a better surgical outcome. In this procedure, the anatomical correction is performed with the division of both great arteries and re-attachment to the respective anatomically correct ventricles.[129-131] Excision and reimplantation of the coronary arteries to the new aorta are also necessary. The success of this procedure depends on adequate preparation of the LV. In patients with intact ventricular septum, the LV pressure and mass are diminished. The LV may not be prepared to tolerate the systemic workload imposed on it suddenly. In the presence of VSD, the LV can tolerate the systemic workload at any stage. PA banding may be performed in patients with intact ventricular septum and who are older, in order to prepare the LV or the correction is undertaken during the neonatal period when the PVR and hence the LV pressures are both high. In addition, myocardial ischaemia and infarction may occur after mobilisation and reimplantation of the coronaries.

Rastelli repair

In patients with a large VSD and subpulmonic stenosis, VSD is closed

obliquely in such a way that the LV flow is directed into the aorta. The RV is connected to the PA with a conduit and the pulmonary valve is oversewn.

Complications include obstruction to the LV outflow across the VSD patch and heart block.

Anaesthetic management

The inhalational induction of anaesthesia is slow as the effective systemic blood flow is relatively low. The patients are severely hypo-xaemic and frequently acidotic. Resuscitation with sodium bicarbonate and calcium chloride may be required. Neonates can be intubated awake and oxygenated with 100 percent oxygen. IV line is secured (which may be difficult) for administration of the narcotic and muscle relaxant. In older infants in whom IV line is difficult to insert, intramuscular ketamine may be used (4 to 7 mg/Kg) along with 100 percent oxygen. IV line is then secured for administration of further medication. This is followed by insertion of the arterial and central venous lines. Bradycardia should be treated aggressively with the administration of 100 percent oxygen, IV atropine and discontinuation of volatile anaesthetic agent. Inotropic support is generally required for terminating the CPB. An anaesthetic technique consisting of low-dose fentanyl, thiopental, atracurium and isoflurane, with satisfactory outcome has also been described.[132] Postoperative period may be complicated following arterial switch operation with low CO and requirement of mechanical ventilation for a prolonged duration. Plasma BNP can predict adverse outcome in the postoperative period after arterial switch operation. It has been shown that a 6 hr BNP concentration of >160 ng/L can predict complicated postoperative course in these patients.[133]

Congenitally corrected transposition

This anomaly has a double discordance (RA to LV to PA and LA to RV to aorta) and the unique feature is that the RV is the systemic ventricle and the LV serves the pulmonary circulation. Although, the physiological correction is achieved, deterioration of the systemic RV function associated with tricuspid regurgitation remains a problem in these patients. The double switch operation is required. It consists of an atrial switch such as a Senning or a Mustard procedure along with an arterial switch. It reverts the physiology to nearly normal, wherein the LV and the RV become the systemic and pulmonary ventricles respectively.

Tricuspid atresia

Anatomical findings include an imperforate tricuspid valve with hypoplasia of the RV. For survival of the infant, an ASD or PFO is essential to allow the circulation of systemic venous blood from the RA to the left side. A VSD and pulmonic stenosis may also be present.

Due to shunting of systemic venous blood into the LA, hypoxaemia and cyanosis are present. The degree of hypoxaemia depends on the magnitude of the pulmonary blood flow. This is dependent on the size of VSD and the degree of pulmonic stenosis.

The operative procedure performed is the Fontan procedure. Since its first description by Fontan and Baudet,[134] advances in techniques and postoperative management have been accompanied by improvement in early survival. The Fontan approach is also applied to a wide variety of anomalies classed together as univentricular hearts. In this procedure, the systemic venous return is directed to the pulmonary circulation by anastomosing the RA or RA appendage to the main PA or right PA. A small residual ASD may be left (fenestrated Fontan) to reduce morbidity and mortality. The total cavopulmonary connection as advocated by de Leval[135] is also widely practised. The extra-cardiac Fontan procedure is yet another modification of the Fontan's original operation. In this, the superior vena-cava anastomosis to the right PA is a direct end-to-side connection as per a bidirectional Glenn, but the inferior vena cava is transected from the RA and attached to the PA.

By diverting the systemic venous return to the PA and separating the systemic and pulmonary circulations, hypoxia is corrected. As there is no contractile contribution from the RA to propel blood, the PVR must be low to allow the forward flow of blood. Children above 4 years who have adequate sized pulmonary circulation with low PVR have good results. Transoesophageal Doppler echocardiography can be performed immediately after CPB to confirm the adequacy of pulmonary blood flow. Biphasic forward flows with peak velocities during systole and diastole have been demonstrated and patients showing forward flows with flow reversal may require reoperation.[136]

Anaesthetic management is aimed at minimising the PVR and optimising CO so that blood flow through the lungs is improved. LV dysfunction causing an increase in the left ventricular end-diastolic pressure and LA pressure is not tolerated as the pulmonary circulation is reduced due to a high

LA pressure. Positive pressure ventilation with high airway pressure decreases the pulmonary blood flow. Early return of spontaneous ventilation should be the aim to improve pulmonary blood flow. Patients should be extubated as early as possible, provided haemodynamics are stable.

In summary, the surgical treatment and perioperative care of the patient with CHD remains an important challenge in medicine. The advances in imaging, clinical monitoring, medical devices and bioinformatics have improved the outcome. However, significant practice variations in the perioperative care of neonates with CHD exist. This is due to physician preference, experience, and lack of evidence in favour of one technique over the other. This, however, may form the basics for investigating the impact of various practices on the outcome. The cardiac anaesthesiologist should actively participate in these investigations in order to improve the outcome of the patients with CHD.

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Chapter 8: Anaesthesia for Closed Cardiac Operations in Adults

Rheumatic fever, which usually causes mitral stenosis (MS) has become exceedingly rare in the developed world. In fact, MS is commonly found in the developed world in patients who have emigrated from the developing countries where rheumatic fever is still endemic. Isolated MS is a frequent presentation of rheumatic heart disease. This particular lesion is amenable to surgical correction without employing cardiopulmonary bypass (CPB) by performing a closed mitral valvotomy (CMV). The operation is still performed in the developing countries, as the facilities for open-heart surgery are not widely available. Tubercular constrictive pericarditis is another condition that is commonly encountered in the developing countries, which is amenable to surgical correction without employing the CPB. This chapter focuses on the anaesthetic management of patients undergoing CMV and pericardiectomy.

Closed Mitral Valvotomy

The typical rheumatic mitral valvulitis causes thickening of the valve leaflets, fusion of commissures, chordal shortening and fusion, and valve calcification. Currently, percutaneous balloon mitral valvotomy (BMV) has become the procedure of choice for isolated, uncomplicated MS with favourable morphology.[1] Unfortunately, facilities to perform BMV are available only in selected centres in the developing countries and, hence, a large number of patients are also subjected to CMV. The CMV is mainly performed in centres where facilities for BMV are not available. The tertiary care hospitals where BMV is performed, also run the training programme for cardiac surgeons. The budding cardiac surgeons may have to work in future

in places where facilities of BMV and open-heart surgery are not available. It is for this reason, at least, that CMV should be continued to be performed in limited numbers in the tertiary care hospitals, so that this operation forms an integral part of the training programme of the cardiac surgeon as well as the cardiac anaesthesiologist.

No doubt, open mitral valvotomy (OMV) is a better operation, because relief of the valvular and subvalvular obstructive elements can be dealt with much better under direct vision.[2-5] OMV provides excellent early and long-term results in a selected group of patients.[6] It offers better haemodynamic and long-term results[3], but is the procedure of second choice because of higher cost and surgery related morbidity. CMV is performed in the developing countries due to the number of patients and economic reasons. The long-term results of this operation have been reported to be satisfactory in young patients.[7-9] It has been compared with BMV and shown to provide comparable short-term (valve area and mean diastolic pressure gradient) and long-term (restenosis free survival) results.[10] It has also been performed at different stages of pregnancy including labour with excellent results offering a cost-effective treatment for developing countries when BMV is not affordable.[11] CMV represents a satisfactory technique in terms of simplicity, high efficacy and lower cost.[9] The major factors that make the valve unsuitable for CMV are the presence of associated significant mitral regurgitation (MR), presence of left atrial (LA) thrombus and dense calcification of the valve. The Wilkins score[12] can be used to assess the valve morphology in order to decide the feasibility of BMV or CMV. This scoring system assigns a value from 1 to 4 for each of valve calcification, leaflet mobility, leaflet thickening, and disease of the subval-vular apparatus. Patients with a score of < 9 are considered suitable for valvotomy provided mitral regurgitation is absent or mild.

The safety and efficacy of CMV has also been demonstrated in patients with severe pulmonary artery hypertension (PAH) with systolic pulmonary artery pressure of more than 100 mm Hg[13] as well as those undergoing reoperation for restenosis.[14] The interest in this operation even today is indicated by the attempts to improve it further by utilising the transoesophageal echocardiography(TOE)[15,16] and less invasive approaches such as port-access surgery.[17]

The suitability of the valve for CMV can be easily detected by

transthoracic echocardiography. It also helps to grade the severity of MS in terms of valve area and PAH. The important factors that come in the way of CMV are the presence of LA thrombus, associated significant MR or other valvular lesions. These also can be easily detected by transthoracic echocardiography. However, it is believed by some[18] that TOE should be mandatory before BMV (and hence, CMV) for detecting the LA thrombus.

Anaesthetic Management

The principles of anaesthetic management are based on the pathophysiology of the condition. The reader should refer to chapter 5, where this has been described in detail. Patients are generally thin built, young adults and often have severe MS (valve area < 1 cm^2) and PAH. In a series of 4850 patients undergoing BMV at G. B. Pant hospital over a 13-year period, the mean age was 27.2 ± 11.2 years and 32 percent patients were under 20 years of age.[19] The anaesthetic considerations are similar to those that are applicable for patients undergoing OMV or mitral valve replacement (MVR), except that elective ventilation for a prolonged period may not be necessary. Therefore, opioids should be used in judicious dosage.

In essence, tachycardia and hypovolaemia are poorly tolerated by these patients. The anaesthetic management, therefore, should be focused with these two issues in mind. The preoperative drug therapy such as digitalis and diuretics should be continued till the day of surgery. The premedication should consist of intramuscular administration of morphine (0.1 to 0.2 mg/Kg) and promethazine (25 mg). Atenolol has been administered orally as a premedication on the night before and 2 hours prior to surgery. It was shown that it provided a lower heart rate (HR) at periods of maximal anaesthetic and surgical stress such as laryngoscopy, endotracheal intubation, surgical incision, and commissurotomy.[20]

Anaesthetic induction can be performed with morphine (0.2 to 0.3 mg/Kg) or fentanyl (5 to 10 µg/Kg) along with small increments of thiopental (50 to 75 mg) as tolerated and needed. Alternatively, a combination of morphine and midazolam has also been used and shown to provide better haemodynamic stability as compared with morphine and thiopental.[21] Propofol in the dose of 2 mg/Kg bolus followed by an infusion (6 mg/Kg/hour) has also been tried, but has been shown to significantly decrease the blood pressure (BP) and cardiac index.[22] Therefore, it appears

that a low-dose opioid technique is suitable for these patients. However, in patients with tight MS (mitral valve area < 1 cm^2) and severe PAH (PA pressure equal or nearly equal to systemic pressure), higher doses of opioids should be used that provide better haemodynamic stability. The respiratory depression and analgesia provided by the opioids are also useful in the postoperative period as these patients with PAH need elective ventilation. Morphine in the dose of 0.5 mg/ Kg or fentanyl in the dose of 10 to 15 μg/Kg can be used.

The choice of muscle relaxant should be determined by the basal HR. Atrial fibrillation is commonly present in these patients and, the basal HR may be high. If the basal HR is fast, e.g. 120 beats/min., vecuronium or atracurium should be selected, both of which have little effect on the HR and in fact can reduce the HR, if opioids have been given for induction of anaesthesia.[23,24] Rocuronium bromide appears to be a good choice in presence of slower heart rate due to its marginal vagolytic effect. Pancuronium bromide can also be used in presence of high-dose opioid anaesthesia (if the basal HR is less).

Maintenance of anaesthesia can be accomplished with nitrous oxide and inhalational agent such as halothane or isoflurane. However, nitrous oxide should be used cautiously in patients with severe PAH. Increments of narcotic agents can also be used for maintenance.

The operation is performed with the patient supine with left side elevated to approximately 30 degrees. A left thoracotomy, usually in the fifth intercostal space is performed. LA appendage and left ventricle (LV) become easily accessible by this approach. The surgeon inserts the right index finger in the LA via appendage. He may allow 50 to 100 mL blood to escape from the appendage, helped by manual inflation of the lungs to remove non-adherent thrombus from the LA. The Tubb's dilator is then inserted by the left hand through the LV apex, and is guided across the mitral valve by right index finger of the surgeon in the LA. The dilator is then opened up so that the fused commissures are opened. The valve is usually dilated in steps until adequate valvotomy is achieved as judged by the surgeon with his right index finger in the LA.

The patient with MS has a low cardiac output (CO) that is easily depressed during intracardiac manipulations of the heart. Severe decreases in BP and HR are very common during the procedure. Therefore, continuous electrocardiographic (ECG) and invasive BP monitoring are very helpful.

Hundred percent oxygenation and the use of inotropes and atropine maybe necessary. Rapid administration of blood/fluid may be needed and, therefore, a good intravenous line should be established during induction of anaesthesia. Another serious complication of CMV is embolisation, either from a thrombus or from calcium deposits. Some anesthesiologists give a head-down tilt during valvotomy and also compress the great vessels externally to prevent cerebral embolisation. If the surgeon is able to feel an obvious thrombus, the patient should be placed on CPB (if the facility is available) and OMV should be performed. If the facility for open-heart surgery is not available, the operation should be abandoned and the patient should be referred to an appropriate centre for OMV in the near future. Sometimes, acute severe MR can occur during CMV that might necessitate urgent mitral valve replacement. Due to these reasons, the operation should ideally be performed in a centre where the facility for open-heart surgery is available. However, in the developing countries, such is not always the case, yet CMV is performed at some centres where facility of open-heart surgery is not available.

CMV is generally considered a simple operative procedure and is often performed without adequate haemodynamic monitoring. It must be remembered that the complications of the procedure can be equally disastrous as any open-heart surgical procedure and hence, the anaesthesiologist must perform adequate haemodynamic monitoring. As already highlighted, direct arterial BP monitoring can be very useful for beat-to-beat pressure monitoring during the intracardiac manipulation by the surgeon. The central venous catheter also is very useful to monitor the right atrial pressure, as the right ventricular (RV) failure is common in these patients. In addition, infusion of inotropes and vasodilators that may be needed postoperatively can be given through the central venous catheter.

Postoperative Care

For an experienced surgeon, the operation is usually straightforward and can be performed within 60 to 90 min. It is also a usual practice to extubate these patients at the end of operation so that the stay in the intensive care unit (ICU) is shortened. This helps in minimising the ICU expenditure as well as allows more operations to be performed. However, it should be remembered that patients with MS often have deranged respiratory functions caused by chronic lung congestion.[25,26] In addition, the LV function may also be

subnormal after valvotomy in some patients because of a ventriculotomy and sudden increases in the flow and distention of the chronically underloaded LV. Therefore, it appears that elective ventilation for some duration in the postoperative period should be beneficial to these patients. Indeed, it has been shown that the patients are mildly hypercarbic if they are extubated at the end of surgery.[27] It has also been shown that this hypercarbia can be deleterious for RV performance at this stage.[27] It is therefore, recommended that elective ventilation should be performed for some duration until the cardiorespiratory functions stabilise and the effect of muscle relaxant wears off completely. This should be strongly considered, especially in patients having severe MS and PAH. Thoracic or lumbar epidural analgesia by fentanyl can be used after the operation. It has been shown that thoracic epidural fentanyl infusion is superior to lumbar infusion because of smaller dose requirement.[28]

Constrictive Pericarditis

In this condition, the thickened pericardium limits the diastolic filling of the heart. Tuberculous pericarditis is still the major cause of constrictive pericarditis in the developing countries. The other rare causes include, idiopathic, neoplastic, uraemic, and post-traumatic pericarditis. The most frequent physical signs of chronic constrictive pericarditis are jugular venous distention and hepatomegaly. In later stages, ascites and peripheral oedema are invariably present. The ECG characteristics include P mitrale (broadened P wave), low QRS voltage and T wave inversion. Atrial fibrillation is also commonly present. Chest radiography may show cardiomegaly and pericardial calcification (Fig. 8.1).

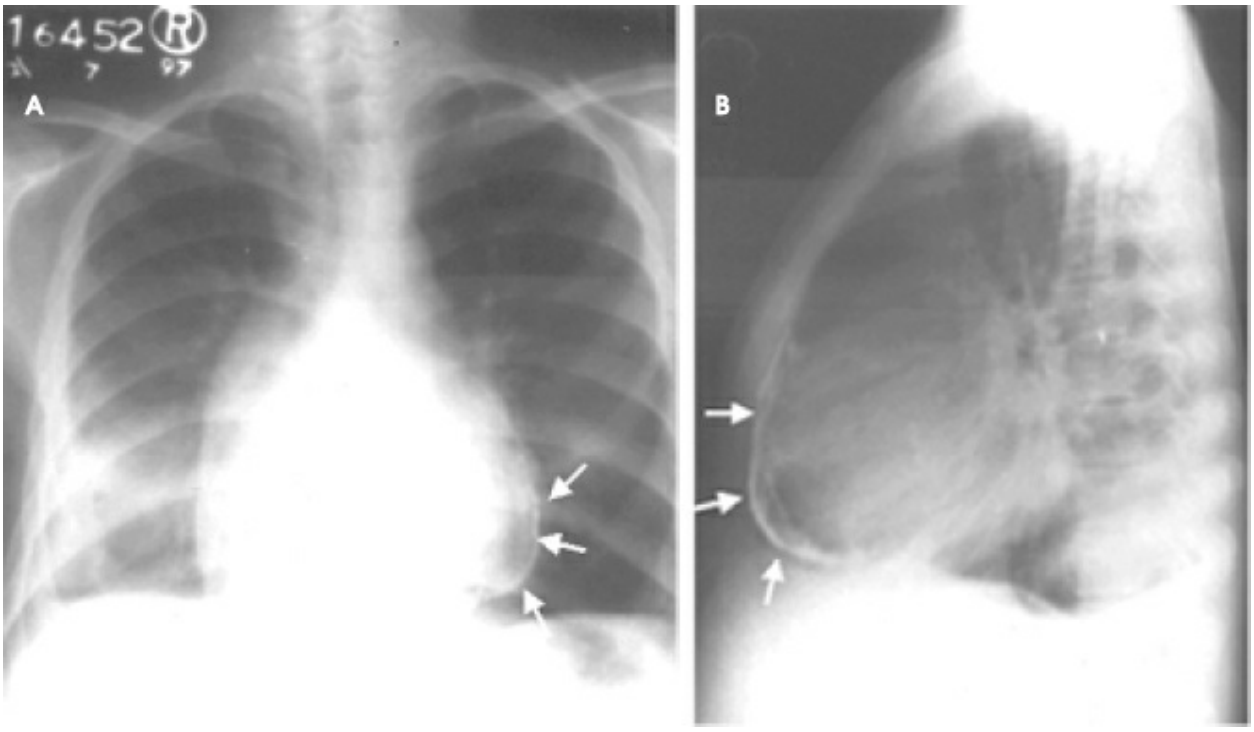

Figure 8.1: Postero-anterior (A) and lateral (B) chest radiographs showing extensive pericardial calcification in a patient with constrictive pericarditis (arrows).

Constrictive pericarditis severely limits ventricular filling with elevation and equalisation of the left and right sided diastolic pressures. Therefore, RV diastolic pressure, pulmonary artery diastolic pressure, right atrial pressure and pulmonary capillary wedge pressures are equal. Prominent 'x' and 'y' waves can be seen on the venous as well as atrial pressure waveforms. An increased diastolic flow velocity in the superior vena cava (SVC) on Doppler examination can be found.[29] Due to the disease, compliance of the pericardium is decreased and end-diastolic volume of the heart is limited by the pericardium. The initial rapid filling of the ventricle is not affected. However, filling is stopped when ventricular volume achieves the limit set by the noncompliant pericardium. After this, there is no further filling and the ventricular pressure shows a plateau until the onset of next systole. Cardiac failure can frequently occur in constrictive pericarditis. This is due to the involvement of myocardium or coronary arteries in the pericardial scar.

Pericardiectomy

The treatment of chronic constrictive pericarditis is pericardiectomy. Mild form of disease can be managed by medical treatment for many years. The

surgical treatment is usually restricted to patients who have disabling symptoms. In the developing countries, patients often present at a fairly advanced stage of the disease with ascites and peripheral oedema. These patients have deranged liver functions due to chronic congestion.

Anaesthetic Considerations

Constrictive pericarditis presents unique perioperative considerations for the anaesthesiologist. He should be well versed with the aetiology, pathophysiology, and diagnostic modalities in order to adequately prepare the patient for surgery. With proper preparation and optimization of patient's condition, successful surgical outcome can be obtained.[30]

Patients should undergo thorough preoperative evaluation. They should be decongested preoperatively with digoxin and diuretics. Some patients will also have pulmonary tuberculosis and accompanying pleural effusion. Moderate to large amount of fluid collection in the pleura should be tapped preoperatively to achieve complete lung expansion. It must be remembered that an absolutely fit patient should not be the objective, as the severity of pericarditis may not permit such a state in many patients. The key is to decongest the patient preoperatively to the optimum extent possible.

Removal of an adherent and scarred pericardium can be technically difficult and may require extensive manipulation of the heart in order to release both right and left ventricles. In addition, relieving the SVC and inferior vena-cava (IVC) from adhesions is also necessary. With the kind of dense adhesions that may be encountered at times, pericardiectomy is a surgical challenge and should be considered a high-risk procedure.[31,32] Calcific constrictive pericarditis is usually associated with severe pericardial tWckening and dense fibrous adhesions making it a technically difficult procedure. Sudden haemorrhage can occur, if a cardiac chamber is accidentally entered during pericardiectomy. Perhaps, due to these reasons, some surgeons advocate median sternotomy and use of CPB for pericardiectomy.[33] Alternatively, percutaneous cardiopulmonary support can also be utilised.[34] In the developing countries, it is a custom to perform pericardiectomy without CPB. Either sternotomy or a left thoracotomy is used for this purpose. However, if profound haemorrhage occurs, especially from such areas which are not accessible without severe retraction of the heart (e.g. IVC), CPB may be instituted (if the facility is available) in an

emergency to tackle the problem. In other words, if the facility of open-heart surgery is not available, the surgeon should not be very aggressive in dealing with dense adhesions particularly in the inaccessible areas.

Decortication of the LV before RV is recommended by some.[35] This is due to the theoretical possibility of producing sudden pulmonary oedema, if the RV is freed first.

The patients have limited preload reserve, and hypovolaemia is poorly tolerated. In addition, CO is rate dependent so that bradycardia is also not desirable. Therefore, induction of anaesthesia, should be performed by agents that cause minimal vasodilatation, bradycardia and myocardial depression. Either morphine administered slowly or fentanyl along with small doses of thiopental can be used. Ketamine is also a good choice in these patients. A cocktail of ketamine and midazolam has been used successfully.[36] Ketamine has a potent analgesic effect, while its tendency to increase blood pressure and HR is countered by midzolam providing relative cardiopulmonary stability. Pericardial surgery has been attempted using high thoracic epidural anaesthesia while fully awake, without endotracheal intubation.[37] However, its use is questionable is patients undergoing pericardiectomy, which is accompanied by haemodynamic disturbances. Venous access with wide bore cannula must be secured for rapid administration of blood. Monitoring should include direct arterial pressure and central venous pressure (CVP) monitoring. A decrease in the CVP may be used as a measure of adequate pericardiectomy. In addition, inotropes can be administered via the central venous line.

Doppler echocardiography performed after the surgery can be useful in assessing the effects of pericardiectomy. The respiratory variation of mitral inflow and pulmonary venous Doppler flows can be studied for this purpose. A decrease in the respiratory variation of the Doppler flows is indicative of adequate pericardiectomy and can be used for evaluating the outcome.[38] It has been shown that B-type natriuretic peptide levels decrease significantly following pericardiectomy and may be used as a marker for LV diastolic dysfunction.[39]

During dissection, hypotension and arrhythmias occur frequently. Occasionally, tearing of atrial or ventricular walls or damage to coronary arteries may also occur.

Haemodynamic improvement does not always occur and patients may

remain in low CO after the operation. Low CO is the most important cause of morbidity and mortality in these patients.[32] One paper has reported that as many as 70 percent of patients were in low CO in the postoperative period.[40] Therefore, these patients should be electively ventilated in the postoperative period and inotropic support should also be continued for 48 to 72 hours. The possible causes of low CO are injury to coronary arteries, residual pericardial scar, constrictive epicardium or underlying myocardial disease.

In summary, pericardiectomy poses a significant challenge and the anaesthesiologist must understand the underlying disease process as well as the surgical considerations. Judicious use of anaesthetic agents with intensive haemodynamic monitoring is required.

Surgery for the coarctation of aorta and ligation of the patent ductus arteriosus are some other closed cardiac operations. These are usually performed in children and have been described in the chapter on congenital heart defects (chapter 7). In the developing countries, sometimes, these patients present for surgery in early adulthood. The same anaesthetic considerations apply in these patients.

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Chapter 9: The Anaesthesiologist and the Management of Cardiopulmonary Bypass

Cardiopulmonary bypass (CPB) means circulation outside of the body via artificial circuitry in which the function of the heart (pump) and lungs (gas exchange) is temporarily taken over by artificial technology. In this manner, the patient's heart and lungs are bypassed (rested) making the surgical field (heart and great vessels) free of blood.

If one takes into account the current scenario of cardiac surgery, it is noticeable that due to an increase in the percutaneous coronary and other interventions performed by the cardiologist, the number of cardiac surgical procedures such as coronary artery bypass grafting (CABG), and repair of some of the congential cardiac defects is on the decline. In addition, a large number of CABGs are now performed without using the CPB. Further, the techniques of percutaneous valve replacement have been refined to the extent that they are being used more commonly in the clinical practice. One may, therefore, question whether CPB techniques are really necessary, and if yes, do they require to be refined any further. However, a variety of other developments are taking place that require CPB and other circulatory support interventions. Surgical procedures for ventricular assist devices are becoming more common. Also, advances are taking place in the surgical correction of complex congenital heart malformations. Minimally invasive cardiac surgical techniques have shown promise. These techniques will continue to require CPB and sophistication would seem mandatory to meet the requirements of some of these techniques.

CPB was first used in the 1950s, after a period of laboratory research on dogs. The first attempts to use heart-lung machine for intracardiac surgery

were carried out on April 05, 1951 by Dennis et al.[1] Two patients were operated, but both died in the operation theatre (OT). On May 06,1953, John Gibbon Jr. successfully closed an atrial septal defect using the CPB.[2] Since then, the progress and developments in CPB techniques have come a long way and now it is being used for the most complex surgical repairs requiring prolonged CPB times and circulatory arrest. Apart from its use for patients undergoing CABG, valve repair/replacement and repair of congenital heart defects, CPB is also used for respiratory support for patients suffering from reversible respiratory dysfunction and some noncardiac surgical procedures facilitated by CPB.

In the early days, the anaesthesiologist was involved in the technical developments of the CPB and was an important member in the management of CPB. Subsequently, however, professional perfusionists were trained who took over the responsibility of managing the CPB. Nevertheless, the anaesthesiologist must understand the CPB completely for the safe conduct of open-heart surgery. Indeed, even today we see anaesthesiologists actively involved in the management of CPB and helping the perfusionist in his everyday practice.

In this chapter, the various issues relating to CPB that are of importance to the anaesthesiologist are discussed.

The Cardiopulmonary Bypass Circuit

The most common form of CPB involves rerouting the patient's entire cardiac output (CO) from both right and left ventricle. The other techniques include left heart bypass, cardiopulmonary support, and extracorporeal membrane oxygenation. The CPB circuit involves systemic venous blood withdrawal from the right atrium (RA) or vena-cavae, the delivery of oxygen (O_2) and elimination of carbon dioxide (CO_2) in the oxygenator (membrane or bubble), and the return of this blood to the ascending aorta. In patients undergoing surgery of the ascending aorta or arch of the aorta and in some reoperations, the blood is returned to the femoral artery or even axillary artery. A heating and cooling device is an integral part of most oxygenators. Water is circulated through this device to either cool the blood at the commencement of bypass, rewarm it towards the end or to maintain the blood and patient at a normal temperature. Blood is drained via venous line, mostly

by gravity into the venous reservoir. The arterial pump draws blood from the reservoir and propels it through a heat exchanger, membrane oxygenator, and the arterial line filter to the aorta. Additional pumps and devices are used to salvage shed blood (the pump sucker), decompress the heart (vent), and deliver cardioplegia solution. Figure 9.1 shows the diagrammatic representation of a normal CPB circuit using a membrane oxygenator. The tubing used for the CPB circuit is made of medical grade polyvinyl chloride (PVC). The newer generation of PVC tubes with surface coatings are also available. The coatings alter the bioactivity of the surface and help to decrease the subclinical coagulation and the inflammatory response.

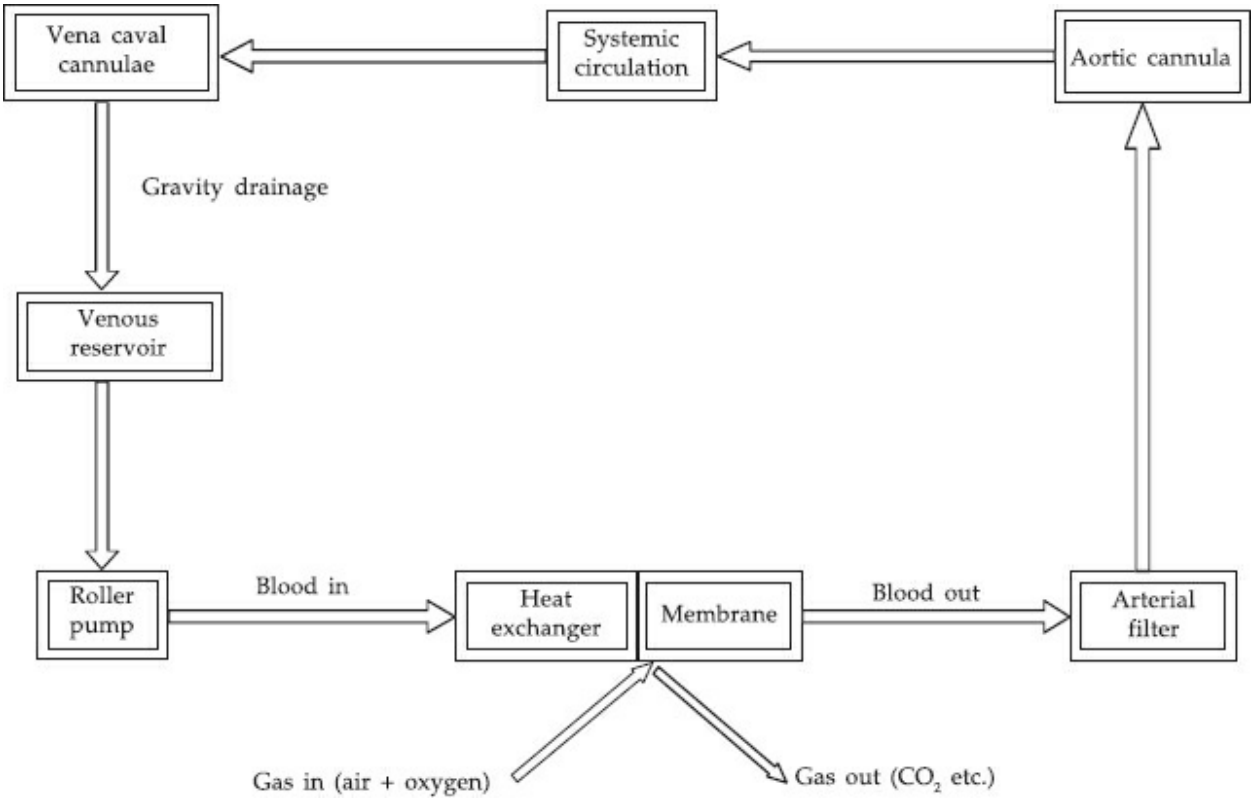

Figure 9.1: Diagrammatic representation of the cardiopulmonary bypass circuit.

The Pump

The most commonly used pump head consists of a two-roller head that compresses the tubing of the bypass circuit against a backing plate as it rotates, thus propelling the fluid in the direction of rotations of the roller head. Simultaneously, fluid is drawn behind the occlusive point. The volume of fluid propelled depends on the volume of tubing occluded by the roller and

on the number of revolutions of the roller. The pump is placed after the bubble oxygenator but before the membrane oxygenator, because the resistance to flow through the membrane is higher. A modern CPB machine consists of between four and five roller pumps on a base console (Fig. 9.2). Each pump has an independent flow control rheostat that can be calibrated with flow constants that correspond to the internal diameter of the tubing that is being used.

The setting of occlusion in the pump head varies among the various pumps used on the bypass console and is extremely important. The arterial pump head occlusion is set in such a way that the perfusate is allowed to drop at the rate of 1 inch/min. when the fluid height is set at 30 inches above the highest water level in the venous or cardiotomy reservoir (whichever is highest).[3] The properly set occlusion results in minimal haemolysis. The pump heads for delivering cardioplegia or venting the left ventricle (LV) should be fully occlusive with no fall in water column. This is done with the intention of preventing a negative pressure generation in the tubing during the period when the cardioplegia is not delivered or the LV vent is turned off. This avoids entrainment of air into the infusion lines that are in communication with the ascending aorta and coronary sinus.

The roller pumps are constant flow generators and continue to pump the set volume regardless of the resistance. They can generate extremely high positive and negative pressures. It is due to this reason, that the circuit will burst at the weakest point, should it be occluded accidentally. Likewise, massive quantities of air can be pumped, if the reservoir becomes empty. The normal resistance offered to the pump is the sum of the resistance of total tubing length, the oxygenator, the heat exchanger, the arterial line filter, the aortic/femoral cannula and the patient’s systemic vascular resistance (SVR). The arterial line pressure that is recorded by the perfusionist while the pump is running depicts the summation of all resistances. With the various components of CPB circuit having a relatively low and constant resistance, the line pressure depends upon the pump flow, resistance across the aortic cannula and the patient’s SVR. Although, the normal limit of line pressure ranges between 100 and 350 mm Hg, a pressure of more than 250 mm Hg is generally not accepted.

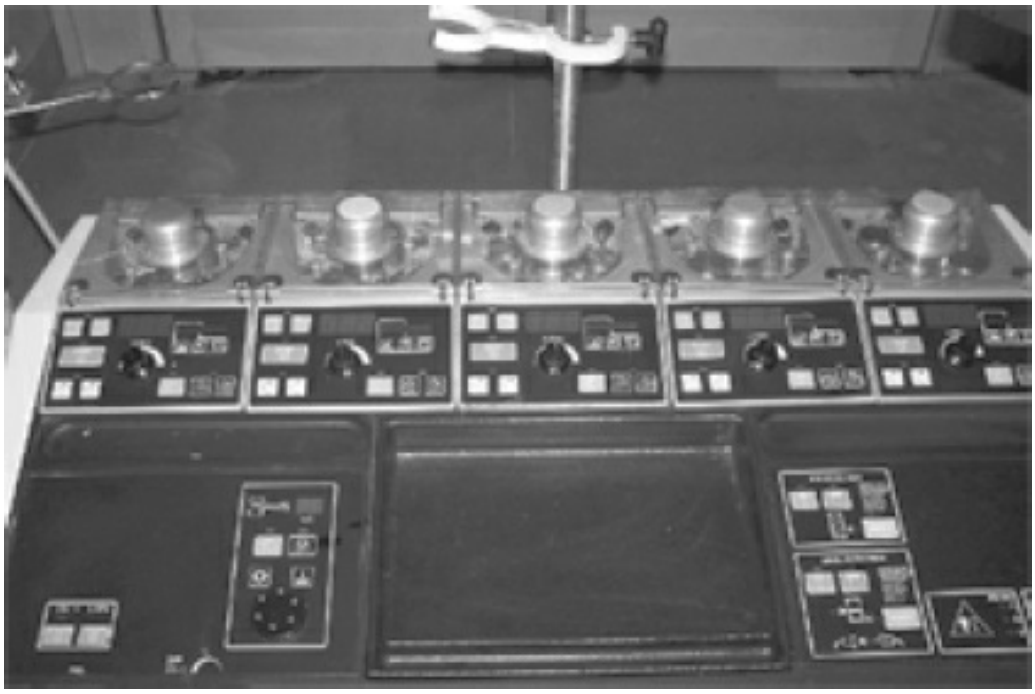

Figure 9.2: Sarns 9000 heart-lung machine with 5 roller pumps (Sams 3 M Health Care, Ann Arbor, Ml).

As a safety measure, a microprocessor controlled alarm that can be set to detect undue increases in the line pressure are being incorporated. They can be used to automatically turn off the pump when the preset limit is exceeded. If dangerously high line pressure develops, two important conditions must be ruled out: 1. accidental kinking of the circuit and 2. malposition of the aortic cannula. If the circuit is kinked, it may burst at the weakest point provided the pump is continued to run. If the aortic cannula is not well positioned in the lumen of the aorta, aortic dissection can occur. The other safety measures that are incorporated in the present heart-lung machines are the level alarm and the battery back-up. The level alarm helps the perfusionist to detect dangerously low levels in the reservoir and thus avoid the accident of infusing massive air emboli to the patient. The automatic battery back-up assures uninterrupted operation of the CPB pump in the event of power loss. Although, most OTs are equipped with emergency generators, cases of power failure even with emergency back-up failure have been reported.[4]

Centrifugal Pumps

The centrifugal pump is an alternative to a roller pump. It is a non-occlusive pump that uses a spinning cone for imparting acceleration to blood by a centrifugal force. The flow is dependent on the pressure changes so that the

accidental disruption of the CPB circuit in the event of unexpected increases in the resistance is prevented. The use of centrifugal pumps has increased over the times and is preferred for long-term CPB, supported CPB in high-risk angioplasty patients, ventricular assistance, etc. The advantages of centrifugal pump over roller pump are; less chances of massive air embolisms, relative lack of trauma to the blood and its components (particularly platelets), and generation of a high volume output with moderate pressure development.

It has been shown that centrifugal pump use can be helpful in reducing the occurrence of some of the most feared neurological complications of adult cardiac surgery patients.[5] A recent survey performed in America has revealed that centrifugal pumps are used as the primary systemic pumps in 54 percent of centres performing adult cardiac surgery, 12 percent of centres performing paediatric cardiac surgery, and 36 percent of centres performing combined adult and paediatric cardiac surgery.[6]

Oxygenators

The oxygenator substitutes for the gas exchange function of the lungs. Up to 10 years ago, bubble oxygenators were used by a number of cardiac centres. However, increasing use of the membrane oxygenators coupled with the advances in efficient production has substantially decreased the cost of the membrane oxygenator. Consequently, membrane oxygenators are used almost universally nowadays. The use of the bubble oxygenators is rare (considered obsolete by some) and only a few centres use if for procedures requiring short periods of CPB. Bubble oxygenators use a direct blood gas interface with dispersion of 100 percent oxygen through the blood. The blood gas interface results in the production of foam, where gas exchange occurs. The antifoam agent present in the defoaming chamber coalesces the foam. The oxygenated blood is collected in an arterial reservoir that is then pumped by the roller pump into the patient. Nevertheless, bubble oxygenators generate substantial gaseous microemboli. In addition, bubble oxygenators increase red blood corpuscles fragility[7] and activate platelets.[8]

The membrane oxygenator keeps the gas separate from the blood by a membrane, which consists of either a sheet or hollow fibre capillary tubes. The first disposable membrane oxygenators were introduced in the 1960s, and were made of silicone rubber. Currently, the majority of membrane

oxygenators are made of polypropylene. The micropores making up the membrane material constitute the micro-channels, which are less than 1 um in diameter. These provide conduits through the polypropylene membrane that gives enough diffusion capability to the membrane for both oxygen and carbon dioxide exchange.

Unlike bubble oxygenators, membrane oxygenators allow independent control of arterial oxygen tension (PaO_2) and arterial carbon dioxide tension ($PaCO_2$). PaO_2 is determined by the fractional inspired oxygen concentration (FIO_2) and the $PaCO_2$ by the sweep rate of the ventilating gas. The membrane oxygenator produces fewer microbubbles than the bubble oxygenator and has less harmful effects on blood.

Heat Exchanger

Some form of heat exchanger is used in the CPB circuit in order to warm and/or cool the patient's blood. During CPB, a large quantity of patient's circulating blood volume is outside the body and is exposed to the ambient temperature, which can lead to hypothermia. Therefore, it is necessary to warm the blood before CPB is terminated. In addition, hypothermia (mild to profound) is an accepted practice to reduce the patient's metabolic rate. Heat exchangers are used to decrease the temperature of blood on initiation of CPB and rewarm it before the termination of CPB. Now, the heat exchanger is an integral part of the oxygenator and lies on its proximal side. The basic design of the heat exchanger consists of two separate phases with water passing on one side and blood on the other. An external heating cooling device is used to regulate the temperature of the water entering the heat exchanger (4°C to 42°C). In this way, the blood perfusing the patient is warmed or cooled, which then raises or lowers the body temperature.

Prime

The CPB circuit is primed with fluid before bypass. Gas bubbles are eliminated to prevent embolisation to the patient. In the early days, when the oxygenators were non-disposable, eight to ten units of heparinised blood were used to prime the CPB circuit. Even in mid- 1970s, one or more units of homologous blood were commonly added to the CPB prime. Subsequently, this practice changed and clear priming solutions were employed. This change in practice was a result of knowledge that the quality of perfusion is

improved by reduction in viscosity and also by studies suggesting a reduction in neurological, renal and pulmonary complications. In addition, the recent increase in concern about transfusion related viral hepatitis has also contributed to this change in practice.

The prime volume is the volume that is necessary to completely de-air the circuit. The addition of clear prime is the main cause of haemodilution associated with CPB. Since haemodilution decreases the blood viscosity, the CO is increased. Therefore, overall oxygen delivery to the tissues may not be significantly affected even in the presence of lowered oxygen carrying capacity. Lower haematocrit values are accepted nowadays during cardiac surgery. A haemoglobin level of 6–7 gm/dL is considered acceptable during CPB with moderate hypothermia except in patients at risk for decreased cerebral oxygen delivery (history of cerebrovascular accident, diabetes mellitus, cardiovascular disease, carotid stenosis) in which case, higher haemoglobin levels may be justified.[9] The patient's predicted haematocirt on CPB can be calculated by the formula: (patient's blood volume x haematocrit)/(patient's blood volume + prime volume). Patient's blood volume is calculated by 75 × weight in Kg.

Addition of crystalloid solutions alone for priming lowers colloid oncotic pressure. This leads to tissue oedema through accumulation of water in the interstitium. Therefore, addition of mannitol, albumin and various high molecular weight colloid solutions has been suggested by some groups. However, the benefits associated with each practice remain controversial. Although accumulation of interstitial fluid especially in the lungs is a matter of concern, fortunately, in clinical practice, lung function does not seem to differ postoperatively with or without oncotic additions to the prime. Balanced electrolyte solution (lactated Ringer's solution) is the commonest priming solution used currently by the perfusionist. An adult circuit requires about 1.5 to 2 litres initially and may need additions during the course of bypass.

Anticoagulation

Before the aorta or cavae are cannulated, the patient must be anticoagulated adequately. Heparin is still the preferred anticoagulant used during open-heart surgery and its aajministration before aortic cannulation must not be forgotten. It is essential that the surgeon, anaesthesiologist as well as the

perfusionist confirm its administration. Further confirmation that the patient is adequately anticoagulated is made by measuring the activated clotting time (ACT). Various dosage protocols are followed to achieve optimum anticoagulation.[10] The definition of optimum anticoagulation also varies. Most commonly, heparin is administered by the anaesthesiologist about 3 to 5 min. before the aortic cannulation. The anaesthesiologist must, therefore, anticipate the surgical steps, particularly if the surgeon is not used to making a verbal request. It is customary to administer heparin once the surgeon starts taking the aortic purse string. Whatever maybe the method that is followed, it must be ensured that heparin is administered before the aortic cannulation is performed. It is also preferable to administer heparin in the central circulation [central venous pressure (CVP) line], by aspirating blood and confkming that heparin is actually reaching the circulation.

Rarely, heparin may be administered by the surgeon (usually into the RA). Even in this case, the anaesthesiologist must be observant and ensure that this critical step is not overlooked prior to cannulation. The anticoagulation management is discussed in detail in chapter 10.

The Cardiopulmonary Bypass

Arterial Cannulation

Arterial cannulation is performed first. The reason for cannulating aorta before vena-cavae is that, the arterial cannula provides a means for transfusing volume to the patient, if necessary. Venous cannula on the contrary provides a means to withdraw blood from the patient. Thus, blood can be transfused to the patient, if the heart fails or other complications arise before or during venous cannulation. The most commonly used site for cannulation is the ascending aorta (Fig. 9.3). However, in patients undergoing ascending aortic and aortic arch surgery and some reoperations, femoral or axillary artery is cannulated. For axillary artery cannulation, a tube graft in anastomosed to the side of the axillary artery to provide access for the arterial cannula without interrupting blood flow to the right arm. Ehiring aortic arch surgery, the axillary artery cannula can be used for antegrade cerebral perfusion during circulatory arrest by clamping the innominate artery. With femoral arterial cannulation, blood flow to the thorax is directed retrogradely

up the aorta. The axillary artery cannulation instead of femoral artery is being increasingly advocated when ascending aortic cannulation is not feasible. The advantages of axillary artery cannulation are; it is less likely to be affected by atherosclerosis, has good collateral flow, healing is better and wound complications are less likely. The other sites for arterial cannulation are innominate artery, brachial artery, and left common carotid artery.

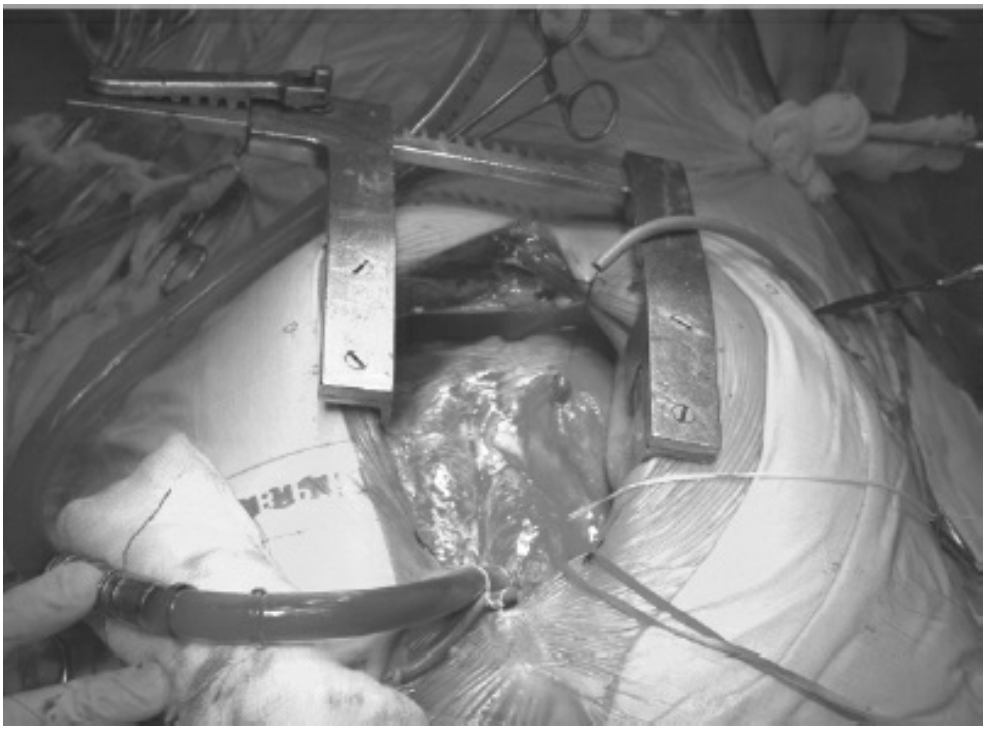

Figure 9.3: Cannulation of the ascending aorta (Picture taken from the head end of the patient).

The aorta allows placement of a large cannula and also carries less risk of arterial dissection, which is a major complication. The other major complications with the placement of aortic cannula are malposition (partial or complete cannulation of any of the arch vessels), disruption of the atheromatous plaque leading to systemic embolisation, and haemorrhage. In aortic dissection, the intraluminal blood enters aortic muscular and elastic layers. Hypertension is considered to increase the risk of aortic dissection during cannulation by increasing the intraluminal pressures and aortic wall tension.[11] The anaesthesiologist should therefore, temporarily lower the mean arterial pressure (MAP) to 80 to 90 mm Hg during aortic cannulation, either by administering inhalational agent or a bolus of peripheral vasodilator. This provides the surgeon with a soft aorta, and also reduces the risk of bleeding during the cannulation.

Atherosclerosis with or without calcification commonly involves the ascending aorta and its cannulation can lead to dislodgement of atheromatous plaque and debris. This may be due to direct mechanical disruption or from the “sand blasting” effect of the jet coming out of the arterial cannula. This constitutes a major cause of stroke following cardiac surgery.[12-14] Therefore, the surgeon may feel the aorta before cannulation in order to select the most appropriate site for cannulation, cross clamping, proximal anastomosis of venous graft and so on. However, this method has a very low sensitivity. Epiaortic ultrasound scanning is a much better method of detecting the atheromatous plaques, but is time consuming and requires special effort. Transoesophageal echocardiography (TOE) is much more convenient in this respect, but it provides limited views of the ascending aorta. Nevertheless, some method or a combination of methods should be utilised by the team managing the patient in order to elinimate/minimize the complications arising out of embolization. In severely calcific aortic disease, aortic cannulation should be avoided and femoral artery utilised for cannulation purposes.[15] The risks involved with femoral artery cannulation are, increased risk of dissection and limb ischaemia. Femoral perfusion can cause cerebral and coronary atheroembolism if there is extensive atheroma in the descending aorta or aortic arch. This can be easily assessed by TOE and should be considered before selecting the femoral route.

Special purpose aortic cannulas that incorporate an inflatable baffle to permit dual stream flow, one to the arch vessels and the other to the distal aorta are available. This cannula permits diverting any emboli away from the brain as well as selective brain cooling while maintaining relative normothermia in rest of the body.

Once the arterial cannula is placed, it is de-aired and connected to the arterial line of the perfusion circuit. Once again the line is inspected to ensure that it is free of air bubbles. The perfusionist at this stage makes a note of the line pressure using an attached aneroid manometer. The pressure should correspond to the patient’s blood pressure (BP). The perfusionist also checks whether the needle of the manometer is swinging nicely. The pulsatile motion of the fluid in the arterial limb (observed at prime/blood interface) should also be noticed at this stage. These observations help to confirm that the cannula is positioned properly inside the lumen of the aorta.

The aortic cannulation is one of the major steps of instituting CPB and may be associated with disastrous complications. Hence, it must be performed

carefully taking all the necessary precautions that have been described.

Although arterial and venous cannulae are considered disposable and intended for one time use, such a practice may be reconsidered in view of cost containment pressures.[16]

Venous Cannulation

Venous cannulation is most commonly performed via the RA. A single two-stage cannula can be inserted through the RA or its appendage. The tip of the cannula is placed in the inferior vena cava (JVC). Two-stage cannula has orifices that are aligned with the RA so that blood is drained from the superior vena cava (SVC) and the RA as well as the IVC (Figs. 9.4 and 9.5a). With this cannula, surgical access to the RA is not possible (air will be sucked in the venous cannula, if the RA is opened) and hence, it is used in surgeries where the RA access is not required, e.g. CABG. In operations where RA access is or may be required (e.g. atrial septal defect, mitral valve replacement), separate cannulation of the SVC and IVC is performed (bicaval cannulation, Fig. 9.5b). The SVC cannula is usually passed through the right atrial appendage and the JVC cannula through the postero-inferior portion of the lateral wall of the RAnear the JVC. Alternatively, the cannulae can be placed directly into the SVC or IVC by taking a purse-string suture. However, this may cause narrowing of the vessel when closed.

Figure 9.4: Different venous cannulae. The cannula on the left is a two stage single venous cannula. The tip lies in the inferior vena-cava and the portion with drainage ports lies in the right atrium (to drain superior vena-cava). Note the markings that help the surgeon to know the length of cannula insertion. The two cannulae on the right are ordinary venous cannulae (one each is inserted in the superior and inferior vena-cava).

Sometimes, venous cannulation is performed via the femoral or iliac veins (reoperation sternotomy, minimal access surgery, percutaneous cardiopulmonary support). A good venous return can be obtained by advancing the catheter into the RA. By inserting tapes around the cannulae and tightening them, all the systemic venous return is diverted to the CPB circuit. This also allows the RA to be opened without air getting sucked in the venous cannula. Blood can still enter the RA via the coronary sinus, if the aorta is not clamped (coronary circulation is going on) or cardioplegia is being delivered (after cross clamping the aorta). It can also enter the RA, if the left SVC is present. The left SVC is present in approximately 0.3 to 0.5 percent of general population, but in 2 to 10 percent of patients with congential heart disease.[17] It usually drains into the coronary sinus and then into RA. Left SVC can be visualised on TOE (Fig. 9.6). This is an important piece of information and helps the surgeon to decide regarding using a separate venous cannula to drain the left SVC. Cannulation of the left SVC is

necessary, if it is large and the right heart is going to be opened during surgery. Proper placement of venous cannulae (bicaval or two stage) is essential for the conduct of CPB. TOE is now commonly used in the cardiac OTs, and it can be used to check the correct placement of the cannulae (Fig. 9.7).

Occurrence of atrial arrhythmias is common during the placement of venous cannulae, however, they are usually self limiting. Sometimes, if the haemodynamics do not permit retraction of the heart to accomplish the placement of IVC purse-string, CPB may be instituted with single cannula placed in the SVC, and IVC cannulation is accomplished on partial CPB. If bleeding occurs during venous cannulation leading to hypotension, the perfusionist may be asked to transfuse volume via the aortic line to restore normotension. Improper size or placement of the venous cannulae will hamper the venous return in the oxygenator and elavate the CVP. This may lead to extravasation of blood from the vascular compartment to the extracellular compartment. Therefore, the performance of the venous cannulae should be carefully evaluated on initiation of the CPB. Proper placement of the venous cannulae can be confirmed by visualising complete decompression of the right side of the heart, which is also indicated by a CVP and PA pressure of zero.

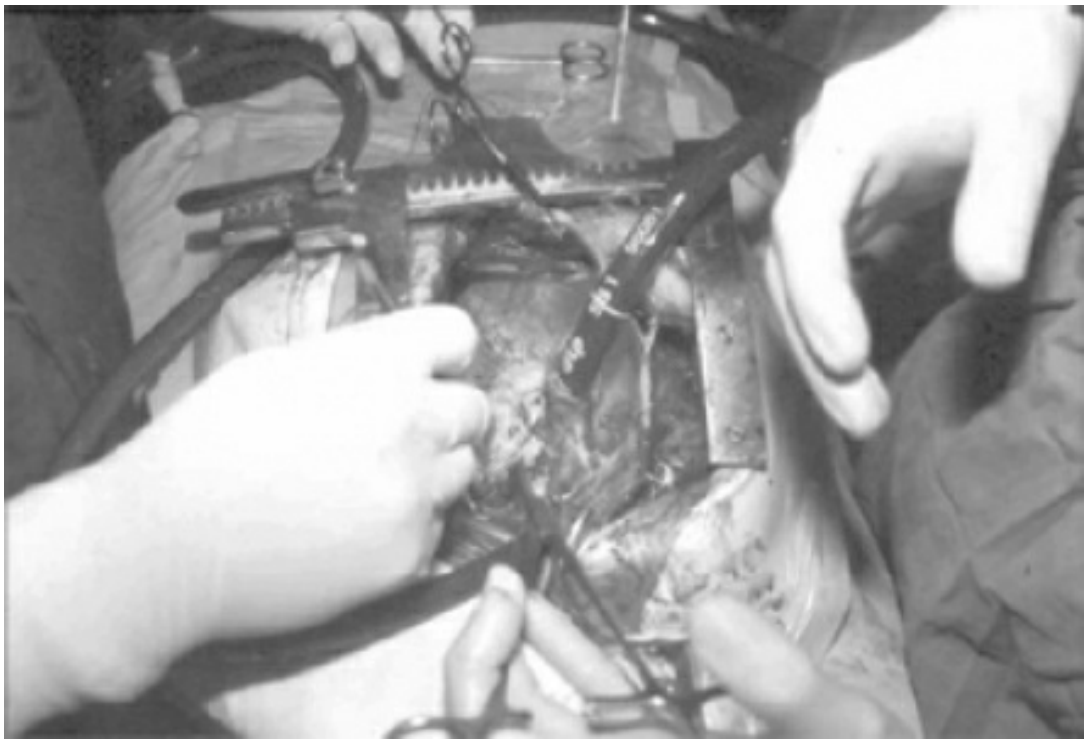

Figure 9.5a: Showing the two-stage single venous cannula (on the right). Arterial cannula is below the hand on the left, and aortic cross clamp (bottom of the picture) is being applied. (Picture taken from the head end of the patient.)

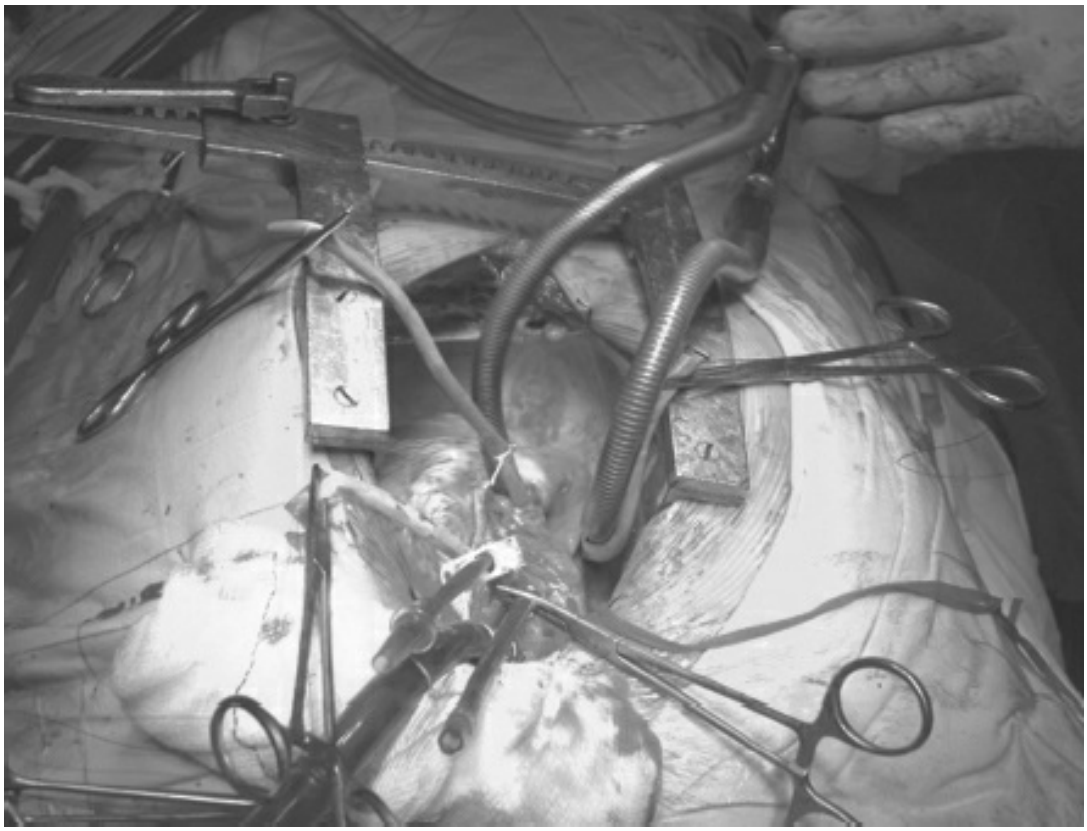

Figure 9.5b: Two venous cannulae (one each in the superior and inferior vena-cava) inserted via the right atrium. (Picture taken from the head end of the patient.)

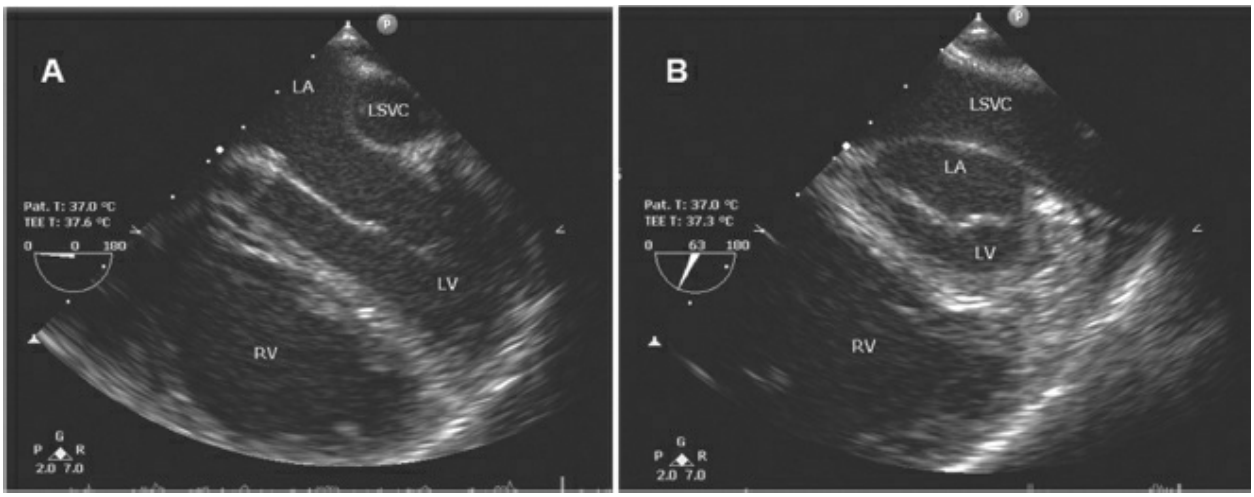

Figure 9.6: A: midoesophageal four-chamber view at 0° showing the left superior vena cava (LSVC) in transverse section, B: by increasing the angle to 63°, a longitudinal section of the LSVC is obtained. (LA: left atrium, LV: left ventricle, RV: right ventricle)

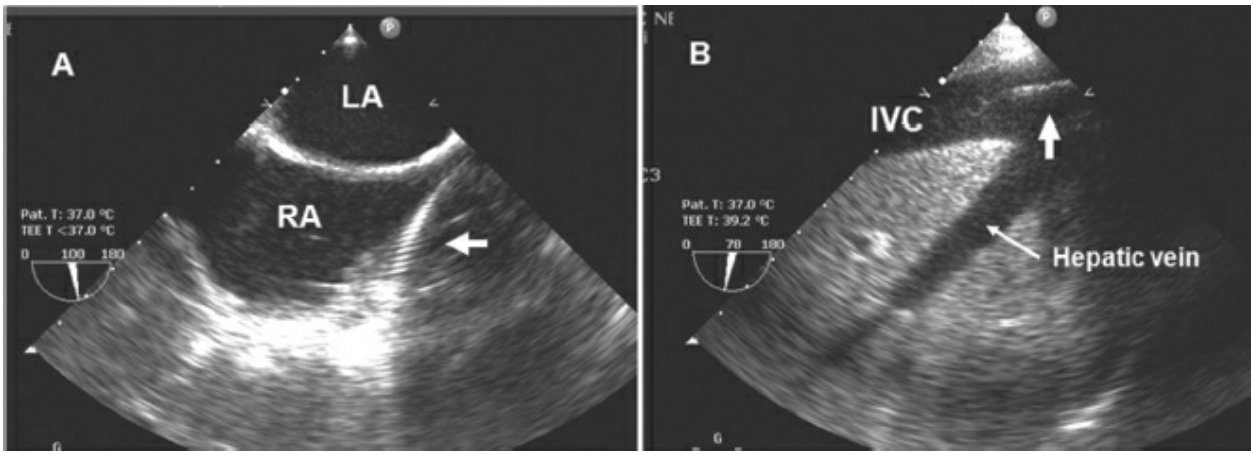

Figure 9.7: A: Bicaval view showing the venous cannula (arrow) entering the superior vena-cava, B: shows the cannula (arrow) entering the inferior vena-cava. (LA: Left atrium, RA: Right atrium, IVC: inferior vena-cava)

Additional vent cannulae are necessary to drain the blood returning to the left side of the heart via bronchial pulmonary vessels. They also allow decompression and de-airing of the heart before the CPB is terminated. The vent cannulae can be inserted via right superior pulmonary vein, left atrium, pulmonary artery or rarely via the apex of the LV.

Initiation of Bypass

After arterial and venous cannulation is accomplished, the perfusionist initiates bypass by gradually delivering the flow from the pump to the arterial system. While doing so, he also drains blood from the venous line (by gravity) in a stepwise manner by gradually opening the clamp on the venous line. The process of drawing blood via the venous line and delivering it after oxygenation via the arterial line in a stepwise manner is continued until the full flow is established. The usually recommended flow rate is 2.2 to 2.4 L/min./m^2 or 50 to 60 ml/Kg when normothermic or when cooling.[18] The recommended flow in infants and children is 2.5 L/min./m^2. The minimum flow rates of 30 ml/Kg/min. at 18°C and 30 to 35 ml/Kg/min. at 27°C to 28°C for maintenance of adequate cerebral blood flow is suggested.[19] During this period of transition to full bypass, the arterial pressure waveform gradually loses its pulsatile waveform (Fig. 9.8). In patients with aortic regurgitation (AR), the pulsatile waveform of the arterial pressure may be maintained till the aorta is cross clamped as the LV continues to receive blood from the aorta via the incompetent aortic valve. Although, gravity

drainage of the blood into the oxygenator has been the standard technique for CPB, the development of minimally invasive techniques for cardiac surgery has renewed interest in using vacuum assisted venous drainage. In this, vacuum is applied to the venous reservoir but, the degree of negative pressure applied should be carefully regulated. Potential problems include haemolysis and aspiration of air from around the venous cannula and holes in the walls of the RA or great veins. In an experimental study, it has been shown that vacuum assisted venous drainage does not increase trauma to blood cells in comparison with standard gravity drainage.[20]

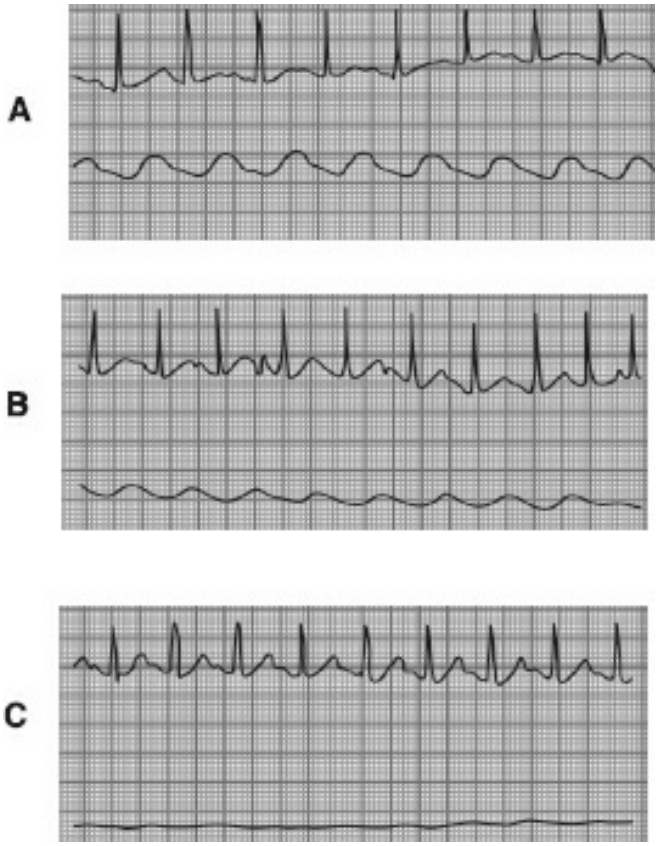

Figure 9.8: A, B and C: showing loss of pulsatile waveform of arterial pressure (lower waveform) on initiation of the cardiopulmonary bypass. A: Recording while the patient is without bypass, B: patient on partial bypass. C: patient on total bypass with full flows. The upper waveform is the simultaneous recording of the ECG.

At the commencement of CPB, the patient is generally cooled to 28°C so that the bypass flows can be reduced safely, if required. The hypothermia increases the viscosity of blood while the decrease in haematocrit lowers it. These two factors together with the nonpulsatile nature of flow and cardiovascular responses to CPB, cause changes in the arterial pressure. The

usual trend is an initial decrease followed by a gradual increase during the course of perfusion. In normothermic bypass, the pressure usually tends to decrease during CPB. These pressure changes are of importance as a low pressure raises the question of adequacy of perfusion, especially of the brain and kidneys. A high pressure may have technical implications necessitating the surgeon to interrupt his operation to investigate and readjust his arterial cannula. Occasionally, it may be due to high SVR. In either case, a high line pressure is noted by the perfusionist. The anaesthesiologist should, therefore, carefully monitor the various pressures at the initiation of CPB. He must notice a gradual reduction in the arterial pressure with loss of pulsatile waveform (except in AR) accompanied by a decrease in the CVP down to zero. The perfusionist, on the other hand, must ensure that he is able to get adequate venous return so as to meet the pump flows that are necessary for the patient. He should also ensure that in doing so, the line pressure (the pressure in the arterial limb of the CPB circuit) remains between 150 and 250 mm Hg.

The aortic cannula is always smaller than the aorta and therefore, there is a pressure drop across the aortic cannula. The pressure drop depends upon the size of the cannula and the pump flow. To maintain the usual MAP of 60 to 80 mm Hg for an adult, the line pressure ranges from 150 to 250 mm Hg. High line pressure can lead to rupture of the CPB circuit or bursting at the level of plastic connections. Therefore, a line pressure of more than 250 mm Hg is generally not acceptable. If bicaval cannulation has been performed, it is also important to snare the SVC and JVC cannulae temporarily at this stage and check that the venous return to the oxygenator is not disturbed. All these manoeuvres confirm that the aortic and venous cannulae are placed properly and that the CPB can proceed in an uninterrupted manner meeting all the perfusion requirements of the patient.

The anaesthesiologist should discontinue administration of nitrous oxide (if it was being administered earlier), before CPB begins, and discontinue ventilation when “full flow” has been established. The state of “full flow” is technically achieved when all the systemic venous blood is draining from the patient to the pump reservoir so that the CVP decreases to near zero and the systemic flow, arterial pressure and oxygenation are maintained at desired values. If systemic hypothermia is to be used, cooling is initiated, and the aorta is cross clamped. Cross clamping the aorta entails placing a large vascular clamp across it. The aorta is occluded between the arterial cannula

and the antegrade cardioplegia cannula (that is placed before clamping the aorta) so that the blood flow from the the arterial line to the coronary arteries is interrupted. This initiates the period of myocardial ischaemia. Cardioplegia is infused during this period (discussed later) to provide myocardial protection. The heart may continue to receive blood even after cross clamping the aorta from the bronchial venous inflow via the left atrium (LA) or from the right heart because of incomplete drainage of systemic venous blood to the oxygenator. This might lead to distention and warming of the LV. As explained earlier, this can be tackled by inserting the LV vent.

Systemic hypotension (MAP 20 to 40 mm Hg) is quite common upon initiation of CPB. Much of this is explained by reduction in the blood viscosity due to nonhaemic prime. However, as hypothermia is initiated, vasoconstriction ensues that restores the MAP towards 60 to 80 mm Hg. The role of increased levels of catecholamines during hypothermic CPB as a cause of this vasoconstriction is however, questionable as it has been shown that the catecholamine levels increase during normothermic CPB (without causing vasoconstriction) more than that during hypothermic CPB.[21] Treatment with alpha agonists is therefore, usually not necessary. However, hypotension at the initiation of CPB is a matter of concern as the patient is warm and the tissue oxygen requirements have not decreased. If normothermic CPB is planned, the MAP is likely to remain low and a large number of patients will require treatment with alpha agonists (norepinephrine or phenylephrine).

The other important cause of persistent hypotension is aortic dissection. This can be suspected, if the line pressure is high, the patient's arterial pressure is low and the oxygenator reservoir level keeps decreasing, due to inadequate venous return (due to reduced systemic perfusion).

Minimally Invasive Extracorporeal Circuits

In recent years, there has been a growing interest in developing minimally invasive extracorporeal circuits. The main features of these circuits are smaller foreign surface area, priming volume and blood-air contact. This is with the objective of decreasing the haemodilution and inflammatory response. These circuits comprise of a closed veno-arterial loop incorporating a single centrifugal pump, and a membrane oxygenator. There is no venous reservoir, cardiotomy suction, heat exchanger, and arterial filter. One of the

major limitations of these circuits is its air handling characteristics and risk of systemic air embolisation. Other limitations include the lack of reservoir to handle excess venous return and immediate volume infusion, if required. Technological advances to eliminate these drawbacks are currently going on. In general, it is believed that the miniaturised systems decrease the post-bypass inflammatory response thereby decreasing the organ dysfunction and transfusion requirements.[22] In high-risk group of patients, better cerebral protection in provided.[23] However, few authors were not able to demonstrate any clinical benefit with the use of these circuits.[24,25]

New biocompatible circuitry, either heparin bonded or polymer coated have been introduced. These have the potential to reduce the perioperative inflammatory response. Such circuits are likely to be beneficial in high-risk patients, provided they are included as a part of an overall strategy to control triggers of the inflammatory response during and after cardiac surgery.[26]

Anaesthetic Drugs during CPB

The anaesthetic goals of hypnosis, analgesia, amnesia, muscle relaxation and attenuation of stress response can be met with ease during CPB. There are several ways in which the pharmacokinetics of drugs can be affected by CPB. These include, haemodilution, hypothermia, alterations in organ perfusion and acid-base status, sequestration of drug into lungs and CPB circuit, and effect of systemic inflammatory response syndrome. The plasma levels of anaesthetic drugs, before, during and after CPB have been investigated by many authors.[27-29] The plasma levels decrease proportionate to the hemodilution. Consequently, lightening of the anaesthetic plane is anticipated. However, haemodilution also lowers the protein concentration and the plasma ratio of free drug to protein bound drug is increased. In addition, the hepatic perfusion and metabolism is reduced and the redistribution of newly administered drug is decreased due to reduced perfusion in some areas. All these mechanisms also tend to maintain the plasma drug concentration present before CPB. These effects have been demonstrated by Dawson et al[30] showing relatively constant unbound plasma concentrations of propofol and midazolam at the onset of CPB. This implies that the drug levels present at CPB onset remain constant without additional drug administration.

It has been shown that there is a marked decline in the plasma

concentration of fentanyl on initiation of bypass but the levels increase at the end of CPB coinciding with rewarming.[31] Remifentanil concentrations decrease with the institution of CPB, but the decrease in elimination clearance with hypothermia results in increased total remifentanil concentrations during CPB.[32] Therefore, more constant remifentanil levels may be obtained by reducing remifentanil infusion rate during hypothermic CPB. The propofol concentration has been reported to decrease significantly 5 min. after the start of CPB and then recover to pre-CPB value in normothermic bypass, but in mild hypothermic bypass no significant changes were observed.[33] Hypothermia induced vasoconstriction can reduce reuptake of drug from peripheral tissues.

For further details on the subject, the reader is referred to the chapter by Hall and Kent.[34]

Neuromuscular Blockers

These drugs have greater water solubility and smaller distribution volumes. Therefore, haemodilution at the onset of CPB can acutely reduce the neuromuscular blocking effect.[35] Clinical studies monitoring twitch height suggest the need for muscle relaxant supplementation at the onset of CPB. The supplemental requirement of muscle relaxants is reduced during hypothermic CPB. Maintaining complete neuromuscular paralysis during CPB is important in order to minimise oxygen consumption and prevent untimely diaphragmatic movement. It is a usual practice in most units to administer boluses of opioids or benzodiazepines and muscle relaxants at the initiation of CPB (some prefer to add it to the pump prime well before CPB). An anaesthetised and immobilised patient is assured at the commencement of CPB. Individual monitoring of neuromuscular blockade may also be considered.

Amnesia

Little scientific data is available on the subject of ensuring amnesia during CPB. The anaesthesiologist, therefore, relies on his own experience and personal preference of managing this problem. Most agree that memory recall is unlikely during hypothermia below 30°C and that the period of greatest risk for intraoperative recall is during rewarming and after CPB. Supplemental doses of thiopental, propofol and benzodiazepines can be

administered during rewarming and continued thereafter till the patient is transferred to the ICU. Alternatively, volatile agents can also be administered, once the pulmonary circulation is established.

Bispectral index (BIS) monitoring to monitor the depth of anaesthesia can be utilised to titrate anaesthetic doses to ensure adequate depth of anaesthesia during surgery so that the memory recall is prevented. (For details refer chapter 14.)

Laboratory Measurements

Regular laboratory measurements are made during CPB by the anaesthesiologist. These include, haematocrit, arterial blood gases, acid-base balance, plasma sodium and potassium, blood sugar and ACT. Samples are drawn at least every 30 min. Base deficit values of –5 or less are corrected by sodium bicarbonate, and ACT values below 400 sec should be treated with heparin bolus. The patient's temperature and urine output are also monitored. The facilities for on-line arterial and venous blood gas and electrolyte analysis are available and practised in some units. However, although, they are of interest, there is little scientific data to prove that this approach is superior to periodic blood gas sampling. Further, these devices may provide misleading information.[36]

Blood Gas Measurements

Two divergent blood gas management strategies have been described: 1. alpha-stat (temperature uncorrected), and 2. pH-stat (temperature corrected).[37-41] In alpha-stat management, the blood gases and acid-base balance is measured at 37°C irrespective of the patient temperature. For instance, blood drawn from the patient undergoing CPB at 28°C is anaerobically warmed to 37°C in the blood gas machine to report the values at 37°C. The principal advantage of alpha-stat strategy is the theoretical preservation of intracellular electrochemical neutrality across all temperatures. The second advantage is the preservation of cerebral autoregulation.[42] As the blood is cooled, CO_2 becomes more soluble, $PaCO_2$ decreases and this results in the blood becoming less acid. In pH-stat management, CO_2 is added to the oxygenator gas supply or the "sweep speed" of air-oxygen mixture is decreased so that the pH, if it was measured at the patient's hypothermic temperature would be maintained at 7.35 to 745.

Carbon dioxide is a potent cerebral vasodilator. Therefore, the increase in $PaCO_2$ during PH stat management makes the ceretral perfusion more pressure dependent (autoregulation is lost) leading to excessive cerebral blood flow.[43] This may increase the embolic material to the brain (air or particulate).

The blood gas management strategy has long been controversial and the debate regarding which acid-base strategy provides the best outcomes in patients is unsettled. In adults, prospective randomized trials have shown the superiority of alpha-stat management during moderate hypothermia in terms of better neurological outcome.[44-46] Therefore, alpha-stat management strategy is recommended in adults undergoing moderate hypothermic CPB.[47] In children, during DHCA, effective and uniform brain cooling becomes an important consideration in reducing cerebral injury. This may be provided by increased cerebral blood flow during pH-stat management. One randomized trial showed no benefit of one technique over the other[48], while some other human and animal studies suggested that pH-stat management may be more beneficial than alpha-stat management for infants.[49,50] The present trend in paediatric CPB is to use pH-stat alone or in combination with alpha-stat (pH-stat during cooling and alpha-stat during rewarming) when deep hypothermia is used.[51]

In addition to blood gas and acid-base measurements, serum potassium, ACT and blood sugar are periodically measured. Despite administration of potassium in the cardioplegia solution, potassium supplementations are frequently required. ACT measurements are necessary to assure adequate anticoagulation and the need for any additional doses of heparin.

Myocardial Protection

In order to provide motionless field for the surgeon, the heart is arrested in diastole by the administration of potassium enriched (20 to 30 mEq/L) cardioplegia solution to the heart. Potassium-induced arrest substantially reduces the myocardial oxygen consumption, which can be further augmented by administering cold cardioplegia solution. In this manner, the myocardium can withstand complete interruption of blood flow for periods up to 20 to 30 min. There are institutional variations regarding the constitution of cardioplegia solution, but potassium is used as the arrest agent by all. Likewise, the choice of substrate for carrying the cardioplegia has

been either crystalloid or blood with most centres preferring to use blood cardioplegia. After an initial arrest dose of approximately 1 to 1.5 litres of cardioplegia, half the dose is repeated every 20 to 30 min. to deliver nutrients to the cells and maintain the potassium concentration. These subsequent cardioplegia doses may contain lower potassium concentration. It is important to ensure that the heart is vented properly by vent lines during this period, as blood returning to heart can warm and distend the heart. Such a state increases the myocardial oxygen consumption and decreases the efficacy of the cardioplegia. Myocardial protection during open-heart surgery is still evolving and newer techniques are being introduced. Retrograde cardioplegia (delivered through coronary sinus) and warm cardioplegia in normothermic CPB are some other methods that have come into practice. For details on the subject the reader is referred to chapter 13.

Hypothermia

Systemic hypothermia is commonly employed during CPB. This is done mainly for two reasons: 1. to reduce the systemic oxygen consumption; 2. to slow the rate of warming of the heart when cold cardioplegia (4° to 10°C) is used for myocardial protection. In vivo, the oxygen consumption decreases exponentially at 9 percent per 1°C.[52] This reduction in systemic oxygen consumption permits reduction of systemic oxygen delivery, thereby allowing haemodilution, lower pump flow and MAP, and a greater margin of safety in the event of some haemodynamic compromise. The main concern is related to neuroprotection. Animal studies have shown that even mild hypothermia (1°C to 2°C) minimizes the severity of cerebral ischaemia.[53] Such studies have further indicated that the mechanisms involved in offering neuroprotection are, decreasing the cerebral metabolic rate of oxygen ($CMRO_2$), delaying the release of excitatory amino acids and neurotransmitters that promote neuronal death[54], stabilization of blood brain barrier[55], and alteration of inflammatory response.[56] However, a meta-analysis has concluded that there is no definite evidence to support hypothermia as a neuroprotective mechanism during routine CPB.[57]

In contrast, hyperthermia is harmful to the brain and reduces the cerebral tolerance to ischaemia. Cerebral hyperthermia during the rewarming period may aggravate the cerebral injury that has occurred.[58] Therefore, active rewarming of patients that was followed to prevent ‘after drop’ of

temperature following CPB is not recommended. In fact, some clinicians advocate that highrisk patients should be weaned from CPB at a temperature slightly lower than normal (34°C).[59,60] Postoperative hyperthermia occurring within 48 hours of surgery can also be harmful, and it is known to increase cognitive dysfunction 6 weeks after cardiac surgery.[61] Therefore postoperative hyperthermia should be actively treated with antipyretics and surface cooling, if necessary. These have been the main reasons for universal application of hypothermia during CPB. However, with the introduction of warm cardioplegia, normothermic CPB is also being employed.

Perfusion Pressure

A MAP of 50 mm Hg during CPB is accepted as normal in many cardiac centres. However, it is by no means certain that this is the optimum pressure. The controversy has once again attracted attention by the publication of data, which suggest that higher MAP (80 to 100 mm Hg) may reduce central nervous system (CNS) complications during CPB.[62] The issue regarding the optimum MAP is important as it is related to the neurological dysfunction following CPB, the incidence of which is still high (1.6 percent after isolated CABG[63] and 53 percent for cognitive decline.[64]) The important causes of postoperative neurological dysfunction are believed to be embolic phenomena and hypoperfusion during CPB. The ideal perfusion pressure has to be carefully balanced as the reduced perfusion pressure and blood flow may decrease the cerebral embolic load, but increase the risk of hypoperfusion. On the contrary, the elevated perfusion pressure and flow may decrease the likelihood of hypoperfusion but increase the cerebral embolic load.

Preservation of cerebral autoregulation at a MAP of 50 mm Hg has been the main argument in favour of this pressure. In addition, this pressure is easily achieved on CPB due to haemodilution and nonpulsatile flows. Concomitant hypothermia provides the cerebral protection and the anaesthetic agents used are known to decrease cerebral oxygen requirements. The low pressure also minimises derangements to blood elements and provides good operating conditions. The question that is being raised is “Is the MAP of 50 mm Hg safe in all patients?” This is relevant in the context of warm heart surgery (protection provided by hypothermia is not there) as well as high-risk group (older and sicker population) being subjected to surgery

nowadays. The older patients are known to be susceptible to neurological injury due to higher incidence of diabetes mellitus, hypertension and atherosclerotic diseases. It thus appears that there is a subset of patients who might be benefited by a MAP of more than 50 mm Hg during CPB. The elevated perfusion pressure during CPB (more than 70 mm Hg) may help to decrease the incidence of hypoperfusion in some patient group. At the moment it appears that patients with severe atherosclerotic disease (aortic arch or cerebrovascular), chronic hypertension and history of cerebrovascular disease should be included in this subset of patients.[65] A recent paper has shown that cerebral oximetry (near infrared spectroscopy) alone with transcranial Doppler can be utilised to assess the lower limit of cerebral autoregulation during CPB.[66] In a group of 225 patients, the authors reported the MAP at the lower limit of autoregulation to be 66 mmHg. The authors concluded that this may provide a more rational means for individualising MAP during CPB.[66] In summary, it is obvious that there is no one pressure that is safe for all the patients. The traditional acceptance of MAP of 50 mm Hg may be applicable to most patients, but there is a room for elevating the pressure further (>70 mm Hg) in a select group of patients.

It may be noted that the femoral artery pressure is more reliable than radial artery pressure during the initial part of CPB.[67] Also, it is not correct to disregard MAP and focus on maintaining a target flow rate. Although MAP and pump flow are physiologically coupled, the primacy of MAP for cerebral perfusion during CPB has been demonstrated.[68]

Cerebral Protection

CNS is at a substantial risk during CPB. Indeed, the incidence of neurological complications following CPB is considerable with the incidence of major strokes being approximately 1.6 percent while that of neuropsychological abnormalities being in excess of 50 percent. Age alone is an independent risk factor for stroke, with patients younger than 60 years having less than 1 percent incidence of stroke, which increases to more than 8 percent at 80 years.[69] As already mentioned, the important causes of neurological dysfunction are embolism and hypoperfusion. Cerebral protection, therefore, is an important consideration during the conduct of CPB.

Multilead EEG monitoring and somatosensory evoked potentials are promising tools, but their use in cardiac surgery is limited as these methods

lack sensitivity and specificity. The clinical significance of some other monitoring tools such as jugular bulb oxygen saturation, regional cerebral blood flow and cerebral oximetry is not clearly defined. Jugular bulb oxygen saturation provides trends in cerebral oxygenation, but it is limited by the fact that it is a measure of global oxygenation so that focal events may remain undetected. It has remained primarily a research tool in cardiac surgery. Near infrared spectroscopy has the potential to provide regional cerebral oxygenation in a noninvasive manner. However, a meta-analysis has concluded that validity of the near infrared spectroscopy has not been clearly established.[70] Although it has many potential advantages over other neuromonitoring techniques, further technological advances are necessary before it can be introduced more widely into clinical practice.[71] Transcranial Doppler provides continuous measurement of the cerebral blood flow by interogating the middle cerebral artery. However, in cardiac surgery, it has found greater use in emboli detection than assessment of the cerebral perfusion.

As far as cerebral protection is concerned, most of the manipulations either physiological or pharmacological remain controversial. As already discussed, the optimum perfusion pressures and flows remain unclear. Perfusion flows of 2.4 L/min./m^2 are adequate at normothermia and can be reduced proportionately during hypothermia because of decreased oxygen consumption.[72] No doubt, hypothermia protects the brain in the event of a planned circulatory arrest or an accidental haemodynamic compromise that leads to compromised cerebral perfusion. However, its role in CNS protection in the absence of any such mishap is controversial.[73] Deep hypothermic circulatory arrest is used in some surgical procedures. It involves reducing the patient's core temperature to 15 to 20°C before interrupting blood flow to the body. All the blood from the body is drained into the venous reservoir. In adults, this procedure is used during surgical repair of the aortic arch. The cerebral cooling can be maintained by putting ice bags on the patient's head. In addition, antegrade or retrograde cerebral perfusion can be used. Nowadays antegrade cerebral perfusion is the major method of brain perfusion during deep hypothermic circulatory arrest. It can help to prolong the duration of safe ischaemic arrest time from 20-25 min. to up to 80 min.[74] Cold antegrade cardioplegia at 10-13°C should be initially applied through the right subclavian or axillary artery and continued bihemis-

pherically through the left common carotid artery at first and later the anastomosed graft, with a mean perfusion pressure of 40-70 mm Hg.[74] Perioperative temperature management is considered important as regards neurocognitive outcome, as it has been shown that slow rewarming is associated with greater improvement in cognitive performance at 6 weeks than conventional rewarming.[75]

Hyperglycaemia is known to be detrimental in the presence of focal or global cerebral ischaemia. It is recommended that hyperglycaemia should be avoided whenever there is significant potential for neurological injury.[76] Serum glucose concentration should be kept below 150 mg/dL during CPB using intravenous insulin.

Barbiturates are known to have cerebral protective effect and it was shown that thiopental is effective in reducing strokes in high as well as low doses.[77,78] Subsequent studies, however, failed to demonstrate any benefit of thiopental.[79,80] Although the role of barbiturates as cerebral protective agents after cardiac surgery is still unclear, some studies have shown thiopental having protective effects against cerebral ischaemia under deep hypothermic circulatory arrest.[81,82] Propofol decreases cerebral metabolic rate and it was speculated that it may have a role in reducing cerebral embolism during CPB through its reduction in CBF.[83] However, large outcome studies on the use of propofol are lacking. Free radical scavengers and calcium channel blockers are also being investigated with regard to their cerebral protective effect. Nimodipine has been investigated, but the results of one trial were inconclusive[84] and the other was interrupted due to increased mortality in the nimodipine group.[85]

Renal Function

Adequate renal function during CPB depends on a previously adequate renal function as well as adequate renal perfusion during CPB. The urine output may decrease when the MAP is low. Adequate urine output during CPB (minimal acceptable urine flow is 1 mL/Kg/hour) should be ensured. This may necessitate administration of diuretics, especially in patients undergoing valve surgery who are on high doses of diuretics in the preoperative period. Occasionally, haemofiltration during CPB can also be used to remove excessive water arid electrolytes when poor renal function is recognised or anticipated.

Renal dysfunction following CPB causes significant morbidity and mortality. However, there is no widely accepted renal protection strategy for cardiac surgical patients. This may be partly due to the absence of a standardised definition of renal dysfunction and a limited number of good quality randomised controlled clinical trials.[86]

Lungs

There is no circulation through the pulmonary artery (PA) during total CPB. Only the bronchial perfusion continues. The lungs can continue to be inflated mechanically, or maintained in an inflated or deflated state. Sustained inflation of the lungs during CPB was thought to preserve lung function best. Both helium and air have been used for this purpose. However, it is a common practice now, to allow the lungs to be deflated when the PA blood flow ceases during CPB (establishment of full flows). It is also important to ensure that they are fully expanded and that normal ventilation is resumed before the termination of CPB. Like heparinisation, this is also an important step that must not be forgotten. It is usual to resume ventilation once the last proximal anastomosis is commenced by the surgeon in patients undergoing CABG while in other surgeries, it should be resumed once the aorta is undamped and a normal or acceptable rhythm has been established.

Termination of Cardiopulmonary Bypass

When the definitive operation approaches near completion, preparations for the termination of CPB should begin. The perfusionist has to start rewarming the patient, (if hypothermic CPB was used) and ensure that the patient is rewarmed adequately by the time proximal anastomosis is completed in CABGs, and aorta is undamped in other procedures. The anaesthesiologist should ensure that normal biochemical parameters are being maintained and if they are not, take appropriate measures to restore normalcy. Of particular importance is the restoration of normal acid-base status, electrolyte levels and haematocrit levels. Most cardiac units prefer a haematocrit of 20 to 25 percent prior to discontinuation of CPB to provide sufficient oxygen carrying capacity. It may be desirable to achieve a haematocrit of 25 percent, especially in patients undergoing CABG after the CPB is terminated. Haematocrit of 25 percent has been shown to be well tolerated by patients undergoing CABG with preoperative ejection fraction of >50 percent.[87]

When the ventricular function is deranged, haematocrit of more than 25 percent may be desirable to support the systemic circulation.

Acidosis impairs myocardial contractility.[88] The ischaemic myocardium is particularly vulnerable to the detrimental effects of acidosis.[89] Therefore, arterial pH should be corrected to near normal before discontinuation of CPB.

Measurement of serum potassium levels is routinely performed in all units. Some units also measure ionised calcium levels before terminating the CPB. Potassium levels can be elevated due to the administration of potassium containing cardioplegia solution. This is more likely in patients undergoing normothermic CPB where a continuous cardioplegia is administered. Potassium may also rise in the presence of beta-blockers, which many patients undergoing cardiac surgery maybe receiving. Values in excess of 6 mEq/L may be found. This can be treated by administration of calcium, insulin and glucose, and diuretics. Haemofiltration can also be used to lower the potassium levels.

Sometimes, the potassium levels can be low due to haemodilution and excessive diuresis. This can be rapidly treated on CPB as the circulation is being supported. Increments of 5 to 10 mEq of potassium chloride bolus can be added to the oxygenator slowly (1 to 2 min.).

Ionised calcium is important for mamtaining myocardial contractility and peripheral vascular resistance.[90] However, ionised calcium levels are shown to return to normal levels prior to separation of CPB and hence, administration of calcium routinely is not recommended.[91] Some authors, however, believe that calcium should be administered, if the myocardial contractility is poor and ionised calcium levels are low.[92] Administration of calcium chloride as a bolus after separation from CPB can significantly reduce the flow through the internal mammary artery (IMA, if used as a graft) increasing the risk of myocardial ischaemia in susceptible patients.[93] Therefore, one should be careful during the adrrunistration of calcium in such patients. Rapid administration of large boluses of calcium that may produce very high concentrations should be avoided.

Rewarming

Rewarming during CPB is achieved by raising the temperature of the heat exchanger in the oxygenator. It is dangerous to overheat the perfusate. Commercial controllers for heat exchangers have an upper temperature limit

of 42°C. A temperature gradient of more than 10°C between the oxygenator and the brain is avoided during rewarming to prevent the increased oxygen in solution in the cold oxygenator coming out of solution and forming bubbles in the patient.[94] Excessive perfusate heating can also lead to the possibility of denaturation of plasma proteins and brain damage by hyperthermia.[58] As the cold patients are vasoconstricted, vasodilators such as sodium nitroprusside may be used to facilitate the process of rewarming.[95] Many centres now employ mild hypothermia (31 °C to 34°C) rather than moderate hypothermia (26°C to 28°C) so that the amount of heat transfer to achieve normothermia is reduced.

The other methods that can be used to aid rewarming are; increased ambient temperature, using heated humidified gases for ventilation and the use of heating blankets. These methods are especially useful after a deep hypothermic circulatory arrest.

The potential for awareness is a matter of concern during rewarming. This may result due to restoration of brain temperature with decreased anaesthetic concentrations that may result in inadequate depth of anaesthesia.[96] Many anaesthesiologists, therefore, administer supplemental doses of benzodiazepines, thiopental or propofol during rewarming.

Removal of intracardiac air and unclamping of aorta

In all operations, where the heart has been opened, (e.g. valve surgery, repair of congenital heart defects) intracardiac air is present. It is necessary to remove as much air as possible before the aorta is undamped so that it does not embolise to the systemic circulation once the ejection is initiated. Various methods are followed to accomplish this task. One of the common methods employs ventilation of the lungs by the anaesthesiologist to drive air from the pulmonary veins towards the LA. The perfusionist is simultaneously asked to partially occlude the venous return, thus causing the LA and LV to fill with blood. While the heart is being filled in this manner, the surgeon squeezes and ballots the LV and LA to dislodge the air bubbles that are vented out via the cardioplegia cannula or a needle vent in the ascending aorta. In addition, the patient is placed in the Trendelenburg position so that the air bubbles will tend to float away from the dependent carotid arteries. Alternatively, some surgeons vent the air out via a cannula placed in the LV apex.

Once, de-airing has been completed, aortic cross clamp is released, and the ventilation stopped by the anaesthesiologist and the perfusionist drains the heart. In patients undergoing repeat surgery, potential for air entrapment is more, as the mobilisation of LV due to dense adhesions may not be possible and therefore, ballotment of the LV is not adequate. In such patients, more meticulous de-airing will be necessary and TOE may be used to ensure that most of the air has been removed. Air ejected from the LV can also embolise into the coronary arteries (usually right coronary artery) resulting in sudden myocardial ischaemia. ST segment changes that coincide with the initiation of ejection suggest coronary air embolism.

After the aortic cross clamp release, the coronary circulation via the native coronary arteries is restored and cardiac rhythm is established in some patients. In the majority of patients, however, ventricular fibrillation (VF) ensues. VF at this stage is not desirable due to increased myocardial oxygen consumption (as compared to beating heart) and LV distention that may result, should the LV receive large amount of blood (aortic insufficiency or bronchial return). LV distention compromises subendocardial perfusion due to increased wall tension.

Defibrillation is accomplished with internal paddles and energies of 10 to 20 joules are routinely used. Biphasic waveform shocks are more effective than monophasic shocks and 5 to 10 joules can be used. Defibrillation may not be effective if the heart is not fully warmed (at least 34°C) and abnormal acid-base and electrolyte status is present. Repeated attempts at defibrillation with increasing energy levels can lead to myocardial injury. Correction of temperature, blood gas, acid-base and electrolyte levels should be undertaken on an emergent basis, if necessary.

As already mentioned, LV distention can occur if the ventricular function does not return following the release of aortic cross clamp. Suction applied on the vent that is placed in the LA or PA at this stage can be useful, as the LV distention during this critical period of rewarming and reperfusion is prevented.[97] In patients with severe hypertrophy of the LV, establishment of cardiac rhythm after the release of aortic cross clamp may be difficult. This leads to progressive LV distention that further enhances the possibility of continuous VF. This should be managed with good suction through the LA vent and defibrillation. In addition, low flows should be maintained to decrease the bronchial return. However, in the author’s experience, it has been found that occasionally, even this therapy does not help and in such

situations, insertion of the vent through the LV apex is found to be useful to decompress the LV as well as in restoration of the cardiac rhythm.[98] Amiodarone injection in the root of the aorta has been reported as yet another method to restore the cardiac rhythm in such a scenario.[99] Sometimes, pacemaker may be required to maintain regular cardiac electrical activity. In addition, pharmacological therapy with amiodarone, beta blockers (esmolol, atenolol), verapamil or adenosine may be used for the treatment of supraventricular tachycardia.

The other problem that is of common concern following the release of aortic cross clamp, is the restoration of normal arterial pressure. It is known that a decrease in MAP often accompanies release of the aortic cross clamp. The reasons ascribed to this phenomenon are reactive myocardial hyperaemia and vasodilator effect of the myocardial stretch receptors[100] and the addition of a fully dilated myocardial vascular bed to the circulation.[101] It has also been shown that in large proportion of patients, the MAP can be less than 50 mm Hg.[102] This finding may be important in the context of cerebral protection as the patients are usually normothermic at this point of time. In patients undergoing CABG, this may have additional importance, in the sense that the coronary circulation is still taking place via the native coronary arteries that are diseased (proximal anastomosis of vein grafts is yet to be completed), unless IMA has been grafted. Myocardial perfusion may be significantly compromised in the presence of a low MAP at this stage. It is therefore, advisable to increase the MAP in the range of 70 to 80 mm Hg using alpha agonists.

Once, the definitive surgical procedure is over, the aorta is undamped and satisfactory cardiac rhythm is restored, normothermia has been achieved and the biochemical parameters are acceptable, the time has come to separate the patient from CPB. The anaesthesiologist should re-zero the pressure transducers at this stage and make an assessment of the myocardial contractility by visual inspection of the heart. Nowadays, TOE is used more commonly to assess the LV contractility objectively, as the LV is difficult to be visualised by the naked eyes (lies posteriorly). Based on the assessment of the myocardial function, the infusion of inotropes, vasodilators and sometimes vasoconstrictors are begun. Once again, it should be ensured that ventilation of the lungs has been initiated. The venous outflow line is gradually occluded by the perfusionist allowing the heart to be filled with

blood. The CVP and/or pulmonary capillary wedge pressure (PCWP) is constantly monitored to know the exact loading conditions of the heart. Ejection is restored by this (can be seen on the arterial waveform) and the pump flows (flows via aortic inflow line) are gradually decreased. The process is continued, if adequate haemodynamic performance as judged by the CVP and BP monitoring and TOE (contractility and volume status) continues to take place, and the bypass is terminated. The anaesthesiologist should be extremely vigilant at this stage and monitor the ECG and various pressures continuously. An increased level of communication and coordination between the anaesthesiologist, perfusionist, and surgeon is required for successful termination of the CPB. Immediately after terminating the CPB, the patient may require volume replacement with the blood remaining in the oxygenator reservoir. Nowadays separation from CPB is a relatively uneventful process in most patients. Preoperative low ejection fraction and prolonged duration of CPB can predict difficulty in weaning the patient from CPB and the need for inotropic support.

If the heart fails to take over the circulation adequately, CPB can be reinstituted. Then steps can be taken to identify and treat the cause of the failure before attempting termination of the bypass again.

When the patient is haemodynamically stable, protamine is administered to reverse the anticoagulation effect of heparin. This step is usually initiated after decannulating the venous lines and stopping the pump suckers. This is in order to avoid the clotting of blood remaining in the circuit that makes it unusable for urgent reinstitution of CPB, if necessary. The dose of protamine is 1 to 1.3 mg for every 100 units of heparin that the patient has received. It should be administered slowly over a period of 5 to 10 min. to reduce the risk of hypotension (incremental boluses or infusion). The aortic cannula is removed after half or full dose of protamine has been administered.

Normothermic Cardiopulmonary Bypass

Hypothermic systemic perfusion during CPB with myocardial hypothermic preservation has been a standard technique in cardiac surgery. The systemic hypothermia was introduced to protect organs from the low-flow state characterised by the early CPB system. It is also being used as an adjunct to the myocardial hypothermic preservation. A technique of “warm heart surgery” has been reported by Lichtenstein et al in 1989.[103,104] The rationale

underlying this approach is based on the following: The hypothermic ischaemic cardiac arrest is an anaerobic arrest and that hypothermia decreases the oxygen consumption so that post-arrest cardiac impairment is minimised. Hypothermia, however, is not without disadvantages and it has adverse effects on enzyme function, membrane stability, calcium sequestration, glucose utilisation, adenosine triphosphate generation and utilisation, and tissue oxygen uptake and osmotic homeostasis. In addition, reperfusion after ischaemic arrest can lead to a progression of the ischaemic injury, termed "reperfusion injury". Therefore, the proponents of the normothermic bypass hypothesised that the ideal state of the heart during an operative procedure would be electromechanically arrested and perfused with blood, that is, aerobic arrest.[104] With this technique of myocardial protection, the maintenance of systemic hypothermia appeared unnecessary. Thus, in normothermic bypass, the heart is maintained at 37°C with continuous warm blood cardioplegia, which virtually eliminates the period of ischaemia. Simultaneously, the systemic temperature is also maintained at 37°C or more commonly, allowed to drift towards 34° to 35°C. The superior myocardial preservation provided by the technique was subsequently confirmed by other authors[105] and hence, the technique is gaining popularity.

There are, however, several issues that must be considered while practising normothermic bypass. Normothermic myocardial preservation has not been as thoroughly studied in the laboratory or fully investigated clinically.[106] Although continuous warm blood cardioplegia appears physiologically sound and effective, it is technically cumbersome. As the warm cardioplegia is delivered continuously, its continued presence in the surgical field hinders visualisation and construction of distal coronary anastomosis and/or replacement of the valve. Some proponents of warm heart surgery term this as a "minor surgical inconvenience" and suggest temporary occlusion of the coronary artery that is being anastomosed, or even temporary discontinuation of the administration of cardioplegia to prevent blood from obscuring the view. The temporary occlusion of coronary artery or discontinuation of cardioplegia is a matter of concern as the myocardium is subjected to normothermic ischaemia during this period.

Continuous infusion of large volumes of cardioplegia can result in systemic hyperkalaemia, hyperglycaemia, excessive haemodilution and generalised oedema. Strict protocols for the management of potassium are, therefore, necessary during normothermic bypass.

As far as the hepatosplanchnic oxygenation is concerned, based on the measurement of hepatic vein oxygen saturation, it has been shown that the hepatosplanchnic oxygenation is better preserved during mild hypothermic CPB (32°C) than during normothermic CPB (> 35°C).[107] A technique of normothermic CPB (35° to 37°C) along with cold cardioplegia (cold heart, warm body) has also been described and shown to simplify the surgical procedure and facilitate postoperative management.[108]

The influence of normothermic bypass on some other systemic effects such as extravascular lung water index (EVLWI), that signifies change in pulmonary permeability and serum cytokines has also been studied. It has been shown that there were no differences in the EVLWI and plasma levels of interleukin (IL)-6, tumour necrosis factor (TNF)-α and IL-10 during and after CPB in patients undergoing normothermic and hypothermic CPB.[109] This indicates that normothermic CPB is not associated with additional inflammatory and related systemic adverse effects.

Many cardiac centres now use normothermic CPB because bypass and operating times are less, and myocardial protection and coagulation function are better preserved. The perceived advantages of this technique are early extubation and fewer perioperative complications.[110] In addition, it avoids any harmful effects of rewarming. The technique has also been successfully applied for neonatal arterial switch operation.[111] However, the patients may be more vulnerable to be aware during normothermic surgery. Schmidlin and colleagues[112] have shown that with similar propofol doses, BIS scores were greater during normothermic CPB than hypothermic CPB, suggesting that more propofol is required for normothermic patients. Yoshitani and colleagues demonstrated that propofol infusion rate of 5 to 6 mg/Kg/hour combined with fentanyl infusion of 5 μg/Kg/hour are associated with measurable EEG burst suppression during normothermic cardiac surgery.[113]

There are of course, other methods of ensuring absence of awareness during normothermic CPB. The administration of volatile anaesthetic agent via a vaporiser in series with the fresh gas flow to the bypass oxygenator is a suitable option. The “anaesthetic preconditioning” that is provided by the inhalational agent is an additional benefit that can be obtained by such a technique.

The use of additional anaesthetic agents during normothermic CPB also fulfills the other requirement, i.e. cerebral protection. The blood cardioplegia

provides myocardial protection for normothermic CPB, but there is no equivalent additional cerebral protection during normothermia. It is reasonable to believe that any reduction in cerebral metabolic rate offered by the anaesthetic agents is likely to be beneficial. There is paucity of information regarding the appropriate doses of anaesthetic agent for maintenance of anaesthesia is such circumstances.

Cerebral Protection during Normothermic bypass

CNS dysfunction remains a major cause of morbidity and mortality after cardiac surgical procedures. In normothermic CPB, the postulated neuroprotective benefits of hypothermia are not applicable. Therefore, evaluation of the technique of normothermic bypass in terms of neurological outcome is essential. Conflicting reports are available in the literature. A three-fold greater stroke rate (warm 3.1%, cold 1%) and a significantly higher incidence of postoperative neurological dysfunction was reported in the patients subjected to normothermic techniques.[114] The authors, in fact, abandoned the study due to the significantly higher cerebral morbidity observed in the normothermic technique and cautioned that normothermic bypass technique may compromise cerebral protection and increase the incidence of neurological injury. In contrast, some other authors reported no significant difference in the neurological outcome between patients subjected to normothermic versus hypothermic CPB.[105,115] A recent report on 300 patients has shown that there are no differences in the neurological and neurocognitive outcomes between normothermic and hypothermic groups and that hypothermic CPB does not provide additional CNS protection in adult cardiac surgical patients.[116] The reader should refer to chapter 14 for a detailed discussion on the subject.

Another important difference with normothermic bypass is the lowered SVR leading to lowered MAP during and in the early hours following normothermic CPB. Although, the optimum level of MAP during CPB is not determined, MAP of > 50 mm Hg is widely accepted. In the absence of hypothermic protection of brain, maintenance of adequate MAP becomes important. Increased use of vasopressors in order to maintain optimum MAP is anticipated and has been reported.[108,117] The use of vasopressors (phenylephrine, norepinephrine) to maintain adequate MAP may lead to vasoconstriction of the arterial graft (internal mammary and radial artery) leading to compromised myocardial blood flow. Indeed, phenylephrine has

been shown to reduce the blood flow through IMA graft.[118,119] However, one study has reported no increased incidence of postbypass myocardial ischaemia, low CO syndrome or myocardial infarction in patients receiving vasopressors during normothermic bypass.[120]

Some other issues relating to the normothermic bypass that need to be addressed are: 1. When to administer heparin repeat dose? 2. Is haemodilution wise during normothermia? 3. What is the potential for awareness during normothermia? 4. Is there a need for more narcotics and less relaxants as there is less risk of shivering?

The normothermic bypass promises better myocardial preservation and absence of disadvantages of systemic hypothermia. It is being practised more frequently. However, as pointed out, many issues regarding normothermic CPB need to be investigated and further clarified.

Accidents and disasters during cardiopulmonary bypass

Accidents and disasters during perfusion have become rare but are not unknown. The anaesthesiologist needs to be well aware of such happenings that can arise during bypass. Those who have seen CPB in its earlier days will have vivid memories of such events. The improvement in the technology as well as the meticulous attention that is given to all the details of the bypass by the perfusionist have considerably reduced such instances. However, it is essential to be familiar with the details of the CPB equipment, as a disaster is waiting to happen every day and will require instant recognition and action by the whole team. In 2000, Mejak et al published the results of a survey that included centres performing cardiac surgery in the United States.[121] The most common types of perfusion incidents were protamine reactions, coagulopathy after CPB, arterial dissection, clot in the circuit while on CPB and transfusion reactions. A survey performed amongst 23,500 Dutch perfusionists during 2006 and 2007 has revealed that the incident rate was 1 per 15.6 perfusions and the adverse event rate was 1 per 1236 perfusions.[122] The three most reported incidents were: (1) persistent inability to raise the ACT above 400 seconds during perfusion (2) an allergic or anaphylactic reaction to drugs, fluids, or blood products, and (3) clot formation in the extracorporeal circuit. Some of the common problems are discussed here.

Malposition of Arterial Cannula

The ascending aortic cannula should be positioned such that, its tip lies freely inside the lumen of the aorta. Occasionally, it may be malpositioned with the jet directed primarily to one of the great arteries arising from the aorta (innominate artery, left common carotid artery or left subclavian artery). When the jet is directed to the innominate or left common carotid artery, unilateral cerebral hyperperfusion with systemic hypoperfusion results. Extremely rarely, when the jet is directed to the left subclavian artery, global cerebral hypoperfusion occurs and preferential perfusion of the left subclavian artery results in hypertension, which can be detected if the left radial artery pressure is monitored. Hypotension (MAP 25 to 35 mm Hg) may indicate cannula malposition. The surgeon should check the position of the cannula, visually and manually. It must not be forgotten that haemodilution and nonpulsatile flow also result in hypotension at this stage. Therefore, some other signs that help to diagnose malposition should also be looked for. These are, unilateral facial and conjunctival oedema and unilateral facial blanching with the onset of CPB. In addition, the hypotension poorly responds to increasing pump flow and/or vasoconstrictors and signs of systemic hypoperfusion such as acidosis or oliguria develop over time. The line pressure (pressure in the aortic inflow line) monitoring also helps in the diagnosis of malposition. It will be high in the presence of malposition (although low pressure may not rule out malposition), but will never be so in the presence of hypotension that is due to a low SVR. A high degree of suspicion is very important to correctly diagnose the condition.

Aortic Dissection

Signs of arterial dissection are almost similar to those of cannula malposition (systemic hypotension unresponsive to increased pump flow, hypoperfusion and high line pressure). Dissection is produced due to intimal disruption or fracture of the atherosclerotic plaque, thereby forcing the blood into the arterial wall. The dissection propagates in the direction of the systemic flow. The perfusion to the vital organs is compromised. As the blood flowing into the dissection does not return to the oxygenator, the venous drainage to the pump decreases. The dissection of anterior or lateral aspect of the ascending aorta can be visualised and help the diagnosis. As with cannula malposition, a high degree of suspicion is important in the diagnosis. TOE and/or epiaortic

scanning can help to confirm the diagnosis.[123] The management includes reducing pump flows so that the progression of dissection is minimised, and instituting hypothermia as much as possible. Simultaneously, an alternative cannulation site (usually femoral) is prepared, and cannulation through this site is accomplished. As hypertension during aortic cannulation can increase the chances of dissection, it is preferable to maintain normotension (systolic BP of 100 to 120 mm Hg) during aortic cannulation.

Massive Air Embolism

The improvement in the techniques of CPB have almost eliminated the occurrence of this rare but disastrous complication. In 1980, the incidence of macroscopic arterial gas embolism was reported to be 0.1 to 0.2 percent.[124,125] Human error, however, can lead to this complication that is known to occur even today. In particular, reversal of LV vent flow can occur due to human error (perfusionist reversing the direction of the vent in the pump head). It is a common practice, therefore, for the surgeon to dip the vent into pericardial blood before insertion, to ensure that the vent is actually sucking and not pumping air.

Retrograde cerebral perfusion[125,126] and hyperbaric therapy[127,128] (to flush air from the cerebral arterial circulation) have been successfully used to improve the neurological outcome in the event of such a complication.

Other Accidents

The anaesthesiologist may be directly involved in some accidents during CPB. One such accident is related to inadequate anticoagulation during CPB. This may be the result of inadvertent omission of heparin administration or the failure of heparin to reach the vascular system. Case reports describing erroneous administration of protamine instead of heparin are available in the literature.[129,130] Therefore, adequate heparin administration before the initiation of CPB must be confirmed by everyone in the OT and the anaesthesiologist must not feel offended, if the surgeon or the perfusionist checks this with him.

The other mishap is related to the initiation of ventilation before termination of the CPB. Instances of anaesthesiologist forgetting to initiate ventilation (that has been stopped while on bypass) before terminating the CPB are not unknown. This may result in disastrous complications due to

hypoxia that ensues. Sometimes, the CPB has been reinstituted before the diagnosis could be made to treat the severe hypotension and bradycardia that follows. Unfortunately, there are no alarms that will remind the anaesthesiologist to resume ventilation before terminating the CPB. It is, therefore, mandatory to remember this simple step and the perfusionist also should ensure that the ventilation has been instituted by the anaesthesiologist before he stops the pump. At some centres, it is a common practice to resume ventilation at some predesignated time ahead of the anticipated time of terminating the CPB. For instance, ventilation may be resumed when the surgeon starts performing the last proximal anastomosis in patients undergoing CABG. Such a practice may help to prevent the omission of this important step at the time of actually terminating the CPB, when the anaesthesiologist is likely to be occupied with some other important job. Some other mishaps that can occur are power failure, administration of wrong medicines, protamine reactions, forgetting to connect oxygen line to the oxygenator, etc.

In summary, in spite of advances in the technology and meticulous attention to perfusion check lists, human error can still lead to accidents during CPB. Anaesthesiologist, must be fully aware of these problems and should be ever vigilant in order to prevent them from happening, and instantly recognise them and initiate early treatment if they happen.

The Inflammatory Response to Extracorporeal Circulation

Inflammation is a normal protective response of vascularised tissue elicited towards antigens or tissue injury. A whole body inflammatory response (such as observed following CPB) can lead to severe organ dysfunction, postoperative bleeding disorders, respiratory distress syndrome and sometimes death. Such a response is attributed to blood interfacing with non-endo-thelial surfaces of the extracorporeal circuit and ischaemia and reperfusion following release of the aortic cross clamp. The whole process consists of activation of the complement system, activation of tissue macrophages and monocytes that release cytokines and other inflammatory mediators, activation of neutrophils with enzyme release, leucocyte migration and accumulation in injured tissue and increased vascular permeability. Cytokines are a class of chemoattractants and white cell activators that are

synthesised by macrophages to act as secondary messengers and induce the synthesis of specific adhesion molecules on endothelial cells and white cells that promote attachment and transmigration of leucocytes during the inflammatory process.[131] mterleukins are a group of cytokines that facilitate communication among (inter) leucocytes (leukin) and produce the inflammatory effects by activating specific receptors on inflammatory cells and the vasculature.

In the early 1980s, only a few measurable markers of the systemic inflammatory response were available. However, a vast number of markers are now known and it appears that the inflammatory response is extremely complex. It is considered to consist of pro-inflammatory and anti-inflammatory part.

The Inflammatory Response

The body reacts to a variety of tissue injuries (e.g. surgery, trauma) with an inflammatory response. After minor tissue injury, the response may be restricted locally without any detectable systemic effects. However, following a more extensive tissue injury a systemic inflammatory response is elicited that is manifested by fever, anorexia, synthesis of acute phase proteins and catabolic hormones. The fulminant inflammatory response that may be observed following cardiac surgery is called “post-perfusion syndrome”.[132] The syndrome is characterised by tissue fluid accumulation, pulmonary and renal dysfunction, haemodynamic instability, coagulopathy, respiratory distress syndrome, shock and death. The degree of systemic inflammatory response following cardiac surgery has been found to be more than other types of major surgery.[133] This has been attributed to the mechanical trauma caused by the foreign surfaces of the extracorporeal circuit, the oxygenator and roller pumps as well as ischaemia and reperfusion associated with aortic cross clamping and unclamping. Figure 9.9 gives a schematic representation of the inflammatory response.

Cytokines

Cytokines are mainly produced by activated macrophages and monocytes. Some of the proinflammatory cytokines are TNF-α, IL-1 a/b, IL-6, and IL-8. The cytokines can diffuse into circulation following an extensive tissue injury and cause systemic inflammatory response. They also stimulate synthesis of nitric oxide from vascular endothelium leading to loss of vasomotor tone in

small arteries.

Following open-heart surgery, the proinflammatory cytokine response is dominated by IL-6, IL-8, IL-1 a/b and TNF-α/β.[134] The plasma levels of IL-6 have been found to correlate with the extent of surgical trauma, and the duration of surgery and CPB.[135] Therefore, IL-6 seems to be a marker rather than a mediator of injury.[136] IL-8 is a potent activator of neutrophils and may contribute in the reperfusion injury caused by activated neutrophils.[137]

The cytokine measurements are performed on peripheral blood and the absence of cytokines does not exclude their local production. Although, the source of pro-inflammatory cytokines during and after CPB has not been well defined, myocardium has been shown to be a major source of TNF-α and IL-6 production.[138]

The anti-inflammatory cytokines have the ability of downregulating the production or blocking the effects of pro-inflammatory cytokines. Some of the anti-inflammatory cytokines that are released to counteract excessive immunostimulation caused by cardiac surgery and CPB are IL-10, IL-4, IL-11, IL-1 receptor antagonist (IL-1ra) and TNF soluble receptors (TNF-sr).[138-141] The adrenocorticotropic hormone and Cortisol with their general immunosuppressive effects are also regarded as antiinflammatory mediators. The anti-inflammatory cytokine response balances the pro-inflammatory cytokine response and thus the harmful effects of cardiac surgery are avoided. IL-10 is predominantly produced by the liver and is known to directly inhibit the release of proinflammatory cytokines. In addition, it exerts anti-inflammatory effects by triggering the release of other anti-inflammatory cytokines such as IL-1ra and TNF-sr.

The magnitude of the inflammatory response to CPB can adversely influence the clinical outcome, as the patients who have an exaggerated inflammatory response tend to bleed more, require more respiratory support, demonstrate greater capillary leak via weight gain and display a decline in independent functioning relative to normal responders.[142]

Granulocytes

The number of granulocytes decreases initially during cardiac surgery (possibly a haemodilution effect) followed by granulocytosis within 2 to 3 hours after CPB. The activated granulocytes are involved in the reperfusion injury after CPB.[143] The granulocytes accumulate in the myocardium and

lungs following CPB. This granulocyte infiltration of the myocardium and lungs plays an important role in the reperfusion injury leading to cardiac dysfunction and decreased pulmonary gas exchange.[143]

Based on an improved understanding of the underlying mechanisms, therapeutic strategies have been developed in order to reduce the inflammatory response and its damaging effects. As the pathophysiology involved appears to be multifactorial, both pharmacological strategies as well as modification of mechanical devices have been tried.

Steroids

Methylprednisolone has been used, especially in children to blunt the inflammatory response. In general, a high-dose (20 to 30 mg/Kg) is administered before the onset of CPB. However, in a comparison of the high-dose (30 mg/Kg) versus low-dose (2 mg/Kg) methylprednisolone, it has been shown that the high-dose was not superior to low-dose in blunting the systemic inflammatory response in paediatric patients undergoing open-heart surgery.[144] Nevertheless, most centres administer methylprednisolone in the dose of 20 to 30 mg/Kg before CPB and repeat half the dose in the postoperative period. Dexamethasone can also be used in an attempt to blunt the inflammatory response. It has been demonstrated that dexamethasone in the dose of 100 mg administered before induction of anaesthesia changes circulating cytokines in an anti-inflammatory direction (decrease in proinflammatory cytokines, IL-6, IL-8, TNF-α and increase in anti-inflammatory cytokines, IL-10).[145]

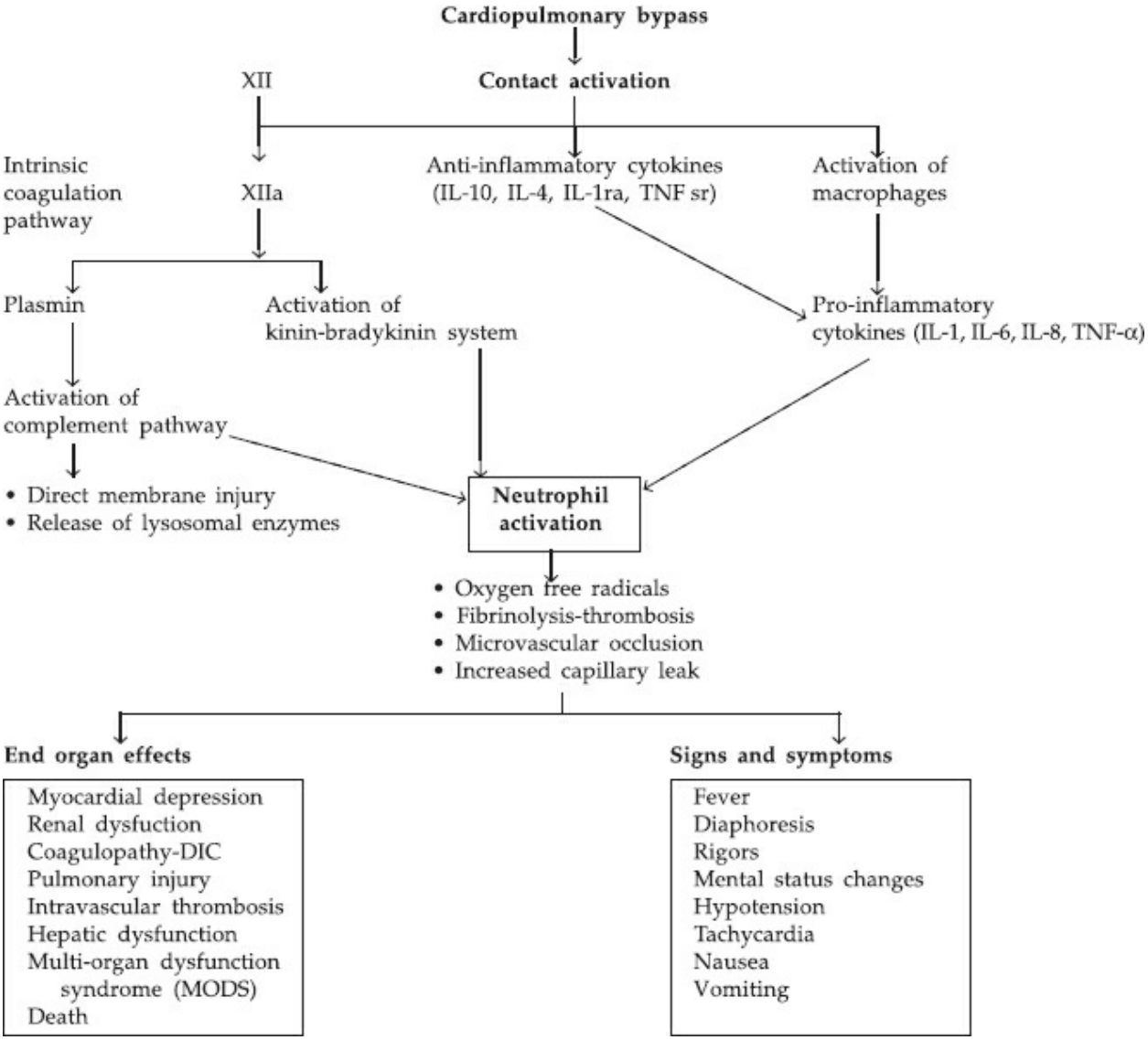

Figure 9.9: Schematic representation of inflammatory response (IL: interleukin, TNF: tumour necrosis factor, DIC: disseminated intravascular coagulation).

Calcium Channel Blocker

Diltiazem infusion during CPB in patients undergoing CABG has been shown to decrease the IL-6 levels after CPB,[146] and thus offers an additional pharmacological means of decreasing the inflammatory response.

Dopexamine infusion and epidural analgesia have also been utilised with the aim of improving the splanchnic circulation so that the alteration of gut mucosal barrier to endotoxins is minimised. However, it has been shown that although, the markers of inflammatory response were significantly decreased with these measures, the splanchnic blood flow and oxygen delivery were similar to the control group.[147] These results suggest that mechanisms other

than an improved splanchnic blood flow by dopexamine and epidural analgesia are responsible for the anti-inflammatory effects.

Leucocyte Filter

Leucocyte filtration aims at physically removing activated leucocytes from the circulation during CPB by incorporating a leucocyte filter in the bypass circuit. The technique has been used since mid 1990s and appears to be beneficial in improving pulmonary outcome by preventing direct neutrophil induced inflammatory injury. Leucocyte filter has been used in combination with aprotinin (high-dose regime) and has been shown to improve post-CPB lung performance by reducing significantly the ventilator times, hospital stay and patient morbidity.[148]

Modification of Bypass Circuit

Standard CPB circuits with their large surface area and volume contribute to postoperative systemic inflammatory reaction. As already mentioned, CPB circuits have been modified on the basis of minimal extracorporeal circulation to minimise inflammatory response. A system with a reduced priming volume, no aortic venting and no venous reservoir has been shown to lower the inflammatory reaction compared to the standard CPB.[149] A new approach with a single disposable, compact arteriovenous loop having integral pumping, oxygenating, air removal and gross filtration capabilities has been used on animals with encouraging results.[150] Some other methods that have been used to attenuate the inflammatory response include use of heparin coated CPB circuits[151], ultrafiltration[152] and aprotinin.[153] Aprotinin has been withdrawn and its use is controversial. For details, please refer to chapter 11.

Beating heart surgery leading to total avoidance of the CPB is yet another option, but is restricted to patients undergoing CABG. The beating heart surgery leads to lesser inflammatory response, renal dysfunction, possibly reduced neurocognitive dysfunction and pulmonary complications.[154,155] A meta-analysis comparing off-pump coronary artery bypass and on-pump coronary artery bypass has confirmed that off-pump coronary artery bypass surgery is associated with reduced risk of stroke and atrial fibrillation.[156]

The different anaesthetic agents and techniques have no effect on the complex intraoperative and postoperative inflammatory response to cardiac surgery. The anaesthetic management should be focused on the maintenance

of homeostasis during the perioperative period. Episodes of hypotension, hypoxia and acidosis all can exaggerate the systemic inflammatory response initiated by CPB. These episodes should, therefore, be avoided and aggressively treated if they occur.

In summary, many measures to decrease the inflammatory response to CPB are available. Likewise, there are many variables that can influence the inflammatory response. Therefore, it is difficult to choose any one particular technique or intervention that can influence the clinical outcome.

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Chapter 10: Anticoagulation and Haemostasis during Cardiopulmonary Bypass

Effective anticoagulation and its safe reversal are important requirements for the safe conduct of cardiopulmonary bypass (CPB). In this respect, discovery of heparin is an important milestone. Heparin was discovered accidentally in 1916 by Jay McLean, a medical student.[1] During the following years, heparin was prepared commercially and underwent clinical trials that proved its ability to prevent clot formation or extension. Protamine was discovered in 1937 and Gibbon in 1938 utilised heparin induced anticoagulation for CPB in animals.[2] Subsequently in 1953, the first human operation using CPB was performed. Although CPB technology has undergone several advances since then, there is no well proven substitute for heparin and its reversal with protamine for the management of CPB.

Normal Coagulation Pathway

The various coagulation factors participate in a series of activating reactions that end with the formation of an insoluble clot. The whole process of clot formation can be divided into four parts: contact phase, intrinsic, extrinsic and common pathways (Fig. 10.1).

Contact phase

The damaged vascular surface exposes the collagen matrix which initiates the surface activation of coagulation proteins. Factor XII binds with the negatively charged collagen material and is autoactivated to factor XIIa. High

molecular weight kininogen (HMWK) binds prekallikrein (PK) and factor XI to the surface. Factor XIIa splits factor XI to form factor XIa as well as PK to form kallikrein.

Intrinsic pathway

The net result of intrinsic activation is the formation of factor Xa from the product of surface activation. Factor XIa converts factor IX to form factor IXa in the presence of Ca^{++}. Factor IXa then activates factor X. For this process, Ca^{++} and factor Villa are also necessary.

Extrinsic pathway

Activation of factor X can also be achieved independently by substances extrinsic to the vasculature. Thromboplastin released from the tissues acts as a cofactor to activate factor X by factor VII. Ca^{++} is also required for this process.

Common pathway

Factor Xa splits prothrombin (factor II) to thrombin (factor IIa). Ca^{++} and factor Va are required for this process. Thrombin splits the fibrinogen molecule to form soluble fibrin monomer and fibrinopeptides A and B. Factor XIII, activated by thrombin, crosslinks these fibrin strands to form a clot.

Fibrinolysis

Fibrinolysis is the dissolution of fibrin. It ensures that the coagulation does not proceed unchecked. It occurs in the proximity of a clot and dissolves it when endothelial healing occurs. Fibrinolysis is mediated by the serine protease plasmin, which is produced from the plasminogen with the help of tissue plasminogen activator (t-PA). Fibrinolysis is a normal response to clot formation and represents pathological condition, when it occurs systemically.

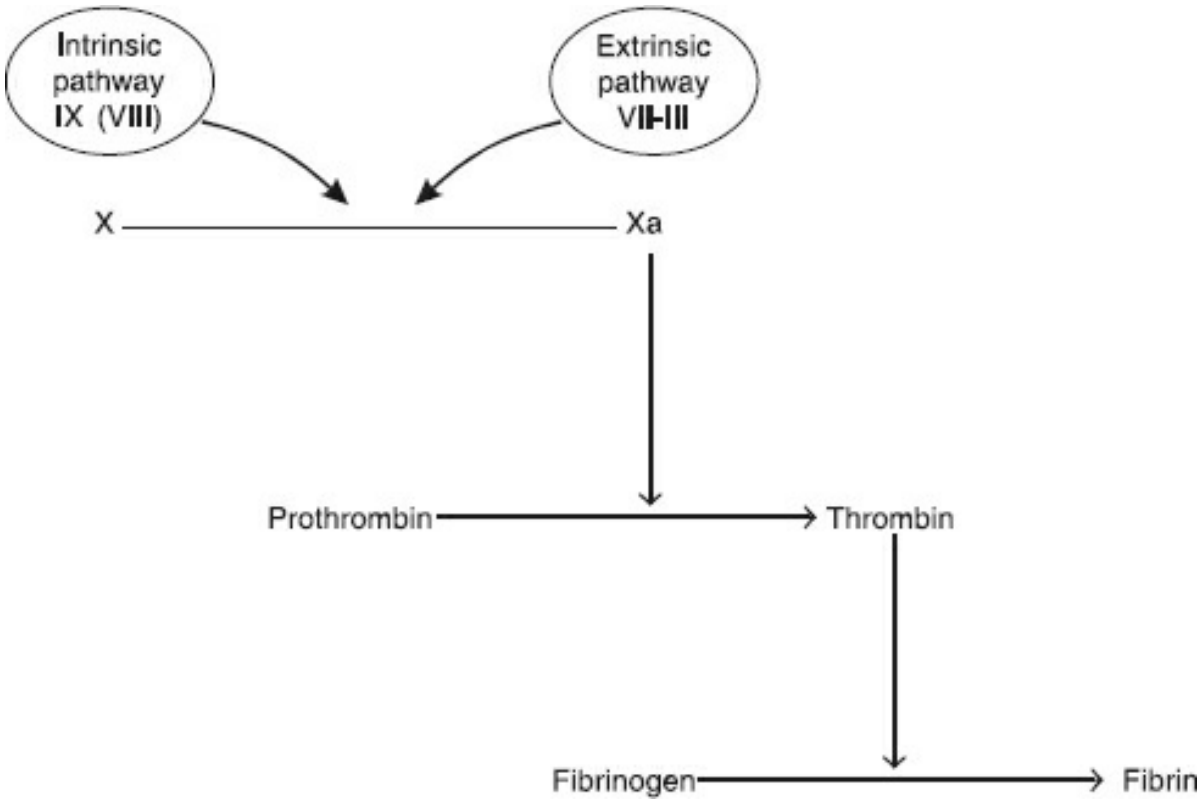

Figure 10.1: Diagrammatic representation of normal coagulation pathway. For additional details refer to the text.

Heparin

Heparin is a glycosaminoglycan, a polysaccharide that resides in the mast cells. The name “heparin” was chosen because the substance was originally isolated from liver extracts. However, intestinal mucosa and lung tissue are the most common sources from which commercial heparin is derived. The heparin compound isolated from animal tissues contains heparin molecules with molecular weights ranging from 3,000 to more than 40,000 daltons with mean molecular weight approximating 15,000 daltons.[3] This factor is of clinical importance as the molecular weight distribution of a heparin compound determines the spectrum of action of heparin.[4] The action and potency of heparin may, therefore, vary between different commercial preparations. The commercial heparin is commonly extracted from pig mucosa (porcine mucosal heparin) and cattle lung (bovine lung heparin). Both the preparations are widely used in clinical practice. Adverse cardiovascular reactions such as decrease in arterial pressure and peripheral vascular resistance may occur after heparin injection. These may be related to

the presence of preservative (benzyl alcohol, chlorocresol), and although, one report has suggested that the cardiovascular reactions are heparin specific phenomena (not related to preservative)[5], some centres use preservative free heparin.

Pharmacology

Heparin is usually administered into the central venous catheter during cardiac surgery. After a bolus injection into the central vein, the peak effect occurs within one minute. The onset is likely to be delayed in low output states or with peripheral venous injection.

As heparin has a bigger molecule, it mostly stays within the plasma compartment of the blood stream. However, a small portion has been found to be redistributed to extracellular fluid, alveolar macrophages, splenic and hepatic reticuloendothelial cells, and vascular smooth muscles. This sequestration of heparin is responsible for heparin rebound (heparin induced anticoagulation after protamine neutralisation).

The elimination half-life of heparin is dose-dependent and has been found to be 126 ± 24 min. with a heparin dose of 400 units/Kg.[6] Hypothermia delays heparin elimination. The mechanism of heparin elimination is uncertain but metabolism by reticuloendothelial system and renal elimination have been suggested.

Heparin causes anticoagulation mostly by potentiating the activity of antithrombin-III (AT-III). It alters the configuration of AT-III by attaching itself to AT-III. The altered configuration, makes it much more attractive to thrombin. In this way, the thrombin inhibitory potency of AT-III is increased several times.

The heparin-AT-III complex also affects several other coagulation factors, but factor Xa and thrombin are most sensitive to inhibition by heparin, and thrombin is 10 times more sensitive to the inhibitory effects of heparin as compared with factor Xa.[7]

The response to a fixed dose heparin bolus measured either by heparin concentration or clotting time varies from patient to patient.[8]

Dosage during CPB

Heparin dosing was accomplished empirically during the early days of open-

heart surgery. Several dosage protocols were practiced and the initial dose ranged between 200 and 400 units/Kg and maintenance dose between 50 to 100 units/Kg that was administered anywhere between 30 min. and 2 hours.[8] In addition, the extracorporeal circulation was primed with bank blood that was heparinised in the dose of 2,500 to 5,000 units/unit of blood. Such a wide variation in the practice was mainly due to the non-availability of an easily applicable test for monitoring the heparin effect or its serum concentration. The introduction of activated clotting time (ACT),[9] however, changed the situation and ACT monitoring was incorporated during CPB.

Activated clotting time

During the initial stages, ACT was performed manually using diatomaceous earth (celite) as an activator. In the manual method described by Bull et al,[8] 2 mL of blood withdrawn from a venous catheter is placed in a glass tube containing celite. The tube is then inverted once per second for 30 seconds before placing it in a heat block warmed by a 40 watt bulb. The tube is then rocked slowly until the clot is formed. A stopwatch is started when the blood first enters the tube and stopped when the first clearly defined clot is visible. The ACT is a bedside test that is performed immediately upon withdrawal of the sample and it should not be performed at a distant location from the patient's bedside.

Manual ACT techniques have been replaced by automated techniques that are currently used by almost every cardiac centre. Hemochron ACT is one such technique that is commercially available. It uses 2 mL of blood with celite as an activator. The blood is mixed in a test tube that contains a small magnet and a plastic baffle. A timer is started as the blood is placed in the test tube. The tube is then placed in a tilted well within a heat block and is rotated continuously. The clot formation engages the magnet and it is rotated along with the clot. This interrupts a magnetic field and stops the timer automatically. The Hemotec ACT is another automated ACT device that is available commercially. It uses kaolin as an activator and requires 0.4 mL of whole blood for the test.

Bull et al in 1975[8,10] pointed out the deficiencies of empirical heparin and protamine dosing protocols and recommended a structured approach using ACT monitoring. An optimal range for ACT or heparin concentration during CPB is controversial. However, Bull et al[8] reported that a clot does not form

in the oxygenator circuit with an ACT exceeding 300 seconds. They further stated that “a much more precise approach is possible, if the effect of heparin or protamine on the clotting time can be predicted in advance.” To achieve this, they proposed the use of a dose response curve.

They adopted an ACT of 480 seconds as the safe value sufficient to prevent it from falling below 300 seconds. The dose response curve is plotted after measuring the baseline ACT (normal range 80 to 120 seconds) and by giving the dose of heparin and measuring the ACT again. This is followed by another dose of heparin and repeat ACT measurement. This helps to create a dose response curve. The appropriate dose of protamine can also be calculated with the help of this curve on the basis of protamine to heparin ratio. Some other recommendations of Bull and co-workers were: 1. ACTs below 180 seconds should be considered to be life threatening; 2. ACTs between 180 to 300 seconds should be considered highly questionable; and 3. maintaining ACTs exceeding 600 seconds would seem unwise. It should be clarified at this stage, however, that ACT of 480 seconds should not be misinterpreted as the minimum safe level for CPB anticoagulation. Young et al[11] demonstrated fibrin formation and depletion of clotting factors in monkeys sustaining ACTs below 400 seconds. This might suggest that the minimum recommended ACT level of 300 seconds is not correct. However, many studies have reported ACT values below 400 seconds for CPB without complications.[12-16] A simplified dosing regimen guided by ACT values but without a dose response curve was proposed in 1979 by Doty and colleagues.[17] These early studies form the basis of current heparin dosing protocols.

It has also been suggested that administration of excessive heparin doses (ACT > 600 seconds and heparin concentration > 40 U/mL) during CPB may predispose to increased postoperative blood loss. But it appears that a need for higher initial protamine doses and higher incidence of heparin rebound are probably the only drawbacks of administering excessive heparin doses. The optimal ACT or heparin concentration range for CPB has not been definitely established, but the ACT minimum of 300 seconds is followed in most places.

Current practice

Unfortunately, Bull et al’s[10] approach was never widely adopted. The current

practice that is being followed at most places is to give a dose of heparin without plotting a dose response curve, use ACT to confirm the maintenance of a minimum value and continue to monitor ACTs throughout the CPB.[18] Gravlee et al[19] have selected the following CPB heparin management protocol while suggesting that other protocols may be equally acceptable.

1. Administer heparin 300 units/Kg intravenously.
2. Draw an arterial sample for ACT in 3 to 5 min.
3. Give additional heparin as needed to achieve ACT > 400 seconds before initiating CPB, to maintain ACT > 400 seconds during normothermic CPB and > 480 seconds during hypothermia between 24°C and 30°C.
4. Prime the extracorporeal circuit with approximately 3 units of heparin/mL (e.g. 5000 U for 1600 mL clear priming solution).
5. Monitor ACT every 30 min. during CPB or more frequently, if the patient proves resistant to heparin induced ACT prolongation. If ACT decreases below the desired minimum value, supplemental heparin doses of 50 to 100 units/Kg most often prolong the ACT sufficiently without the aid of precise calculations (dose response curve).

Limitations of activated clotting time for heparin monitoring

Although, ACT is generally accepted as the standard test for monitoring heparin anticoagulation during CPB, it has important limitations. ACT values may be affected by several clinical variables. Factors such as haemodilution, hypothermia, thrombocytopenia, platelet inhibitors and aprotinin prolong the ACT, and platelet lysis and surgical stress shorten the ACT. Therefore, ACT may not always accurately reflect the anticoagulant effect of heparin during CPB. It has been shown that heparin levels decreased to levels below 2 units/mL during CPB in the presence of ACT of 400 to 480 seconds, implying that hypothermia and haemodilution may be responsible for increasing the ACT.[20] Thus, with ACT monitoring, heparin levels can decline to levels that may be inadequate to suppress thrombin activity. This problem can be of significance when CPB duration is long. In addition, intrinsic and extrinsic pathway coagulation occurs in presence of heparin, and platelets can be activated by contact with the bypass circuitry and by heparin directly.[21,22]

Heparin concentration

Because the ACT correlates poorly with the measured heparin concentration, and also several clinical variables can affect the ACT, it has been argued that ACT may not prove to be an adequate monitor of heparin efficacy and simultaneous monitoring of heparin concentration should also be performed.[20]

It has not been firmly established whether it is better to monitor heparin concentration or heparin effect. The case report by Nielsen et al[23] demonstrating clots in the surgical field as well as extracorporeal circuit despite maintaining whole blood heparin concentration of 4 units/mL or higher suggests that, perhaps, monitoring heparin effect (ACT) is a better method of ensuring anticoagulation during CPB. The ACTs of this patient who had previously undiagnosed AT-III deficiency were not reported. Since, there are no reports of clots in the extracorporeal circuit with ACT > 300 seconds, it seems likely that this clinical picture could have been avoided by monitoring ACT.

One paper has shown that in comparison to heparin management with ACT, heparin concentration based anticoagulation management during CPB leads to a significant reduction of thrombin generation, fibrinolysis, and neutrophil activation, but there is no difference in the effect on platelet activation.[24]

A novel method using hollow core photonic crystal fibre (HC-PCF) in conjunction with Raman spectroscopy has been explored for real time monitoring of heparin concentration in serum. In this method, an enhanced Raman signal (> 90 times) is obtained from various heparin-serum mixtures filled HC-PCFs compared to its bulk counterpart.[25] The utility of this method in clinical practice is yet to be proven.

Protamine titration test

This is a modification of Lee-White whole blood clotting time (WBCT). One mL of blood is added to several glass tubes at 37°C containing a known concentration of protamine. Each tube is tilted every 30 seconds. The first tube to clot determines the concentration of heparin in blood. Suppose the tube containing 10 pg of protamine clots first, it means that blood contains 1 unit/mL of heparin (presuming that 10 pg of protamine neutralise 1 unit of heparin).

The Hepcon is an automated protamine titration test. It uses cartridges with several chambers containing various amounts of protamine. The method is expensive but provides quick results. It can be used both for calculating heparin and protamine doses in the patient. Despotis et al[26] used this method and concluded that it facilitated maintenance of a therapeutic heparin concentration and identification of an accurate protamine dose that can result in reduced use of blood products.

Anticoagulation during off-pump coronary artery surgery

Off-pump coronary artery bypass grafting (CABG) has recently gained popularity. Because the use of CPB is avoided, it is thought that full anticoagulation is not necessary. However, heparinisation prevents thrombus formation in the native coronary arteries and bypass grafts and allows emergent institution of CPB if needed. Also, patients undergoing off-pump CABG are not immune to thromboembolic complications, which have been found to be similar to those undergoing traditional on-pump CABG.[27] In one study, a dose of 180 units/Kg plus 3000 units every 30 min. was used. It was shown that platelet counts and fibrinogen levels were preserved while a peak ACT of 445 ± 73 seconds was achieved.[28] Further, there was no immediate hypercoagulable state (residual heparin effect in the early postoperative period was observed) and the total doses of heparin and protamine were lower in the off-pump CABG group compared with the conventional CABG group.

A survey performed among 750 European cardiothoracic surgeons (with 43.7 percent respondents) revealed wide variation in heparin dosing.[29] Intraoperative heparin dosage ranged between 70 units/Kg to 500 units/Kg with 60 percent respondents preferring a low-dose regimen ($\leq$ 150 units/Kg). The lowest acceptable ACT was 200 seconds by 24 percent, 250 seconds by 18 percent, and 300 seconds by 26 percent of surgeons.

Heparin resistance

Heparin resistance can be defined as the need for higher than normal heparin doses to induce sufficient anticoagulation for the safe conduct of CPB.[19] In the majority of cases, administration of additional heparin doses is sufficient

to achieve safe levels of anticoagulation. The reported incidence of heparin resistance is 20 percent with risk factors as AT-III levels less than 60 percent of normal, preoperative heparin therapy, and platelet counts greater than 3,00,000/mm^3.[30] Some patients having normal or supranormal AT-HI activity may depict heparin resistance that is unresponsive to administration of AT-III. AT-III deficiency can be inherited or acquired. Patients most often present between the ages of 15 and 30 years and have AT-III levels below 50 percent of normal (normal: 22 to 39 mg/dL or plasma AT-III activity level 80 to 120 percent). Lower limb thrombosis or pulmonary embolism are the common presenting features. Newborns and infants have AT-III levels averaging 60 to 80 percent of adult levels till approximately 3 months of age.[31] Therefore, they have relative heparin resistance compared to adults.

The diagnosis of AT-ITJ deficiency in a patient about to undergo CPB is based on substantial heparin resistance that is noticeable from inability to attain an ACT of > 300 seconds despite administration of large doses of heparin (> 600 units/Kg). Transfusion of fresh frozen plasma (FFP) which contains normal concentration of AT-III has been used as a treatment. Two to three units are usually sufficient for most adults. The ACT prolongation after administration of FFP, however, does not establish that AT-III deficiency caused the heparin resistance, because increasing AT-III level is likely to increase heparin induced anticoagulation whether or not initial AT-III levels are inadequate.[32]

Human AT-III concentrates are available and have been successfully used to potentiate the heparin effect to meet the necessary ACT to allow for CPB.[33,34] Five hundred units of AT-III concentrate should be administered and ACT should be measured. If the target ACT is not achieved, a further dose of 500 units can be administered. The AT-ITJ concentrate is usually given slowly (100 IU/min.) due to fear of anaphylaxis, however faster rate of infusion (250 IU/min.) have been used without any problem.[35] In the absence of FFP or AT-III concentrate, whole blood can also be transfused, since it also contains AT-III. Blood transfusion, however, should be avoided in the postoperative period, as the excessively administered heparin may precipitate its anticoagulant effect in the presence of AT-III and cause postoperative bleeding.

Attenuation of ACT response to heparin may also be observed during CPB in patients receiving heparin infusion during preoperative period. High dose

thrombin time (HiTT) can be a useful tool for monitoring adequate anticoagulation in such patients. The HiTT correlates well with the heparin concentration,[36] and unlike the ACT, HiTT is not affected by haemodilution and hyperthermia. It has been shown that heparin resistance is not observed when HiTT is used to monitor anticoagulation.[37] A target HiTT of 190 seconds should be maintained during CPB, which corresponds with ACT value of 480 seconds.

Heparin induced hyperkalemia

Although, heparin is widely used during cardiac surgery, its adverse effects other than bleeding and thrombocytopenia are poorly recognised. A recent case report has demonstrated hyperkalaemia following administration of heparin for CPB.[38] Another report in an 85-year-old lady clearly demonstrated hyperkalaemia on starting heparin that returned to normal after discontinuing heparin.[39] This is a rare but serious complication.

Heparin induced thrombocytopenia

Unfractionated heparin has been safely used during CPB for a long time. However, heparin can induce thrombocytopenia in some patients. The thrombocytopenia occurring as a consequence of direct platelet activation by heparin (HIT type I) is mild and self limiting and does not require any treatment. The thrombocytopenia caused by immune mediated mechanism (HIT type II) occurs when antibodies (predominantly IgG) are produced against platelet factor 4 (PF4) - heparin complexes. The macro-molecular complex of heparin, PF4, and IgG causes platelet activation, platelet destruction, and the release of prothrombotic microparticles from platelets.[40] The net result is low platelet count (< 50 percent) and a paradoxic prothrombotic state leading to life-mreatening arterial and venous thrombosis. With advances in the therapy of acute coronary syndromes, repetitive exposure to heparin has become common place. Therefore the incidence of HIT has increased. A wide range of incidence rates (up to 30 percent) have been reported. However, the incidence of this increasingly recognised antibody-mediated complication of heparin therapy has been estimated to be 0.5 to 5 percent of patients receiving heparin for at least 5 days.[41] Some studies have found a higher incidence with bovine lung heparin than with porcine mucosal heparin.[42,43]

The mechanism by which heparin causes thrombocytopenia is incompletely understood, but is likely to be immune mediated, (antibodies formed against PF4/heparin complex) as it appears 7 to 14 days after heparin therapy. This is further supported by laboratory investigations. The serum and purified IgG from patients with HIT induce platelet activation that results in generation of procoagulant platelet derived microparticles. These microparticles have been identified in blood of patients with HIT. They provide a phospholipid surface that accelerates formation of thrombin.[44,45] Thrombin generation further activates the platelets and generation of fibrin clot. This is thought to be the mechanism by which HIT initiates thrombosis. Pre-existing vascular endothelial damage may further aggravate the thrombosis associated with HIT.

Diagnosis and management

HIT typically presents as an unexpected decrease in the platelet count that occurs within 5 to 10 days of heparin administration, as this is the approximate time period required to generate HIT antibodies. Occasionally, HIT may present within hours of the administration of heparin, if the patient has had an earlier exposure to heparin within previous 100 days.[46] This is likely caused by the presence of residual HIT antibodies induced by the previous heparin exposure. Platelet counts also decrease (up to 50 percent) during the first 2–3 days following cardiac surgery. However, this is attributable to haemodilution and platelet consumption during CPB and not to HIT. Platelet counts are restored to baseline value by postoperative day 3. A decrease in platelet count $\geq$50 percent from this peak postoperative value occurring within 5 to 10 days of heparin exposure should be considered as HIT.[47]

HIT should be suspected in the presence of a decreasing platelet count following exposure to heparin therapy. The diagnosis should be confirmed by laboratory testing. Enzyme-linked immunosorbent assay (ELISA) is highly sensitive for detecting anti-PF4/heparin antibodies. Platelet aggregation assay or serotonin release assays have a lower sensitivity than ELISA tests but have a greater specificity for the diagnosis of HIT.[47]

Cardiac anaesthesiologist will need to manage the patient with a previous history or a current event of HIT. Sometimes this may be on an urgent basis, as a large number of patients with acute coronary syndrome receive heparin

and some of them need urgent surgery. Occasionally, patients may develop HIT in the postoperative period following cardiac surgery. The management of these patients requires careful planning as the risk of thrombosis with associated mortality is high, and additional heparin cannot be administered.

A large number of papers have evaluated the use of alternative non-heparin anticoagulants in patients with HIT undergoing on-pump as well as off-pump procedures. These have mostly been case reports, prospective observational or retrospective studies. Almost all the heparin alternatives suffer from the drawbacks of not being able to monitor the anticoagulation effect and having no effective method of rapidly reversing the effects of these agents. One of the approaches that can be used is to discontinue heparin therapy for 4 to 8 weeks (if feasible), which results in resolution of the antiplatelet-antibody reaction.[48] Changing the tissue source of heparin may also be tried.

Alternatives to Heparin

Low molecular weight heparin

Different components of unfractionated heparin possess differing affinities for platelets and AT-III. The unfractionated heparin contains polysaccharide chains with molecular weight above 5,400 and has antifactor Xa and anti-thrombin actions in the ratio of 1:1. Heparin can be fractionated into different compounds for different indications. Shorter heparin chains (e.g. low molecular weight heparin, LMWH) are less capable of inhibiting thrombin (factor IIa), but are potent inhibitors of factor Xa. Moderate inhibition of factor Xa prevents thrombus formation without impairing haemostasis as intensely as simultaneous inhibition of Xa and IIa. Thus prophylaxis against deep vein thrombosis can occur with a lower incidence of bleeding complications.[49] Fractionation of conventional heparin to develop different LMWH compounds has been performed and has been used effectively for prevention of deep vein thrombosis, during haemodialysis and in the treatment of thrombosis occurring with HIT.[50-52] However, a nearly 100 percent cross-reactivity rate of LMWH with HIT antibodies has been reported using sensitive platelet functional assays.[53] A few case reports have described the use of LMWH for the conduct of CPB in patients with HIT.[54-56] It has important limitations such as possible cross reactivity with HIT antibodies,

no effective neutralising agent, and difficulty in monitoring the effect. Therefore, currently it is recommended that LMWH should not be administered for anticoagulation during cardiac surgical procedures or postoperatively in patients with acute HIT.[57]

LMWH is now recommended in the treatment of unstable angina. Some of these patients may undergo CABG. The LMWH that these patients have received might influence the postoperative bleeding. It has been shown that the blood loss is significantly more in patients who have received LMWH within 12 hours of surgery.[58] It is, therefore, important that the risks of bleeding and transfusion must be weighed against the risk of ischaemia, if LMWH is discontinued more than 12 hours before operation.

Danaparoid

Danaparoid sodium consists of a mixture of low-molecular-weight glycosaminoglycans (heparin sulfate, dermatan sulfate, and chondroitin sulfate). It produces the anticoagulant effect primarily via inhibition of factor Xa.[59] The incidence of cross-reactivity with HIT antibodies is significantly lower with danaparoid as compared with LMWH (17 percent versus 100 percent).[60] Its elimination is dependent on kidneys and there is no reversal agent for this drug. The first use of danaparoid for CPB was reported by Doherty and colleagues in 1990.[61] However, significant postoperative bleeding and transfusion requirements were observed. A variable dosing protocol has been used for the management of patients with HIT that includes intermittent bolus doses, and continuous infusion.[62,63] However, none of the protocols have been shown to be satisfactory and results in inadequate anticoagulation (formation of clots) and severe postoperative bleeding necessitating large quantities of blood transfusion. The clinical utility of danaparoid is limited due to its long plasma half-life, the lack of neutralising agent and requirement of complex monitoring (anti X-a). Perhaps, the use of danaparoid may be more appropriate during off-pump surgery. In this scenario, effective anticoagulation can be achieved with lower doses of danaparoid. It has been used in patients without HIT undergoing off-pump surgery in the dose of 40U/Kg.[64] However, further trials are needed to define appropriate dosing and monitoring strategies in this group of patients.

Defibrinogenating agents

Ancrod

Ancrod is derived from Malayan pit viper venom. It lyses fibrinogen thereby preventing formation of fibrin polymers. Zulys et al[65] have reported the successful use of ancrod for CPB anticoagulation. The average dose used was 1.65 U/Kg. It takes a long time (at least 12 hours) to achieve enough fibrinogen depletion to produce adequate anticoagulation for the conduct of CPB. Similarly, its elimination by reticuloendothelial system may take several days. It has also been used in patients with acute HIT undergoing cardiac surgical procedures.[66] Important limitations include delayed onset (cannot be used for urgent or emergent situation), and increased need for homologous blood products. In addition, since ancrod does not inhibit thrombin generation, thrombotic complications can occur after CPB. Further, there is no method of monitoring ancrod anticoagulation during CPB and rapid effective reversal. Fibrinogen concentrate, cryoprecipitate and FFP need to be administered to restore fibrinogen levels. Due to these disadvantages, the manufacturer of ancrod has discontinued its production in 2002.[46]

Streptokinase and Urokinase

Although these thrombolytic agents are capable of producing defibrinogenation, the increased plasmin formation that they produce can lead to hyperfibrinolysis. This can lead to increased bleeding following CPB and hence, they are considered undesirable heparin substitutes.

Argatroban

Argatroban is a synthetic direct thrombin inhibitor that binds reversibly to the active site of the thrombin molecule. It is primarily metabolised in the liver and has a short half-life (3951 min.), which may be prolonged in patients with moderate hepatic impairment (152 min.).[67] It has been used in patients undergoing percutaneous coronary interventions (PCI), but its use during cardiac surgical procedures has not been widely studied. Case reports describing its use for CPB, even in patients with HIT are available.[68,69] For PCI, a dose of 2 to 3 μg/kg/ min. has been used with the goal of achieving an ACT of > 200 seconds. Similar dosing can be used for off-pump procedures. For CPB, a dose of 5 to 10 μg/Kg/min. has been successfully used to maintain an ACT of 300 to 400 seconds.[68,69] Inadequate anticoagulation during off-pump cardiac surgery despite an ACT of > 380 seconds[70] and

during mitral valve replacement[71] has been described. Further, the safe and effective dose of argatroban for cardiac surgical procedures and the most appropriate method of monitoring the anticoagulant effects is undetermined.[46] Therefore, it is suggested that, at present, the use of argatroban as a substitute of heparin during CPB should be restricted to those cases where the other thrombin inhibitors are contraindicated.[71]

Hirudin

Hirudin is isolated from medicinal leeches and it inhibits thrombin directly without requiring AT-III. It is now produced by using the recombinant technology (r-hirudin). Among the two commercially produced r-hirudins (lepirudin and desirudin), lepirudin has been used more commonly. It is effective in inhibiting free as well as clot-bound thrombin.[72] It is eliminated primarily by the kidneys and the plasma half-life may be prolonged as long as 120 hours (normal 80 min.) in the presence of renal failure.[73] Therefore, it should be used with caution in presence of renal failure. Modified ultrafiltration may be utilised to enhance the elimination of hirudin during CPB.[74,75] The methods used to monitor the anticoagulant effect of r-hirudin during cardiac surgery include, ACT, aPTT, thrombin time, ecarin coagulation time (ECT), plasma modified ACT, and thromboelastography. The ECT was specifically developed to assess the anticoagulant effect of direct thrombin inhibitors. Ecarin is derived from the snake venom and converts prothrombin to meizothrombin, which has moderate clotting activity. Meizothrombin binds to direct thrombin inhibitors and neutralises their action, thus precipitating clot formation. The commercial device to measure ECT is no longer available.[46] For plasma modified ACT, an equal volume of citrated commercial normal plasma is added to the sample of blood to which lepirudin has been added.[76]

r-hirudin was used first to induce satisfactory anticoagulation in dogs in 1991.[77] A number of case reports have described successful use of r-hirudin in patients with HIT undergoing cardiac surgery.[75,78-80] A bolus dose of 0.25 mg/Kg followed by an infusion at 0.5 mg/min. with additional 0.2 mg/Kg added to the prime can be used.[78] Smaller doses have been used in patients undergoing off-pump surgery.[81] The dose required can be further decreased by the concomitant use of minimised extracorporeal circulation.[82]

The limitations of r-hirudin are; there is no effective reversal agent, excessive bleeding can occur in patients with renal insufficiency, the optimal dosing regimen has not been defined, and anaphylactic reaction may occur.[83]

Bivalirudin

Bivalirudin is a bivalent direct thrombin inhibitor that inhibits free as well as clot-bound thrombin thus preventing thrombin-mediated platelet activation. Bivalirudin has a short elimination half-life of approximately 25 to 30 min. and has no antidote. It primarily undergoes dual elimination via proteolytic cleavage and renal elimination. It requires dose adjustment in the setting of severe renal dysfunction, as the clearance of bivalirudin is reduced by nearly 80 percent in patients with renal failure.[84] The elimination of bivalirudin can be improved by haemofiltration. Koster et al have demonstrated that zero-balanced modified haemofiltration significantly reduced the elimination half-life of bivalirudin and also reduced the 12-hour postoperative blood loss.[85] The author concluded that zero-balanced haemofiltration should be considered for the augmented elimination of bivalirudin in complex surgical procedures with high risk of bleeding complication.

The effect of bivalirudin can be monitored by the prothrombin time, aPTT, international normalised ratio (INR), thrombin time, and ACT as all increase after bolus administration of bivalirudin. The ACT has been used as a guide to monitor dosing of bivalirudin during off-pump surgery[86] as well as during CPB.[87] A plasma-modified ACT has also been used to monitor bivalirudin effect. Preliminary clinical investigations have suggested that bivalirudin may be an appropriate alternative anticoagulant in HIT patients requiring on- or off-pump cardiac surgery. The typical dosing protocol includes a bolus of 1 to 1.5 mg/Kg, 50 mg added to the pump prime and an infusion of 2.5 mg/Kg/hour. Proportionately lower doses can be used for off-pump surgery. The rapid breakdown of bivalirudin entails certain precautions during and after CPB. Clots may be observed in the pericardium in the areas of pooled blood, this may not necessarily mean that additional bivalirudin is required. Similarly, blood remaining in the CPB circuit after tennination of CPB can rapidly clot. Therefore, a cross limb should be added to the circuit to allow for continued circulation of blood after termination of CPB.

The EVOLUTION-off,[88] and-on[89] trials; and the CHOOSE-off[90] and-on[91] trials provide further evidence to the utility of bivalirudin as a substitute for

heparin. The EVOLUTION-OFF trial randomised patients to receive either bivalirudin or heparin for off-pump surgery, and the EVOLUTION-ON trial randomised patients undergoing cardiac surgery with CPB. Likewise, the CHOOSE-OFF trial was performed on patients with HIT undergoing off-pump surgery and CHOOSE-ON trial on patients with HIT undergoing cardiac surgery with CPB. A single centre large experience as well as a recent review have concluded that in experienced hands, bivalirudin anticoagulation can be safety performed during on-pump and off-pump cardiac surgery with and without HIT.[92,93]

Heparin + platelet inhibitors

Administration of a potent platelet inhibitor immediately before heparinisation with unfractionated heparin is yet another method used to manage HIT patients undergoing cardiac surgery. Iloprost, a stable analog of prostacyclin has been used for this purpose. Successful use of iloprost along with heparin has been described in a series of 22 HIT patients undergoing cardiac surgery with CPB.[94] Platelet counts were maintained perioperatively, and no significant thrombotic or bleeding complications were noted. Epoprostenol, a freeze-dried preparation of prostacyclin has also been used before administration of unfractionated heparin.[95] An infusion of epoprostenol (15-30 ng/Kg/min.) can be started and due to its short half-life (6 min.), prompt recovery of platelet function is achieved. Iloprost and epoprostenol both can produce significant hypotension and may necessitate the use of potent vasopressors.

A short acting platelet glycoprotein IIb/IIIa antagonist, also has been used with heparin to provide anticoagulation in HIT patients.[96] Fondaparinux a parenteral factor Xa inhibitor has also been used in a patient with HIT requiring valve surgery.[97] From the above discussion, it is clear that there are many ways of dealing with HIT patients. There is no single heparin alternative that can be appropriate in all situations. The clinicians should consider the availability of agents, the monitoring capabilities, the presence of coexisting diseases that might influence the elimination of the drug, and the familiarity of the team with the agent. The guidelines on the management of HIT patients have been published by the American College of Chest Physicians (ACCP).[98] They are summarised as follows:

1. In patients with a previous history of HIT who is HIT-antibody negative, heparin should be used. This is based on the fact that risks of developing HIT upon heparin re-exposure are less than the risks associated with the use of heparin substitutes.
2. In patients with acute HIT (thrombocytopenia and a positive HIT antibody test), if possible, cardiac surgery should be delayed until HIT antibodies are negative, and then heparin can be used. If surgery cannot be delayed bivalirubin should be used. Off-pump surgery should be preferred over on-pump procedures as smaller doses of anticoagulation are required. Epoprostenol can be used if ECT monitoring is not available and renal dysfunction is present. Tirofiban can be used but, further studies are necessary to define the safety.
3. In the patient with subacute HIT (recent history of HIT with recovery of platelet count, but HIT antibodies are detectable), the risk of developing HIT with re-exposure to heparin is real, hence heparin use should be avoided. Surgery may be delayed, if possible, otherwise they should be treated as those with acute HIT.

Heparin Coated Surfaces

When the CPB in used, the blood comes into contact with foreign surfaces. To diminish this impact, various types of biocompatible coated surfaces have been developed. The different types of biocompatible coatings have included, heparin, trillium, bioline, phosphorylcholine, and polymethoxyethyl acrylate. Heparin can be bound ionically to plastic surfaces. This can decrease thrombus formation and platelet adhesion upon artificial surfaces. By binding heparin to the internal surfaces of the CPB circuit, the need for systemic heparinisation during CPB may be reduced. Surfaces such as cardiotomy reservoir, inline filter and inside and outside surfaces of venous and arterial cannulae will also require heparin coating. Bound heparin inhibits the binding of factors Xa, Ha and XII[99] inhibiting thrombus formation. This technique has also been shown to decrease the release of granulocyte factors because of lower activation of leucocytes[100] and better platelet preservation.

It was shown that the use of heparin coated circuits in combination with full systemic heparinisation is better than the uncoated circuits in terms of

platelet preservation and postoperative bleeding.[101] However, a retrospective analysis comparing heparin coated circuit and full heparin dose (ACT > 480 seconds) versus reduced heparin dose (ACT > 250 seconds) has revealed that the reduced anticoagulation decreases postoperative bleeding, haemoglobin loss, the intubation time and the incidence of postoperative atrial fibrillation in patients undergoing CABG.[102] The same group of authors have recently shown in a large series that heparincoated circuits and reduced level of systemic heparinisation (ACT > 250 seconds) is safe and results in a very satisfactory clinical course without any signs of clotting.[103] Similar results with reduced early postoperative blood loss without enhancing the risk of complications have been published by other authors.[104]

The heparin coated circuits have also been used in other settings such as renal dialysis catheters, extracorporeal membrane oxygenation, miniature extracorporeal circulation, and left ventricular assist devices.[105] The effect of heparin coated circuits on the complement activation and cognitive dysfunction has also been studied. Although, it has been shown that there was less postoperative cognitive dysfunction with the use of heparin coated circuits, it did not correlate with decreased compliment activation intraoperatively and activation of coagulation postoperatively.[106] Thus, heparin coated bypass circuits appear to be a useful alternative to the conventional circuits.

Haemostasis during Open-Heart Surgery

Protamine has been the mainstay of heparin neutralisation for more than 3 decades. Although it is very effective, it has some serious cardiovascular side effects including life threatening and fatal reactions.

Protamine

Protamine is derived from the sperms of salmon fish and is a polycationic protein. It binds with heparin to produce a stable precipitate. It is also capable of producing a mild anticoagulant effect that is independent of heparin. Large doses of protamine are necessary to produce clinically significant anticoagulant effect.[107] Platelet dysfunction has been suggested to be the

mechanism of anticoagulant effect of protamine.[108]

Dosage

At the conclusion of CPB, the remaining heparin in circulation should be neutralised in order to restore normal coagulation. Although it is widely accepted that 1.3 mg of protamine neutralises 100 units of heparin, many different dose regimens for protamine reversal of heparin anticoagulation have been described. This is mainly due to the difficulty in assessment of the residual heparin at the conclusion of CPB. The residual heparin estimation is difficult due to considerable inter-patient variability in heparin metabolism. Nevertheless, it is important to estimate the residual heparin accurately, as un-neutralised heparin can increase postoperative bleeding. The methods that have been used to calculate residual heparin include, ACT/heparin dose response curve, heparin/protamine titration curve and actual measurement of residual plasma heparin level.

The easiest and commonly followed method of calculating the protamine dose, is a fixed dose ratio of protamine to heparin. In this method 1 to 1.3 mg of protamine is administered for each 100 units of heparin. The amount of heparin to be neutralised is taken as the total dose of heparin administered during CPB or the initial dose of heparin.[109] This method is quite simple, as no assays are required and there is no need for ACT measurement. Usually, higher than required dose of protamine is administered, hence, the risk of heparin rebound is reduced. However, it may increase the risk of anticoagulant effect of protamine.[110]

Due to these drawbacks, Bull et al[10] suggested calculations of protamine dose based on heparin dose-response curve. The ACT measured at the end of CPB is utilised to calculate the amount of residual heparin on the basis of dose-response curve. The calculated amount of heparin is neutralised by giving protamine 1.3 mg/100 units of heparin. The advantages offered by using this method are: 1. more accurate calculations of protamine dose than the fixed regime; 2. reduced quantity of protamine administered; 3. possibly decreased infusion of blood, platelets and FFP.[111] The disadvantage of this method is that the method relies on ACT that is affected by many factors and has no correlation with heparin levels.[112]

Measurement of plasma heparin concentration at the end of CPB (protamine titration test-Hepcon) has also been utilised for the purpose of

calculating protamine doses. Decreased protamine doses are likely to be required by this method as compared with ACT/heparin dose-response curve. In this method, tubes with several dilutions of a standard protamine solutions are used. A fixed volume of whole heparinised blood is added to these tubes. The lowest protamine concentration resulting in the shortest clotting time represents the optimal neutralisation of heparin. The total protamine dose is calculated based on the estimated blood volume.

There is evidence that higher than necessary doses of protamine offer no additional benefits and may lead to excessive bleeding and other adverse haemodynamic events.[113]

In clinical practice, the most widely used method of protamine reversal of heparin anticoagulation is to administer protamine in the ratio of 1.3 mg for each 100 units of initial dose of heparin. Following this, ACT is measured, and if found to be more than that of baseline, additional bolus of protamine (25 to 50 mg) is administered. Some anaesthesiologists also like to give this additional bolus dose if bleeding persists even though the ACT is restored to baseline value.

Protamine Reactions

Haemodynamic compromise following protamine administration during cardiac surgery is well known and well documented. The haemodynamic compromise may range from mild hypotension with normal or low filling pressure to profound increases in the pulmonary arterial (PA) and central venous pressure (CVP) with dramatic decreases in left atrial (LA) and systemic arterial pressures.[114] In addition, evidence of bronchoconstriction with elevated airway pressure can be present. The catastrophic pulmonary vasoconstriction after protamine occurs in about 1.5 percent of adult cardiac surgical patients.[115] The important risk factors amongst the many that have been suggested are, valvular heart disease (particularly mitral), preexisting pulmonary hypertension and rapid administration. Kimmel and associates have found that neutral protamine Hagedorn (NPH) insulin use, documented fish allergy, and a history of nonprotamine medical allergies were independent risk factors for protamine reaction.[116] Other unconfirmed risk factors include previous exposure to protamine and a history of vasectomy.

The rate of administration has been shown to be an important factor leading to pulmonary vasoconstriction.[117] The manufacturers recommend

that protamine should not be administered faster than 5 mg/min. This rate of administration is not practical as an average dose of 200 mg will require 40 min. Nevertheless, it is very important that the protamine be administered slowly and carefully. Most anaesthesiologists prefer to administer a bolus of 25 to 50 mg and then carefully observe haemodynamics for a short period of time. If no change is observed, another bolus is administered. If haemodynamic change is observed (hypotension or increased PA pressure), the next bolus is withheld until the haemodynamics stabilise. Slow and careful administration of protamine is perhaps the easiest method of preventing protamine reaction and must be observed (even though there is a temptation to administer it quickly), especially in sick patients.

The site of protamine administration is also considered to be important. Vasoactive substances are released upon exposure of the pulmonary vasculature to protamine. Hence, to avoid drug reaching the pulmonary circulation directly in high concentration, it has been suggested that it should be given in the left side of the circulation (LA, aorta) or via a peripheral vein with subsequent dilution. Conflicting results have been observed in animals, using different sites of injection.[118,119] Studies on humans have not been able to demonstrate any advantage to left-sided versus right-sided protamine administration.[120] The site of injection (central or peripheral vein) has not been shown to influence the incidence of protamine reaction.[121]

There are possibly 3 causes of protamine reaction: 1. pharmacological histamine release; 2. true anaphylaxis mediated by a specific anti-protamine immunoglobulin, and 3. thromboxane release leading to pulmonary vasoconstriction and bronchoconstriction (anaphylactoid reaction). A systematic literature review has revealed a very low incidence of anaphylactic reaction; 0.69 percent in prospective studies, and 0.19 percent in the retrospective studies.[122] However, severe life-threatening protamine reactions have been reported, and still continue to be reported.[123] Regardless of the cause, the end result of protamine reaction is hypotension, the severity of which varies from patient to patient. The diagnosis of protamine reaction in the operation theatre is based on hypotension during or following protamine administration. If the PA catheter is in place, concomitant increase in PA pressure and pulmonary vascular resistance (PVR) can be noticed. In some patients, a diminished contractility of the right ventricle (RV) can be visualised by the naked eye. Transoesophageal echocardiography is a better

way of diagnosing RV dilatation and failure.[124] All these factors should lead to the diagnosis of protamine reaction and appropriate therapy should be instituted.

Therapy

As already emphasised, protamine should be administered slowly and carefully. If adverse haemodynamic response is noticed during administration, the injection should be stopped immediately. Administration of fluids and epinephrine should be instituted. Prophylactic histamine H_1 and H_2 blockers or corticosteroid administration have also been used. A variety of supportive strategies to treat pulmonary vasoconstriction and hypotension can be used. These include, pulmonary vasodilators such as, nitroglycerin and sodium nitroprusside, along with virtually all inotropic drugs. Rarely, reinstitution of CPB may be necessary. Nitric oxide has also been used as a therapy for pulmonary vasoconstriction induced by heparin-protamine complexes in sheep,[125] suggesting that it can be a useful alternative. Inhaled prostacyclin was used to treat acute pulmonary hypertension in a severe life-mreatening protamine reaction.[126] The PA pressure decreased from 70/37 to 45/23 mm Hg within 10 min. of administration of inhaled prostacyclin in this patient.

Avoidance of protamine administration altogether may also be considered, if there is a known food allergy including fish. In one report, heparin coated bypass circuit was used to minimise the amount of heparin necessary for anticoagulation during CPB and haemostasis was achieved without the administration of protamine.[127] In another, bivalirudin was used to perform off-pump surgery.[128]

Other agents used for reversal of anticoagulation

Platelet factor 4

PF4 binds and neutralises heparin when released during platelet aggregation. The PF4 is released at the site of vascular injury and binds heparin, thus facilitating thrombin accumulation and clot formation. Recombinant PF4 is capable of neutralising the heparin. The effect is achieved by neutralising

heparin's inhibition of factor Xa and thrombin. Recombinant PF4 has been shown to effectively neutralise the heparin effect[129,130] and can be a useful alternative to protamine in patients undergoing cardiac surgery.

The enzyme heparinase has been investigated as an alternative to protamine, especially for patients with known hypersensitivity to protamine. Initial results indicate that heparinase may be useful as an alternative to protamine, not only in patients who have protamine allergy but also as a general method for reducing blood loss after CPB.[131]

Other drugs that have been used for heparin reversal include polybrene and toluidine blue. In the earlier days, polybrene was commonly used to reverse heparin following CPB in humans.[132,133] It was withdrawn in 1962 because of suspected nephrotoxicity.[134] Increase in PA pressure and decrease in systemic arterial pressure are other drawbacks of this agent.

Toludine blue has also been used for heparin reversal but is less effective than protamine and is associated with methaemoglobinaemia.[135]

Protamine has remained the heparin neutralising agent for over 3 decades. However, the need to reduce homologous blood use during cardiac surgery is widely recognised. The increasing awareness of risks associated with homologous blood transfusion has been mainly responsible for this. Consequently, several methods of blood conservation have been described. This has also been due to the fact that more and more patients at increased risk of bleeding are being subjected to cardiac operations. These include, patients undergoing repeat surgery, patients with sepsis and endocarditis, urgent/emergency CABG in patients receiving aspirin pretreatment, and heart transplantation. The use of pharmacological agents such as aprotinin, desmopressin acetate, epsilon aminocaproic acid (EACA) and tranexamic acid (TA) is widely practised in this subset of patients. They are discussed in detail in chapter 11.

Recombinant activated factor VII

Recombinant activated factor VII (rFVIIa), a coagulation factor is now available and has been used for the management of excessive bleeding during cardiac surgery. It exerts its pharmacological action by inducing thrombin generation on locally activated platelets and leads to formation of a stabilised fibrin clot at the site of vessel injury.[136] In the initial period, several case reports demonstrated the utility of rFVIIa in refractory bleeding associated

with trauma and cardiac surgery. Its utility in terms of reducing the blood loss, transfusion requirements, and reexploration rates has been shown in cardiac surgery in adult and paediatric population[137,138] as well as vascular surgery.[139] However, safety concerns were raised on the potential danger of severe thromboembolic events with its usage.[137,140,141] The Canadian Consensus Conference in 2007 recommended that due to lack of evidence, rFVIIa should be considered only in cardiac surgical patients who develop refractory haemorrhage.[142]

A wide range of dosage has been used, but most authors recommend a single dose of 90 μg/Kg for refractory bleeding during cardiac surgery. A lower dose 20–40 μg/Kg can also be used and repeated, if necessary. The results of rFVIIa therapy have been analyzed in two recent meta-analyses. The first one by Levy et al[143] in 2010 included 35 randomised clinical trials with a total number of 4468 patients in various clinical settings. They demonstrated a significantly increased risk of arterial (5.5 percent versus 3.2 percent, $P < 0.003$), but not venous thromboembolic events. The second one by Ponschab, et al[144] in 2011 included 6 clinical trials in cardiac surgery patients ($n = 470$) and concluded that administration of rFVIIa in cardiac surgery patients could result in a significant increase in stroke with a trend towards reduction of the need for surgical reexploration.

Therefore, it seems that rFVIIa should be considered with caution only in the setting of refractory haemorrhage.

Patients on Anticoagulants

Patients with ischaemic heart disease are managed acutely or chronically with pharmacological agents including aspirin, heparin, and antiplatelet agents. Likewise, patients with valvular heart diseases or with low left-ventricular ejection fraction may be receiving antithrombotic agents including warfarin.

The advances in PCI such as intracoronary stent placement have led to the use of antiplatelet medication to maintain stent patency and prevent stent thrombosis. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend administration of dual antiplatelet therapy (aspirin and clopidogrel) for a period of one year following drug eluting stent placement.[145] In addition, glycoprotein IIb/IIIa receptor antagonists and LMWH are recommended during post-intervention

period.[145] These patients may require urgent or emergency surgical revascularisation. They pose considerable challenge regarding management of postoperative bleeding. The various strategies to minimise bleeding in such patients include stopping the anticoagulation therapy, platelet, and/or coagulation factor transfusion, and considering rFVIIa administration for refractory bleeding.

It has been shown that patients receiving clopidogrel within 24 hours of surgery are at an increased risk for transfusion and haemorrhagic complications.[146] A strategy to delay surgery after clopidogrel treatment is suggested, but the optimal waiting period after clopidogrel treatment is controversial. Some suggest that this period should be at least 5 days before CABG[147], others say that elective CABG should be delayed for 7 days[148], and yet others consider that this period should be at least 2 days.[149] For patients undergoing off-pump CABG, discontinuation of clopidogrel for 3 days has demonstrated similar blood loss pattern as compared with a control group.[150] It appears that balancing individual risks for thromboembolism (if clopidogrel is discontinued), and excessive bleeding (if clopidogrel is continued) is an important consideration, and the results of randomised controlled trials should further clarify the antiplatelet management of CABG patients.[151]

Evaluation of Coagulation Abnormalities

Excessive bleeding after CPB is a persistent problem in cardiac surgery. It occurs in 5 to 25 percent of patients and is a major contributor to morbidity and mortality.[152] Many factors are considered to be responsible for bleeding following cardiac surgery. After surgical control of bleeding has been achieved, these include heparin and protamine administration, platelet dysfunction, fibrinolysis, decrease in the various coagulation factors, and patients who have received thrombolytic therapy and aspirin. Amongst these, acute acquired platelet dysfunction is considered to be the main cause of nonsurgical bleeding after CPB.[153-156] There is a significant decrease in the platelet count after CPB. The major portion of the decrease occurs in first 2 to 5 min. In addition, the function of platelets (adhesion and aggregation) is

significantly reduced after CPB. The various causes attributed to these effects are haemodilution, platelet aggregation on foreign surfaces, platelet sequestration and destruction. The degree of platelet dysfunction is proportional to the duration of CPB and the depth of hypothermia and is usually partly reversed within one hour after the termination of CPB. Usually, the platelet abnormalities occurring after CPB are not clinically important because coagulopathies requiring platelet therapy do not develop in most patients undergoing cardiac surgery.[157] Despite heparin anticoagulation, thrombin and, in consequence, plasmin (both are effective platelet stimulators) are generated during CPB to some extent. This is due to the fact that heparin is not capable of inhibiting thrombin action completely. In particular, the thrombin that is bound to fibrin is not accessible for the heparin AT-III complex. This inability of heparin to suppress thrombin action completely, appears to play a major role in coagulation disorders after CPB.[158]

Tests for coagulation mechanism

(Table 10.1)

Whole blood clotting time

The Lee-White whole blood clotting time (WBCT) is the simplest coagulation test. Blood is placed in a glass tube at 37°C and it is tilted every 30 seconds until fluid does not run along the side of the tube. The coagulation process is initiated by the glass surface of the tube. The normal WBCT is 5 to 12 min. The test is simple and inexpensive but is cumbersome and takes time. WBCT is prolonged excessively after heparin administration and timely results cannot be obtained to guide anticoagulation for CPB.

ACT and protamine titration tests are other clinically useful tests that have already been discussed.

Table 10.1: Tests for coagulation abnormalities.

Tests for coagulation mechanisms
Whole blood clotting time
Activated clotting time
Protamine titration test
Prothrombin time
Activated partial thromboplastin time
Tests for platelet function
Platelet count
Bleeding time
Platelet aggregation and adhesion
Tests for fibrinolysis
Fibrinogen and fibrin degradation products
Thromboelastograph

Prothrombin time and activated partial thromboplastin time

The prothrombin time (PT) and the activated partial thromboplastin time (aPTT) are commonly used to evaluate the extrinsic and intrinsic pathways of coagulation respectively. Although, PT and aPTT are accurate and reproducible, they carry a high false positive rate with respect to diagnosis of coagulopathy after CPB. Therefore, they have limited usage. Prolongation of PT and aPTT in the immediate post-bypass period is known to occur,[159,160] but an acceptable prolongation of PT and aPTT values after CPB is not well defined. An elevated PT and aPTT after CPB may be associated with coagulopathy and severe blood loss or merely an abnormal test value without any obvious clinical significance.[161] Therefore, platelet function tests should be used along with PT and aPTT to evaluate excessively bleeding patients after CPB.

For the performance of these tests, supernatant obtained by centrifugation of anticoagulated blood is utilised. The tissue extract thromboplastin is added for PT whereas, only a portion of thromboplastin along with an activator (celite, kaolin) is added for aPTT. Time required for the formation of gel after addition of Ca^{++} is recorded. Normal PT and aPTT are 12 seconds and 32 seconds respectively. However, the response varies with the quality and type of thromboplastin and activator used. Therefore, the results should

accompany the control reading indicating the result for normal plasma.

The calculation of INR permits the comparison of PT results from different commercial thromboplastin reagents. INR=PCR^{ISI}, where PCR is the ratio of the PT of patient sample and control sample, and ISI is the international sensitivity index, which is a measure of responsiveness to decreased concentrations of vitamine K-dependent factors.

Bedside automated monitors for PT and aPTT are available, the results of which correspond well with the laboratory measurements.

Thrombin time

Addition of thrombin to a plasma sample will lead to fibrin formation within 10 seconds, if fibrinogen is present, and heparin and fibrin degradation products (FDP) are absent. However, detectable prolongation of thrombin time requires significantly lower and higher levels of fibrinogen and FDPs respectively.

Tests for Platelet Function

Platelet Count

The normal platelet count is 1,50,000 to 3,50,000/mm^3 but it does not signify that the platelets are functionally normal. Abnormal platelet function in the face of normal platelet count can be a cause of excessive bleeding. However, it is an important test as platelet count below 1,00,000/mm^3 is associated with excessive bleeding during and after surgery.

Bleeding time

It measures the duration of blood seepage following a standard skin incision. A template device (template bleeding time) is used to make an incision on the forearm. The wound is blotted every 30 seconds until staining of the paper stops. The normal bleeding time is 4 to 10 min. and indicates platelet counts greater than 1,00,000/mm^3 with normal function.

Platelet aggregation and adhesion

Platelet aggregation and adhesion can be studied in the laboratory and offers the functional status of the platelets. Platelet aggregation is studied by adding aggregating agents (adenosine diphosphate, collagen, adrenaline). Maximum

increase in light transmission after addition of the aggregating agents is defined as maximum aggregation (read as percentage increase). For platelet adhesiveness, glycoprotein Ib (GpIb) receptors on platelets are measured which are the platelet adhesive receptors. Fluorescence flow cytometry is utilised for this purpose.

Tests for Fibrinolysis

Fibrinogen and fibrin are broken down by plasmin giving rise to fibrinogen and FDPs. Estimation of the fibrinogen and FDPs provides a measure of fibrinolysis.

The results of FDP are provided as negative (< 10 µg/mL) or positive (> 10 µg/mL). Quantitative analysis giving actual levels of FDPs are available, but are expensive

D-Dimer

D-Dimer is a specific degradation product of fibrin and can be detected in a semiquantitative or fully quantitative manner. It is more specific for secondary fibrinolysis than the FDP, and is normally less than 0.5 µg/ml.

Clot dissolution and lysis of normal clot also indicate the fibrinolytic activity.

Thromboelastograph

Thromboelastograph (TEG) provides a measure of global coagulation function and measures the haemostatic process in the whole blood from the start of clotting to clot lysis. The blood sample is placed in a cuvette that is rotated. A piston is placed at the centre of the cuvette leaving small blood filled rim around the piston. When the fibrin strands are formed, the piston is engaged and the rotatory motion is transferred to the piston which is recorded on a slowly moving chart recorder. The test can be performed rapidly by addition of celite to the cuvette.

The TEG recording depicts the time on ‘x’ axis and coagulation on the ‘y’ axis in mm. Various parameters on TEG recording should be noted. These include the time from sample placement to initial pen deflection (reaction time r: normal 6 to 8 min.), the time from initial pen deflection to tracing width of 20 mm (amplitude-K, normal 3 to 6 min.), the angle formed by a tangent of the amplitude tracing at the initial pen deflection (α, normal 45 to

50 degrees), the maximal amplitude (MA, normal 50 to 60 mm) and the amplitude 60 minutes following its maximum (A_{60}, normal within 5 mm of MA). The normal TEG has a characteristic shape (Fig. 10.2). Since it reflects a global physical property of clot formation, its results are not diagnostic of any specific abnormality.

TEG is useful to know if abnormal coagulation exists which indicates that further tests are necessary. TEG based coagulation monitoring has been shown to be effective in reducing the reexportation rate.[162] It is also useful for the diagnosis of fibrinolysis where it gives a characteristic “tear drop” shaped tracing. This can be confirmed by restoration of normal tracing by addition of antifibrinolytic agent to the sample.

Heparinase has been used to neutralise the heparin effect in a blood sample before performing TEG. This has been shown to improve the management of bleeding and transfusion of blood products in the postoperative period by doing TEG either during CPB[163] or 10 and 60 min. after protamine administration.[164]

Routine application of TEG-based transfusion algorithm for blood and blood products has been utilised following cardiac surgery. It has been shown that this leads to reduction in consumption of blood and blood products in patients undergoing CABG.[165] TEG has also been shown to be beneficial in guiding rFVIIa therapy in patients with refractory haemorrhage. The odds of response to rFVIIa therapy was greater in presence of one abnormality in TEG measures (r time, K time, alpha angle, and maximum amplitude) as compared with two or more abnormalities.[166]

Despite controversies regarding, whether laboratory coagulation results are useful in managing the postoperative bleeding, clinicians continue to use them. The ways on how the monitoring technology can be used to derive maximum benefit to the patient will continue to be sought.

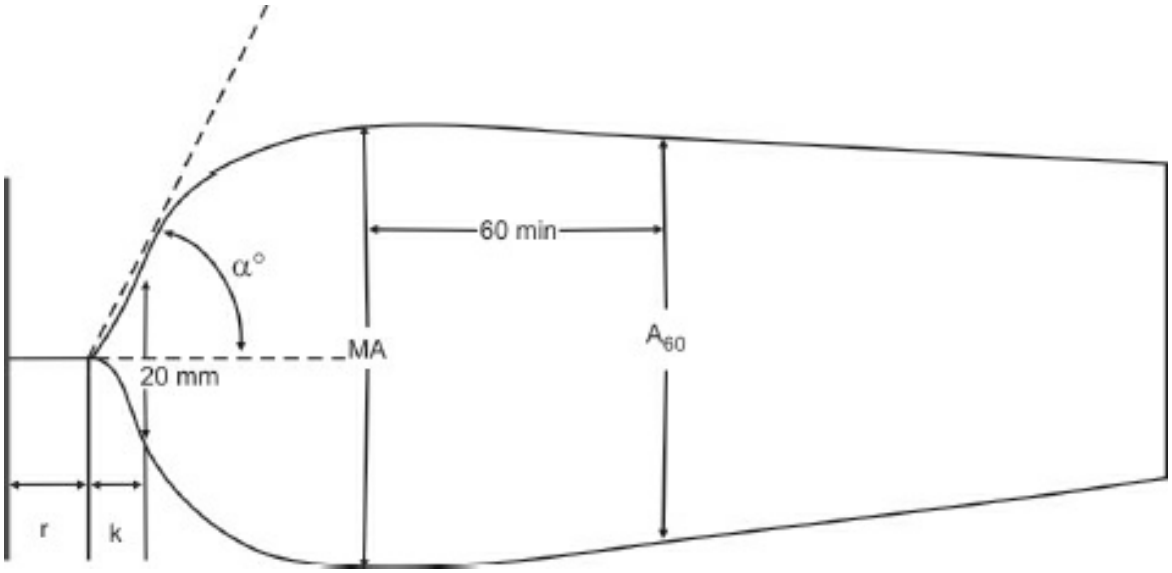

Figure 10.2: Schematic representation of thromboelastograph (for details refer to the text).

Excessive bleeding after cardiac surgery continues to be an important problem and the protocols for the management of excessive bleeding vary from centre to centre. However, in general, platelet dysfunction is considered to be an important reason for haemostatic abnormality following CPB and adequate therapy is directed to achieve better platelet preservation.

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Chapter 11: Blood Conservation during Cardiac Surgery

Cardiac surgery is one of the largest users of blood and blood products. It is estimated that in the U.K., about 15 percent[1] and in the USA, 10 to 20 percent[2] of the blood stocks are used for cardiac surgery. Approximately 20 percent of patients have significant bleeding after surgery and 5 percent require re-exploration for cardiac tamponade.[3,4] The increased blood loss is due to the surgical interventions performed on major vascular structures as well as the coagulation abnormalities that accompany extracorporeal techniques. The damage and the shortened life span of red blood cells and coagulation factors due to cardiopulmonary bypass (CPB) increase the need for blood and blood products with these procedures. Advanced age, low preoperative red blood cell volume (preoperative anaemia or small body size), preoperative antiplatelet or antithrombotic drugs, complex procedures or emergency operations, and patient comorbidities are some of the risk factors for increased bleeding.

Despite the fact that a large proportion of cardiac surgical work has been replaced by the interventional procedures performed by the cardiologists, the number of cardiac operations is increasing. In addition, the number of reoperations is on the rise. These patients have dense adhesions and more chances of injuries to the vascular structures. Therefore, they are likely to bleed more, increasing their transfusion requirements. This has obviously placed tremendous load on the blood banks.

In the early days, use of 8 to 12 units of blood during each open-heart surgical procedure was not uncommon.[5,6] Acceptance of normovolaemic anaemia along with better understanding of the coagulation management during CPB, autologous blood donation and scavenging of shed blood with

reinfusion as well as development of pharmacological methods of reducing blood loss led to substantial decrease in the blood usage. A large number of operations could be performed without transfusion, but until recently transfusions were still required in more than 50 percent of all cardiac surgery patients.[7]

There is growing recognition of the fact that transfusions are independently linked to increased short- and long-term morbidity and mortality. Murphy et al[8] found no benefit from transfusion for haematocrits as low as 21 percent (haemoglobin of 7gm/dL), and the risk of death within 30 days of surgery was almost 6 times greater for patients who received blood. Further, transfused patients were more likely to experience increased infections and ischaemic complications (myocardial infarction, renal compromise, and stroke). Even transfusion with as little as one unit of red blood cells has been associated with decreased 10 years survival after coronary artery bypass grafting (CABG).[9]

In a comparison of 123 Jehovah's Witnesses (who did not receive any transfusion) versus a control group, it was shown that there was no difference in the outcome in the two groups.[10] This shows that avoidance of blood transfusion is possible and perhaps, implies that the transfusions may be unnecessary. Also, the CPB related technology has refined further and the expertise of the team has improved. However, the blood transfusion practice has not shown much further change in recent times and even shows a wide variation.[11]

One of the reasons for such a practice is related to the reluctance to accept normovolaemic anaemia, which is an integral part of blood conservation. Also, there is a general belief that transfusion of one or two units of blood is safe. It has now been shown that blood conservation is safe and effective in reducing transfusions and tolerance of perioperative anaemia does not increase the complications, or death in cardiac surgery.[12] In fact, avoidance of transfusion reduces the risk of complications.[12]

The Society of Thoracic Surgeons (STS) and the Society of Cardiovascular Anesthesiologists have recently updated the practice guidelines for blood conservation.[13] They admit that much has changed since the previously published 2007 blood management guidelines by them. The areas of major revisions include:

1. Management of dual anti-platelet therapy before operation,
2. Use of drugs that augment red blood cell volume or limit blood loss,
3. Use of blood derivatives including fresh frozen plasma (FFP), factor XIII, leukoreduced red blood cells, platelet plasmapheresis, recombinant factor VII, antithrombin III, and factor IX concentrates,
4. Changes in management of blood salvage,
5. Use of minimally invasive procedures to limit perioperative bleeding and blood transfusion,
6. Recommendations for blood conservation related to extracorporeal membrane oxygenation and cardiopulmonary perfusion,
7. Use of topical haemostatic agents, and
8. New insights into the value of team interventions in blood management.

It seems that there is a need to re-evaluate the use of blood transfusion in elective cardiac surgical patients with the intention to avoid unnecessary blood transfusions, thereby reducing the adverse effects and costs. Reduction of blood product use during cardiac surgery is a desirable goal for all patients.

In this chapter, the various blood conservation techniques that are commonly utilised during cardiac surgery will be discussed (Table 11.1). The choice of technique varies from place to place and a multimodal approach, especially in high-risk patients should be practised.

Table 11.1: Showing the various blood conservation techniques used in cardiac surgery

Autologous blood donation – preoperative – intraoperative (acute normovolaemic haemodilution) – retrograde autologous priming
Autologous platelet-rich plasma
Intraoperative blood scavenging
Postoperative blood scavenging
Ultrafiltration – conventional – modified
Pharmacological therapy – EACA – TA – Desmopressin acetate – Aprotinin
Low prime, surface-coated bypass circuits

EACA: Epsilon aminocaproic acid, TA: tranexamic acid

Autologous Blood Donation

The preoperative autologous blood donation for postoperative reinfusion was first reported in 1921.[14] However, it was not practised actively until open-heart surgery became commonplace. It was known that normal healthy volunteers[15] as well as debilitated patients[16] could tolerate preoperative donations before planned surgical procedures with maintenance of haemoglobin over 10 g/dL with supplemental iron. The fact that patients readily tolerated haemodilution during CPB, further led to the development of interest in preoperative autologous donations. Subsequently, the collection of autologous blood intraoperatively during the planned open-heart surgical procedures, utilising haemodilution techniques was described for reducing homologous blood usage.[17] It has been shown that preoperative autologous blood donation reduces the need for allogeneic blood products in adults as well as children undergoing cardiac surgery.[18-20] Predonation of as many as 3 units of blood has been practised, with allogeneic blood transfusion rate being inversly related to the number of predonated units.[18] However, preoperative autologous donation is not widely practised, and much more

common is the intraoperative collection of autologous blood either before the institution of CPB or during the very early phases of bypass process. This may be partly related to the fact that preoperative autologous donation is expensive and can be applied to elective patients only. In the developing countries, preoperative donation of blood is rarely practised due to logistic reasons.

Intraoperative autologous blood donation (also called as acute normovolaemic haemodilution, ANH) and its reinfusion provides the patients with fresh blood that is richer in 2,3 diphosphoglycerate (DPG), platelets and clotting factors than bank blood.[21] The technique involves intraoperative withdrawl of a part of circulating blood volume and the substitution with crystalloid and colloid solution to obtain fresh whole blood to transfuse after the end of surgery. Generally, the autologous blood is collected intraoperatively after induction of anaesthesia, but before the initiation of CPB. Normovolaemia is maintained by simultaneous infusion of crystalloid or colloid which leads to haemodilution. A reasonable quantity of blood from the patient is withdrawn and collected into sterile blood collection bags containing citrate phosphate dextrose (CPD) anticoagulant and stored at room temperature and is saved from the deleterious effects of the heart-lung machine. Reinfusion of this blood after the termination of CPB offers coagulation factors and platelets. In addition, it acts as an excellent volume expander. The autologous blood can be collected from almost all the patients undergoing open-heart surgery. However, the patient should be haemodynamically stable and have adequate haemoglobin concentration.

Physiology of anaemia and Oxygen Transport

One of the most debated issues is the degree of haemodilution. An understanding of the physiology of anaemia and oxygen transport is necessary for this purpose. Oxygen supply should be adequately matched to tissue oxygen needs to ensure aerobic cell respiration. The whole body oxygen delivery (DO_2) is the product of cardiac output (CO) and arterial oxygen content (CaO_2) (DO_2 is in mL/min, CO in L/min, and CaO_2 in mL/L). CaO_2 is the sum of haemoglobin based oxygen and the oxygen dissolved in plasma.

CaO_2 = (arterial oxygen saturation, SaO_2) (1.39 × Hb) + 0.003 × (arterial oxygen tension, PaO_2)

Under physiological conditions, DO_2 (800–1200 mL/min.) exceeds oxygen consumption (VO_2, 200–300 mL/min.) with an oxygen extraction ratio (O_2ER) of only 20–30 percent.

Thus, a marked isolated decrease in haemoglobin concentration (with all other determinants of DO_2 remaining constant) will still be able to meet tissue oxygen requirement. However, below a critical threshold of haemoglobin concentration, there will be a decrease not only in DO_2, but also in VO_2. This is described as critical DO_2, the level of DO_2 at which there is a decrease in the VO_2 signifying tissue hypoxia. Ideally, it seems that the trigger for transfusion should be VO_2 rather than the haemoglobin concentration. The alternative triggers that indicate tissue hypoxia are O_2 ER of 0.44, mixed venous oxygen tension 34 mm Hg, and mixed venous oxygen saturation 56 percent. However, these are not commonly used criteria for deciding blood transfusion.

The physiological adaptations to nomovolaemic anaemia that help to maintain tissue oxygenation are; increase in CO (due to reduced, blood viscosity, decreased systemic vascular resistance and afterload, increased sympathetic activity), redistribution of blood flow (to heart and brain), rightward shift of the oxygen dissociation curve (due to increased synthesis of 2, 3 DPG in red cells) and increase in O_2ER. In addition to these adaptive measures, general anaesthesia and induced hypomermia further assist by decreasing the tissue oxygen requirement. The literature suggests that tissue oxygenation is maintained in healthy normovolaemic persons with a haemoglobin of 6–7 g/dL and haematocrit of 15–20 percent[22,23] and that there is no increase in mortality rate among cardiac surgery patients until perioperative haemoglobin was < 5 g/dL.[24] In addition, no change in myocardial lactate extraction or production after CPB with haemodilution to haemoglobin of 5 g/dL has been shown[25] and in a large series of Jehovah's Witness (4722 patients), it was shown that most patients who died had haemoglobin of < 5 g/dL.[26] These reports, however, need confirmation in patients with compromised left ventricular function, as compensatory increase in CO may not occur in them.

According to the STS guidelines[13], during CPB with moderate hypothermia, transfusion of red blood cells for a haemoglobin of 6g/dL or less is reasonable except in patients at risk for decreased cerebral oxygen delivery (i.e. history of cerebrovascular accident, diabetes mellitus, cerebrovascular disease, carotid stenosis), in which case higher haemoglobin levels may be justified. The haemodilution can be cardioprotective, and it has been shown that the troponin-I levels, and myocardial fraction of creatine kinase were significantly lower in patients undergoing CABG and aortic valve replacement.[27,28] Optimization of pre-ischaemic myocardial oxygen delivery and/or consumption and the post-conditioning effects of endogenous erythropoietin are the potential mechanisms for the cardioprotection.[28] In addition, moderate acute normovolaemic haemodilution does not compromise left ventricular systolic and diastolic function in patients with coronary artery disease, as shown by transoesophageal echocardiography (TOE).[29]

The quantity of blood that can be safely donated is determined by the patient's blood volume, the preoperative haematocrit and the acceptable haematocrit on CPB. It is crucial to balance the amount of blood withdrawn and the acceptable haematocrit on CPB, as excessive haemodilution may lower the haematocrit below the transfusion threshold necessitating transfusion of autologous blood during CPB. This will negate the beneficial effects on erythrocytes and coagulation protection. In general ANH is performed when the haematocrit is over 35 percent and the patient is haemodynamically stable. The amount of blood withdrawn has been variable. Some authors have removed 15 percent[30], while others have removed as much as 40 percent of the estimated blood volume.[31]Thus, the volume of blood removed has ranged from 700 mL[30], 700–1000 mL[32], and 1280 mL.[33]

Some other authors have harvested substantially less blood. In one study, a volume of only 360 ml was withdrawn as the patients were small with low preoperative haematocrit[34], while in another, 500 ml was withdrawn, as the authors wanted to use it as an adjunct to a standardised intraoperative blood sparing protocol.[35]

During donation, haemodynamic stability should be maintained. It is, therefore, essential to perform careful haemodynamic monitoring during the process of donation. Normovolaemia is maintained by simultaneous administration of crystalloid (twice the volume of donated blood) or colloid

(equivalent amount of donated blood). Many techniques have been described for obtaining blood. The most widely accepted access routes are through a central venous catheter, an arterial catheter or the venous tubing of the heart-lung machine. If the blood is collected from the central venous catheter, the blood collection bag containing anticoagulant CPD is connected to the central venous catheter via a sterile intravenous tubing. The blood collection bag is then placed below the level of patient's heart and the blood is allowed to collect into the bag by gravity to limit shear effects on the platelets. Simultaneously, crystalloid solution is infused through a peripheral intravenous line to replace the blood volume. This technique is attractive as it is simple and the blood loss is gradual so that it can be easily compensated by intravenous fluid replacement. The major limitation of the technique is that it is relatively slow. The period from the start of anaesthesia to the institution of CPB is generally short and is not enough to allow blood collection by this method. Therefore, a three way tap may be incorporated between the central venous line and the tubing of the blood collection bag. A 50 mL heparinised syringe can then be used to aspirate patient's blood and push it into the blood collection bag by turning the three way tap. However, this may be associated with increased blood trauma. Alternatively, a separate wide bore cannula may be inserted into the internal jugular vein for this purpose.

Another method of blood collection is through an arterial cannula which allows for a fairly rapid collection of blood. However, there is an increased risk of transient hypovolaemia and hypotension with the procedure. In addition, if only one arterial cannula is in place, monitoring the blood pressure may become a problem during removal of blood.

The blood can also be collected immediately prior to the institution of CPB via the venous line. This can be achieved by placing a 'Y' connector in the venous line near the reservoir. At the time of initiating the bypass, the patients blood can be directed into the blood collection bag by the perfusionist by clamping the appropriate limb of the 'Y' connector. Initially the limb of the 'Y' connector that leads to collection bag is clamped and the pump prime is allowed to drain into the reservoir. When the venous blood starts entering the reservoir, the limb of the 'Y' connector leading to the reservoir is clamped and the blood is diverted into the collection bag by releasing the clamp on the tube leading to it (Fig. 11.1). Simultaneously, the pump prime is transfused through the arterial cannula to replace the volume loss. After the required quantity of blood has been collected, the drainage

tubing to the collection bag is clamped and the venous return is redirected to the reservoir.

This method is attractive, as large volumes of blood can be collected quickly, without disturbing the haemodynamic stability. At the time of blood collection, the patient is fully heparinised so that the collected blood also contains significant heparin. This will require neutralisation by protamine after it is transfused back to the patient. The preservation of platelets and coagulation factors by using this technique is reported to be satisfactory.[30]

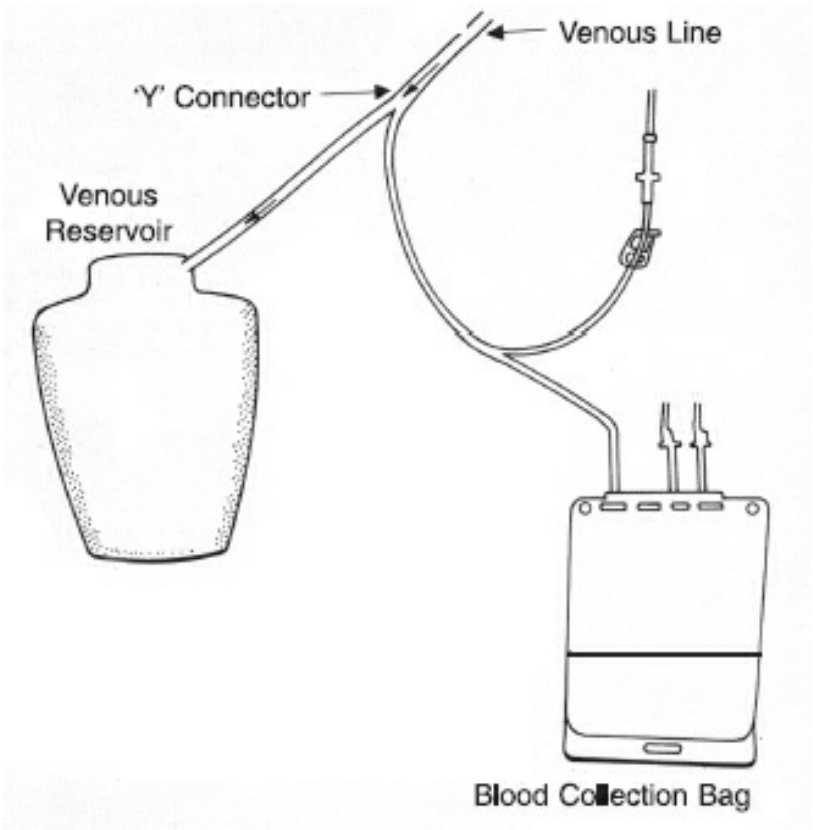

Figure 11.1: The technique for autologous blood collection from the venous line of the bypass circuit is shown. The blood is collected via 'Y' connector into the blood collection bag. For details refer to the text.

Since the time when the ANH was first proposed in the 1960s[17], it has been used extensively in cardiac surgery. However, the benefits of this technique have been reported to be variable. Some of the earlier studies[36], as well as recent ones [37,38] failed to demonstrate any desirable effect of ANH. Some recent studies have demonstrated the benefit of ANH in terms of reduction of postoperative bleeding or reduction of the need for allogeneic

transfusion or both.[39-41]

The improvement in the platelet number and function utilising this technique has also been demonstrated.[30,42] This method, however, does not provide any additional benefit, if it is combined with intraoperative cell saver and high-dose aprotinin.[31] One of the problems with most of the studies has been the fact that they were not prospective randomized, leaving scope for bias. Withdrawing less volume has not been shown to be beneficial[34,35,43] and some authors consider that only high volume ANH is necessary to achieve the beneficial effects.[44] It seems that the technique should be used judiciously with the aim of harvesting large volumes of autologous blood. In case, withdrawl of large volume is not feasible (low body weight and/or haematocrit), the benefits may be obtained by combining the technique with other techniques, such as a cell saver.[34] The simplicity of this technique makes it attractive, especially in patients in whom larger quantities of blood can be withdrawn. It requires minimal preoperative preparation and is suitable for emergency and elective procedures. One should be careful while using this technique so that complications such as mistaken transfusion to a different patient, bacterial contamination of the collected blood, and haemodynamic instability are avoided.

Retrograde Autologous Priming

The haemodilution produced by the CPB prime can be minimised by increasing the hematocrit of the prime. One of the ways of doing this is by retrograde autologous priming of the CPB circuit by the patients's blood. In this method, after cannulation of the aorta, blood is drained retrogradely into the reservoir just before initiating the CPB. Around 400 to 500 mL of blood can be drained in this fashion so that the volume of crystalloid prime is reduced. Careful haemodynamic monitoring should be performed to guide the retrograde withdrawal of blood. This method has been shown to be safe and effective in patients undergoing CABG.[45] The value of this method lies in small patients in whom large quantities of blood cannot be withdrawn during ANH. In a recent study performed on patients with body surface area of less than 1.5 m^2, with autologous priming, a mean volume of 615 ml of priming solution was replaced with autologous blood.[46] This allowed a significantly higher haematocrit value during CPB and reduced the blood transfusion requirement as compared with the control group. It has also been

shown to be particularly useful in Jehovah's Witness utilising a low-prime perfusion circuit.[47]

Intraoperative Blood Scavenging

Blood lost from the operative field can be salvaged and after processing, it can be reinfused. This is called auto-transfusion. The first application of auto-transfusion dates back to 1918, when patients with severe postpartum haemorrhage were transfused the shed blood.[48] It was rarely used thereafter, mainly due to the nonavailability of the equipment that is necessary for washing and processing of the shed blood. The developments in the techniques of blood storage and banking during this period led to wide acceptance of the homologous transfusion. In the 1970s, increase in the number of open-heart surgical procedures along with the concerns about disease transmission associated with homologous blood transfusion led to the revival of interest in auto-transfusion techniques. Devices for red blood cell washing and reinfusion (cell saver) were developed. Some of the devices currently in use are; Bentley, Haemonetics, Dideco-Shiley, etc. (Fig. 11.2). These devices wash the red cells and remove the activated coagulation factors, free haemoglobin and blood cell debris.

Techniques of blood scavenging

When the patient is on CPB, he is fully heparinised. Any blood that is shed in the pericardial cavity during this period can be sucked by the cardiotomy suction of the heart-lung machine and can be returned to the patient. However, due to the fear of clot formation in CPB circuit, the cardiotomy suction cannot be used before heparinisation and after neutralisation of heparin with protamine. Any blood loss occurring during this period is normally wasted. The cell washing devices can collect this blood via a heparinised suction tubing into a reservoir. As patients undergoing repeat surgery are more likely to bleed excessively before and after CPB, the cell washing devices are particularly useful in them.

The blood collected in this fashion into the reservoir of the cell washing device is first of all filtered to remove any clots and debris. The filtered anticoagulated blood is then processed in a centrifuge bowl, where the blood components are separated. The heavier, more dense blood components are

centrifuged outward and the lighter, low density components float inwards towards the bowl's centre. The lighter supernatants are discarded and the red cells are washed with saline to remove debris, plasma free haemoglobin and anticoagulants. The remaining red cells are collected into a collection bag. The haematocrit of the blood processed in this fashion can be as high as 70 percent.[49] Many studies have demonstrated that the use of this technique is safe and effective in reducing homologous blood transfusion during open-heart surgery[34,50-52] The fear that reinfusion of a platelet and coagulation factor depleted blood product can lead to coagulation defects and that processing might alter the stability of the cell membrane, has been proved to be wrong.[50] A meta-analysis that included thirty one randomized trials involving 2282 patients has concluded that the use of cell saver reduces the exposure to allogeneic blood products or red blood cell transfusion for patients undergoing cardiac surgery.[53] Subanalysis of the results suggest that a cell saver may be beneficial only when it is used for shed blood and/or residual blood or during the entire operative period. Processing cardiotomy suction blood with a cell saver only during CPB has no significant effect on blood conservation and increases FFP transfusion.[53] The published studies have limitations such as inconsistent use of other blood transfusion-sparing strategies. The recently published Cochrane Database review on the subject acknowledges this fact, but suggests that cell salvage is efficacious in reducing the need for allogeneic red cell transfusion in adult elective cardiac and orthopaedic surgery without adversely impacting the clinical outcomes.[54]

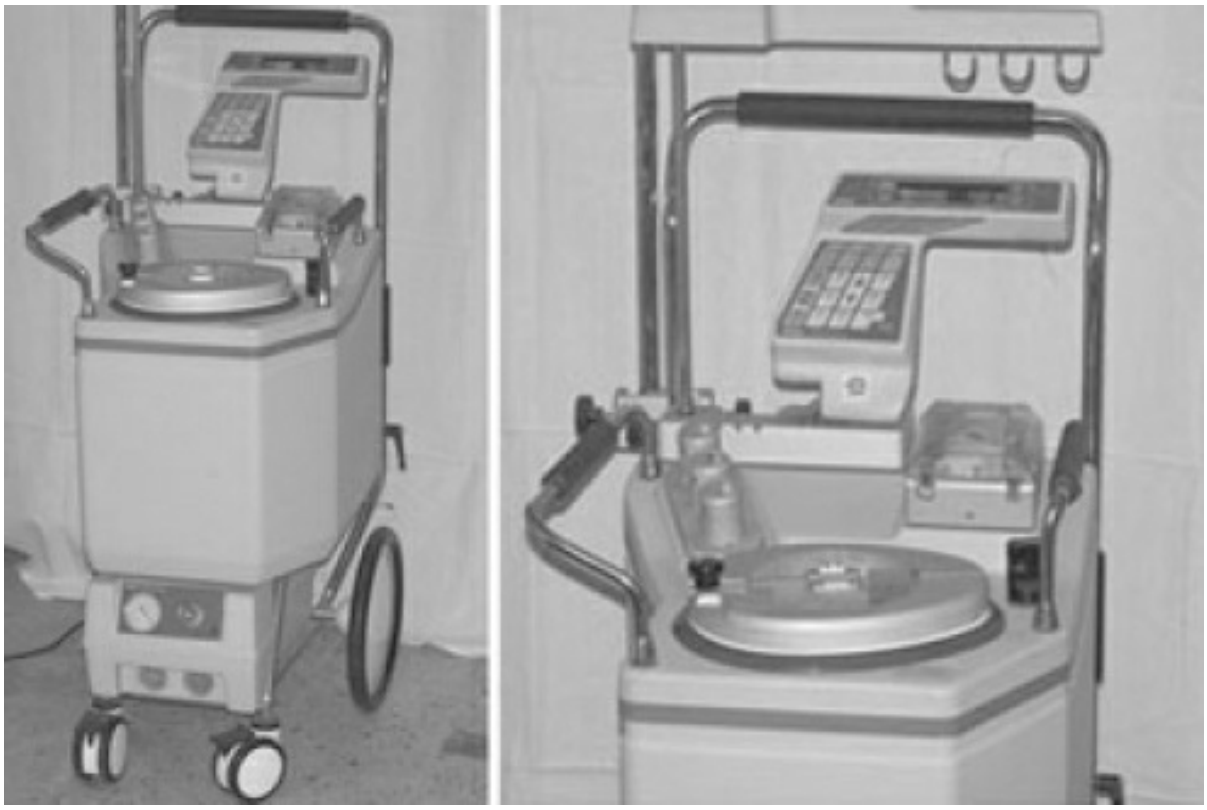

Figure 11.2: A cell washing device (Dideco-Shiley, Mirandola, Italy).

It is reasonable to believe that this technique would be effective in those patients who are likely to bleed more, as the cell saver reduces the requirement of homologous blood by making patients own concentrated blood available for transfusion. Studies have shown that routine use of cell saver in all cardiac operations or low-risk patients did not reduce the need for transfusion.[55,56] In one study, only in 7 percent of patients, the volume of blood loss was sufficient enough to be washed and returned.[55] It is therefore suggested that cell salvage should be considered in all cases where significant blood loss (> 1000 mL) is expected or possible.[57] The examples are, re-do surgery, complex surgery, and surgeries requiring prolonged CPB time. The indications can be extended to those patients who refuse allogeneic blood products, are anaemic or have a rare blood group.

The effect of transfusion of processed blood by the cell saver on inflammatory markers has been studied. It has been shown that the cell saver reduced the levels of pro-inflammatory markers IL-6 and IL-8 at 6 hours after CPB.[58] The blood left in the oxygenator at the end of CPB should also be processed by cell saver for subsequent reinfusion. Some authors have

combined ANH along with intraoperative cell saver, but this has not been shown to provide any additional benefit.[59]

The cell washing devices do not completely remove bacteria, malignant cells and certain medications. Therefore, salvaging blood from an infected surgical site should be avoided. Similarly, blood collected from an area of malignancy should not be reinfused since it can lead to diffuse metastasis.

The disadvantage of this technique is that it is expensive.[60] This involves an initial cost of the equipment as well as the recurrent expenditure by way of special disposable circuit that is necessary during each use. In addition, trained personnel are necessary for running the equipment. Despite these drawbacks, it is a popular technique and a survey performed by the author revealed that 55 percent of centres in India possess cell washing devices (unpublished data).

Postoperative blood scavenging

Although, cell saver can be used to perform blood scavenging in the postoperative period when the patient is transferred to the intensive care unit (ICU), it is rarely used in this setting. More commonly, the blood is collected from the chest drains in a sterile system and is transfused back to the patient. The cardiotomy reservoir from the heart lung machine can be used to collect the shed blood from the chest tubes. The rationale of using autotranfusion of mediastinal shed blood after cardiac surgery is to preserve haemoglobin levels and reduce the need for allogeneic blood transfusions. The shed mediastinal blood can be retransfused hourly to the patient and has been shown to reduce postoperative homologous blood requirements.[61] However, the efficacy and safety of the technique has been questioned on the basis of some possible adverse effects. In a multicentre observational study, it has been suggested that the shed mediastinal blood is ineffective as a blood conservation method and may be associated with a greater frequency of wound infection.[62] Another concern is related to the high levels of cytokines present in the blood drained from surgical field.[63] Some studies have shown that shed mediastinal blood contains high levels of cytokines but autotransfusion of this blood does not modify the inflammatory response of the patients to CPB and that it seems to be an excellent source of red cells.[64,65] One recent study has demonstrated that small to moderate amounts of mediastinal shed blood does not influence haemostasis or the cytokine

levels following CABG,[66] while another one has shown that transfusion of shed mediastinal blood resulted in less postoperative drainages and less allogeneic blood transfusions, but no difference in FFP or platelet transfusions and complications.[67] It seems that transfusion of shed mediastinal blood is one of the options for blood conservation, but it is still controversial and is not widely practised.

Ultrafiltration

This is a method by which excess fluid is removed by the filtration of blood through ultraporous membrane (hollow fibres). Initially, it was used to concentrate blood of a patient who has been severely haemodiluted on CPB. Its use was then extended to patients with compromised renal function undergoing CPB. It is now recognised as a useful method for removing water from excessively haemodiluted blood[68] and also as a method of preservation of platelets and coagulation factors, thereby helping blood conservation.[69]

The ultrafiltration device uses a semipermeable membrane for the separation of plasma water and low molecular weight solutes (Fig. 11.3). Adialysate solution is not required. In this respect it differs from the dialysis that uses dialysate solution to achieve diffusion of solutes through a semipermeable membrane via a concentration gradient. Ultrafiltration uses hydrostatic pressure gradient in removing plasma water without an osmotic gradient. The hydrostatic pressure across the ultrafiltration membrane can be increased by increasing the perfusion pressure applied to the blood side of the membrane. Negative pressure on the effluent side of membrane can also be applied to improve filtration.

Blood may be drawn from the venous line, the venous reservoir or the arterial line, and the filtered blood may be returned to the venous line or the cardiotomy reservoir. When the blood is taken from a high-pressure source (e.g. arterial line), a pump is not necessary, otherwise a pump is required to propel blood through the device.

A variety of ultrafiltration devices are available and each device varies as to its efficacy in producing ultrafiltration. The rate of fluid removal may vary, but is generally in the range of 30 to 50 mL/min. The pore size of the membrane allows filtration of small molecules such as sodium, potassium, chloride, urea, creatinine and glucose. These molecules are filtered at a rate

equal to their concentration in the plasma. Large molecules such as albumin, haemoglobin, fibrinogen and blood cells are not filtered. Therefore, a higher concentration of the nonfiltered elements results following a period of ultrafiltration. Heparin is also filtered out by ultrafiltration, necessitating careful anticoagulation monitoring when ultrafiltration is used during CPB.

The ultrafiltration can be performed at the termination of CPB to concentrate the blood left in the reservoir. This concentrated blood can then be transfused back to the patient either directly via a pump or through a blood bag into the venous line.

Patients undergoing cardiac surgery may receive large volumes of crystalloid load. They may, therefore, develop a large increase in extravascular volume. This is more likely to happen in paediatric patients due to their smaller blood volume. Ultrafiltration can be used to reduce the risk of volume overloading in these patients. As already mentioned, it can also be used in patients with compensated renal function.

It has also been used to reduce the requirement of blood products. It has an ability to concentrate and preserve platelets as well as clotting factors.[70] It seems to be an effective and safe means of salvaging red blood cells and reducing homologous blood transfusion in paediatric patients.[71] However, it has a limited role in adults undergoing elective surgery and it has been suggested that direct transfusion should be considered an appropriate approach for returning residual blood in the CPB circuit to the patient due to its cost effectiveness.[72]

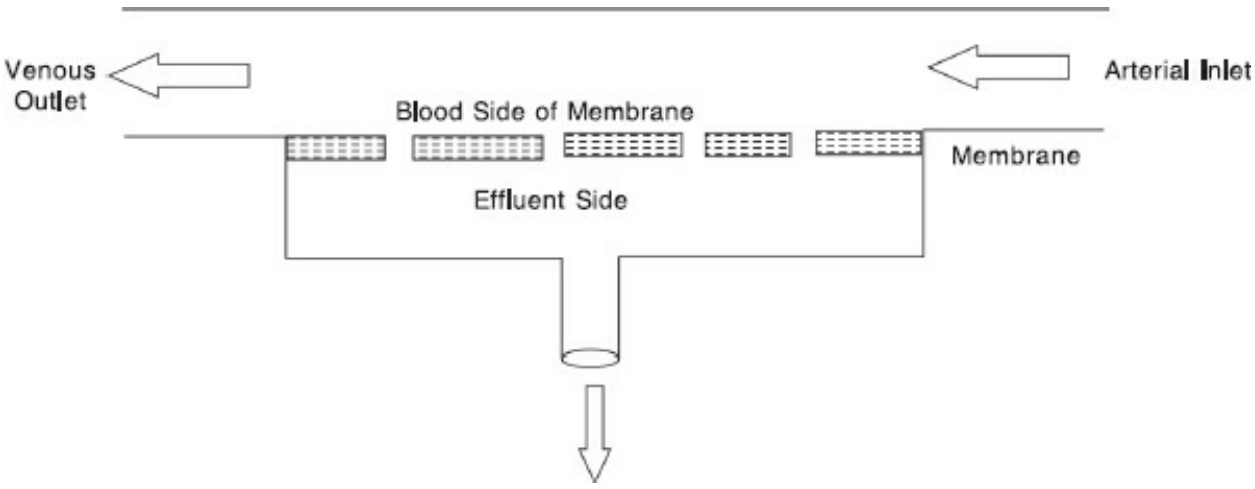

Figure 11.3: Diagrammatic representation of ultrafiltration. Water and solutes are filtered across the semi-permeable membrane due to pressure difference across the membrane.

Modified ultrafiltration

It is a technique after cardiopulmonary bypass whereby blood withdrawn from the aortic can nula is passed across the ultrafiltration device to haemoconentrate. The blood is pumped back into the patient through the venous cannula. Generally, arteriovenous configuration is used, but veno-venous circuit can also be used. Some groups have used blood cardioplegia system as the modified ultrafiltration circuit. It is more useful in paediatric population because the benefits may be greater due to smaller circulating volumes. In adults, it does not change the coagulation values as measured by thromboelastography, number of allogeneic unit transfusions or chest tube drainage[73], but it is effective for haemoconcentration after CPB in patients with low body weight.[74]

Autologous Platelet Rich Plasma

The device used for this purpose draws patient's blood into a reservoir and platelet rich plasma is separated by centrifugation. The separated red blood cells are returned to the patient. It can be performed after induction of anaesthesia using internal jugular vein for withdrawing blood. A greater concentration of platelets can thus be saved from the adverse effects of CPB than obtained in whole blood. Since the separated red blood cells are returned to the patient, haemodilution is not produced and it can be used even in patients having lower haemoglobin concentration.

Earlier studies have reported increased postoperative platelet counts, diminished blood loss and reduced homologous blood use with the help of this technique.[75,76] However, current opinion seems to indicate that its effectiveness remains controversial and more studies are needed before it can be employed routinely in cardiac surgical patients.[77]

Pharmacological Therapy

The necessity to reduce homologous blood use during cardiac surgery has gained wide acceptance. Consequently, many attempts have been made to reduce the bleeding tendency and blood requirement by pharmacological interventions. Antifibrinolytic drugs are widely used for this purpose and

previous reviews have found them to be effective in reducing blood loss, the need for transfusion, and the need for reoperation. In the last few years, comparative performance of these drugs has been questioned.

Aprotinin

Aprotinin is a naturally occurring protease inhibitor isolated from bovine lung tissue. It was introduced in clinical use in 1950s, but its role was limited to the treatment of pancreatitis. Subsequently, its ability to reduce bleeding was recognised. This led to its usage for reducing surgical bleeding and the need for donor blood transfusion, especially in the field of cardiovascular surgery.

The interest in aprotinin began after Royston et al published a report showing that the drug resulted in an 8-fold decrease in the need for blood transfusion in patients undergoing repeat cardiac surgery.[78] Aprotinin inhibits serine proteases such as trypsin, plasmin or tissue and plasma kallikrein. The concentration of aprotinin required to inhibit each one of them is variable with concentration of approximately 50 kallikrein inactivator units (KIU)/mL required to inhibit plasmin and approximately 200 KIU/ mL to inhibit plasma kallikrein. The result is inhibition of the contact activation and plasmin mediated fibrinolysis. Aprotinin also has the ability to inhibit various aspects of platelet function. The second phase response of platelet aggregation following stimulation with adenosine diphosphate is effectively inhibited by aprotinin at concentrations of 100-400 KIU/mL. van Oeveren[79] have demonstrated that the improved haemostasis observed during and after CPB in patients treated with aprotinin can be attributed to preserved adhesive capacity of platelets (Glycoprotein lb receptor). Thus, anti-fibrinolytic effect and preservation of platelet function are the principal mechanisms of action of aprotinin.

Until recently, aprotinin was one of the most effective and widely used agents in cardiac surgery for decreasing perioperative bleeding as well as the need for donor blood transfusion. On November 5, 2007, after consultation with health regulatory authorities, marketing of aprotinin was suspended by the Bayer Pharmaceuticals Inc. This decision was a fallout of the results of the Blood Conservation Using Anti-fibrinolytics in a Randomised Controlled Trial (BART).[80] The BART study was a multicentre, double-blinded study that compared full-dose aprotinin with standard dose epsilon- amino-caproic

acid (EACA) or tranexamic acid (TA). The study was halted prematurely because of a higher rate of death in patients receiving aprotinin. Before, the current controversies on this issue are discussed, it is worthwhile considering briefly the pre-BART era of aprotinin.

Background

The classical high-dose regime of aprotinin consists of 2×10^6 KIU loading dose administered over a 20 min. period after induction of anaesthesia, followed by a continuous infusion of 5,00,000 KIU/hour until the patient is transferred to the ICU. In addition, 2×10^6 KKJ is added to the oxygenator to overcome the dilution effect.[81] In addition, many low-dose protocols have been used in an attempt to reduce the cost and potential adverse events. Aprotinin, 2×10^6 KIU given into the oxygenator prime as the only therapy[79], and the use of half of the classical high-dose are some other dose regimes that have been reported.

The therapeutic efficacy of aprotinin was demonstrated in a variety of patient population. The classical high-dose regime was first used in patients undergoing repeat surgery through a prior median sternotomy.[81] This study showed that postoperative blood loss in the aprotinin treated patients was 286 ± 48 mL as against 1509 ± 388 mL in the control group. Consequently, only 4 of the 11 patients in the aprotinin group received a total of 5 units of donor blood. All the patients in the control group required blood transfusions (total 41 units). Similar results were subsequently reported by other authors in this group of patients.[82-84]

The beneficial effects of aprotinin were also demonstrated in less complex primary myocardial revascularisation, especially those pretreated with aspirin (without increasing the risk of myocardial infarction),[85-87] patients with sepsis and endocarditis and vascular surgery.[88] Even topical application of aprotinin (spraying it on internal mammary region and pericardium) in a smaller dose (1.25×10^6 KIU) was shown to be as effective as the systemically given aprotinin.[89] It was also shown that aprotinin attenuates the increase in pro-inflammatory cytokines IL - 6 and IL –10[90], and it reduces the incidence of stroke and death.[91] Maintaining the celite ACT above 400 to 450 seconds was not considered a reliable indicator of adequate heparinization in presence of aprotinin. Celite ACT of > 750 seconds or use of monitoring tests which do not rely on celite activation (Kaolin ACT, heparin-protamine

titration) were recommended.[92]

Many people, however, restricted its use to high-risk patients such as those undergoing repeat surgery, complex procedures, or patients with endocarditis.

The major adverse events with the use of aprotinin that were recognised included the risk of anaphylactic reaction[93] renal dysfunction[94] and the possibility of graft occlusion following CABG.[95] Nevertheless, due to variability in the results and lack of concrete evidence against its use, the use of aprotinin during cardiac surgery continued.

The Controversy

Although the clinical use of aprotinin continued, controversy regarding the safety issues of the drug did not stop. The Multicenter Study of Perioperative Research Group, Ischemia Research Education Foundation (McSPI) published a report in 2006 that claimed, “The association between aprotinin and serious end-organ damage indicates that continued use is not prudent. In contrast, the less expensive generic medications EACA and tranexamic acid are safe.”[96] Further, the report highlighted that withdrawl of aprotinin would reduce the renal failure and the associated cost of dialysis leading to direct and indirect savings. The final event leading to withdrawl of aprotinin was the suspension of the BART trial by the medical safety monitoring board. The board’s concern was the increase in the mortality (nearly statistically significant) in the aprotinin group as compared with others. Some other studies performed nearly during the same period on large number of patients concluded that it is the use of blood and sickness of the patients and not aprotinin that was responsible for the renal dysfunction,[97] and there was no evidence of increased short- or medium-term mortality because of aprotinin usage.[98] However, aprotinin was still withdrawn.

Since the withdrawl of aprotinin (now nearly 4 years), the cardiac anaesthesiologists and surgeons have resorted to alternative pharmacological means (mainly EACA and TA) of blood conservation or have not used any means. It would be interesting to evaluate the results of blood conservation techniques in the post-aprotinin era. Of note, whether the mortality decreased after discontinuation of aprotinin or not also needs to be evaluated. A large report from a single centre in China evaluated the results of patients for 6 months before (n = 1699) and 6 months after (n = 2225) the withdrawl of aprotinin.[99] During the 6 months in which aprotinin was used, all patients

received the drug, and afterwards no annfibrinolytic medications were given. There was a significant increase in the blood loss, reoperation for bleeding, and overall transfusion of coagulation products in the group where no antifibrinolytics were given. However, the non-use of aprotinin did not lead to decrease in renal failure. An increase in the mechanical ventilation time attributable to increased use of FFP, platelets and other blood products was observed. In addition, the aprotinin group had a significantly better PaO_2/F_iO_2 ratio.

A group from Chicago published a preliminary report saying that discontinuation of aprotinin did not lead to increase in red cell usage in their patients.[100] But, another report noted that the use of FFP, cryoprecipitate, platelet pheresis packs, and red blood cell transfusions were significantly higher when they changed from aprotinin to TA.[101] They also noted a higher reexploration rate for those receiving TA. In addition, the use of factor Vila was more in the TA group, which may offset the cost that was saved by the non-use of aprotinin.

A retrospective analysis of observational data reported that TA was associated with higher cumulative drainage losses and a higher rate of repeated thoracotomy for bleeding as compared with aprotinin.[102] Further, in a subgroup of patient's having surgery with open cardiac chamber, the mortality was higher in TA group. Similar increses in blood loss have been reported in neonates with EACA.[103]

In a study performed on piglets, Ishibashi and colleagues demonstrated that aprotinin reduces cerebral leukocyte activation and accelerates neurological recovery in a dose-dependent fashion.[104] No measurable impact on standard indices of renal function were seen in these young piglets. Therefore, the authors have suggested that the current lack of availability of aprotinin is a serious disadvantage for paediatric patients undergoing CPB.

A survey performed in Great Britain in 2009, revealed that about 33 percent of doctors felt their patients have suffered because of the lack of aprotinin.[105] No physician reported that their patients were doing better with non-use of aprotinin. Another group reported that aprotinin use was associated with a 3.8-fold increase in odds of death one year later compared to no aprotinin use, regardless of the level of preoperative kidney dysfunction after adjusting for other perioperative variables.[106]

The other important issue that needs to be considered is the side effects of

TA and EACA. It is known that TA causes seizures by a gamma-aminobutyric acid (A) receptor antagonistic effect[107] and this has been reported in patients undergoing cardiac surgery.[101,108,109] EACA also has been shown to induce seizures and delirium[110] and a recent report has suggested that seizure rate is doubled with TA compared to EACA.[111]

So, has the withdrawl of aprotinin led to improved patient outcome and lowered cost without causing undue increase in bleeding and transfusion requirements with the use of alternatives such as EACA and TA? At the moment, there does not seem to be any such definite evidence. It is true that in the absence of evidence (or if the evidence is conflicting), opinions may be the deciding factor. However, even opinions in this matter are conflicting.[112,113] Spiess has vehemently argued in favour of aprotinin saying that "the entire series of events have been most unfortunate in that they were not driven by science, level I evidence, and cool heads.[112] Milas believed that the practice of cardiac anaesthesia has not significantly changed after the withdrawl of aprotinin. Further, he suggested that point of care testing should be used to direct the blood transfusion decisions (rather than empiric administration of blood products) in the post-aprotinin era.[113]

Every drug has a side effect, and its utility is determined by the risk-benefit ratio. It has been shown that aprotinin may have a better risk-benefit profile in truly high-risk patients as compared with TA, and therefore its use in high-risk cases may be warranted.[114] An independent and separate analysis of BART trial has shown that aprotinin is not associated with increased mortality, specifically, in patients who are at high-risk of massive blood loss (emergent or urgent surgery, and in whom excessively prolonged CPB is anticipated).[115] In this subgroup, the evidence supports the contention that aprotinin maintains a risk-benefit ratio that is superior to all other antifibrinolytics.[115] It remains to be seen what is the eventual fate of aprotinin, but it appears that there is a scope for its judicious use on an individualized basis in those patients who are at a high-risk of bleeding.[116]

Epsilon aminocaproic acid and Tranexamic acid

These lysine analogues having antifibrinolytic effects have been used in cardiac surgery to minimise blood loss and transfusion requirements. Since,

the withdrawl of aprotinin from the market, EACA and TA are used more frequently. It is common to administer a loading dose before the CPB, followed by a continuous intravenous infusion. EACA has been commonly administered in the loading dose of 5 gm (doses up to 10 gm have also been used) followed by a continuous infusion of 10 to 15 mg/Kg/hour till the protamine is administered.

In addition, a dose of 2 to 2.5 gm/L of priming solution can be added to the oxygenator. A prophylactic pre-CPB administration of EACA was shown to be effective in decreasing the postoperative chest-tube drainage without inducing hyperthrombotic complications.[117] A comparison of EACAbefore incision and after heparin to placebo revealed that both EACA protocols reduced chest tube drainage.[118] Hence, EACA may be administered after anticoagulation for CPB (but before initiation of CPB) in order to avoid prothrombotic effects of EACA, if any. Some other reports have also demonstrated the utility of EACA comparable to that of aprotinin in patients undergoing primary CABG.[119]

TA is a synthetic antifibrinolytic agent that is 6 to 10 times more potent than EACA. The typical loading dose is 10 to 15 mg/Kg over 10 to 15 min. followed by an infusion of 1 to 1.5 mg/Kg/hour. However doses as high as 50 mg/Kg before CPB and 50 mg/Kg into the prime have also been used.[102] Its efficacy has been reported in terms of reducing the chest drainage as well as blood transfusion requirements in patients undergoing open-heart surgery.[120,121]

It has been compared with aprotinin and has been shown to provide similar clinical effects on bleeding and allogenic transfusion in patients undergoing primary elective[122] as well as high transfusion risk cardiac operations.[123] As already pointed out, with the suspension of aprotinin from the market, TA and EACA are the only antifibrinolytics that are left as pharmacological options to reduce bleeding complications during cardiac surgery. This is especially so with those who believe that all patients undergoing cardiac surgery should be administered antifibrinolytic agent. As already discussed, there is no clear evidence that following suspension of aprotinin, the mortality has decreased without increasing the bleeding and related complications or the costs of cardiac surgery have gone down. EACA and TA are useful antifibrinolytics, but are not devoid of side effects. A recent meta-analysis of 25 randomised trials including more than 10000 patients has

concluded that compared with aprotinin, TA has less effective blood conserving effect and mortality risk.[124] Further, given the potential to increase neurological complications, the current trend towards indiscriminate use of TA for all cardiac patients needs to be re-evaluated. A recent review has analysed the current data and concluded that in a dose-dependent fashion, TA is associated with an increase in adverse events, particularly the observation of seizures.[125] The authors further concluded that in these studies, the TA has been highly overdosed.

Thus, indiscriminate use of EACA and TA in all patients should be discouraged. It is necessary to reevaluate these agents, especially in terms, of their safety, and recommended and approved doses.

Desmopressin acetate

Desmopressin acetate releases a variety of coagulation system mediators from vascular endothelium (factor VIII, factor XII, prostacyclin and tissue plasminogen activator). The overall effects of desmopressin favour haemostasis. It is administered in the dose of 0.3 ng to 0.4 μg/Kg by intravenous, intranasal or subcutaneous route. Rapid administration may produce transient hypotension. It has been reported to diminish the postoperative chest tube drainage and blood transfusion requirements in patients undergoing open-heart surgery. In one study performed on patients with severe aortic stenosis, it was shown that desmopressin increased the von Willebrand factor related indices and reduced the postoperative blood loss by 42 percent.[126] It has also been shown to augment platelet function and to reduce blood loss in patients with platelet dysfunction.[127] However, there is insufficient evidence to recommend the use of desmopressin for reducing bleeding and transfusion requirements in cardiac surgery.[128]

In addition to the specific measures described above, there are certain general measures that are equally important and should be applied rigorously. The first and foremost is the firm belief by all the members of the cardiac operation team that blood conservation is possible and a large number of patients can actually undergo open-heart surgery without homologous blood transfusion. The other important measure should include meticulous surgical haemostasis. In addition, the use of crystalloid oxygenator prime and accepting the haemodilution should also be practised.

Although, it is reasonable to conserve blood in all the patients, it carries

special importance in certain patient groups such as those expected to require prolonged CPB, patients having rare blood groups and emergency procedures where there is no time to discontinue anticoagulation and anti-platelet medications (warfarin, streptokinase, aspirin, clopidogrel). The choice of techniques will vary from centre to centre and will depend upon the availability of facilities and the preferences of the team. The use of cell saver, platelet rich plasma and ultrafiltration is expensive and needs trained personnel. EACA and TA are other attractive cheaper alternatives as they do not require trained personnel. Some novel perfusion techniques such as vacuum assisted venous drainage, a short arterial venous loop, retrograde autologous prime, and saline prime removal from the primary cardioplegia circuit along with use of polymer-coated perfusion circuithave been described.[129] Amultidistiplinary approach using a combination of techniques has been suggested to be an effective method of blood conservation in cardiac surgery.[130,131]

Blood Conservation in Off-Pump CABG

Coronary artery bypass grafting on the beating heart through median sternotomy is being increasingly performed nowadays. Since, the CPB and its harmful effects on coagulation are avoided in these patients, it is expected that these patients will bleed less and hence will require less blood transfusion. Indeed, it has been shown that CABG on the beating heart is associated with a significant reduction in postoperative blood loss, transfusion requirement, and transfusion related cost when compared with conventional CABG with CPB and cardioplegic arrest.[132,133] Nevertheless, some authors have tried to further decrease the bleeding and transfusion requirement by utilising some pharmacological means. Aprotinin in the standard doses has been used and shown to significantly reduce the blood loss.[134] Inhibition of enhanced fibrinolysis was also observed in this prospective randomised study. TA has also been used and shown to be effective in reducing postoperative bleeding and the need for allogeneic blood products.[135,136] Amongst the pharmacological means, although, aprotinin in standard doses has been shown to significantly reduce the blood loss[134], it is

no longer available. TAhas also been used and shown to be effective in reducing postoperative bleeding and the need for allogeneic blood products.[135-137] A bolus dose of 1 gm before skin incision followed by maintenance dose of 400 mg/hour during surgery can be used. A recent meta-analysis of eight trials has shown that TA significantly reduced the overall risk of allogeneic blood component transfusion and packed red blood cell transfusions.[138] No adverse events were noted, but the population sample size was too small to detect rare but clinically significant adverse events. The authors concluded that a well designed randomised controlled trial is required to confirm the effectiveness and safety of TA in off-pump CABG.

Sometimes a considerable amount of blood loss can occur during the intraoperative period, especially if the surgeon is not experienced in the technique of off-pump CABG. The blood loss occurs from the arteriotomy site during anastomosis. In such a situation, use of a cell saver or a cardiotomy reservoir can be especially useful to collect the blood and retransfuse it later on, thereby minimising the need for allogeneic blood transfusion. A survey performed amongst the European surgeons has revealed that widely different intra- and perioperative anticoagulation strategies are used for off-pump CABG.[139] The cell saver was used by 70 percent and antifibrinolytics by 40 percent surgeons. Fifty six percent of respondents did not think that bleeding is reduced in off-pump CABG as compared with conventional CABG.

Blood Conservation in Paediatric Patients

Certain characteristics are unique to the paediatric patients undergoing congenital heart surgery (Table 11.2).[140]

Neonates have decreased levels of coagulation factors up to approximately 6 months of age. In addition, considering the relatively high priming volume of the CPB circuit, severe dilution of coagulation factors may occur. The children may have delayed hepatic maturation secondary to poor organ perfusion. Further, the type of operation done in neonates influences the blood loss. The surgery usually involves complex procedures with a long duration of CPB and multiple extracardiac suture lines that are often located

in high pressure locations. The use of deep hypothermic circulatory arrest is associated with an increased incidence of fibrinolysis after CPB. Consequently, paediatric patients, particularly those undergoing surgery for cyanotic congenital heart disease (CCHD) are prone to excessive haemorrhage after corrective surgery. Indeed, children receive blood and blood products, such as platelet concentrates, cryoprecipitate, and FFP more frequently than adults and are exposed to a large number of donors. Minimising the bleeding can be an important factor in modulating surgical outcome. Unlike adult patients, the therapy for bleeding in paediatric patients has not been well addressed, and controversies exist. Meticulous surgical haemostasis and a comprehensive approach towards the management of bleeding are essential to minimize the blood transfusion requirements.

Table 11.2: Characteristics specific to paediatric patients that make them prone to excessive bleeding.[140]

- Decreased levels of coagulation factors compared with normal children of the same age group.
- Haemodilution resulting from high priming volume relative to small blood volume.
- Delayed hepatic maturation secondary to poor organ perfusion.
- Complex operative procedures requiring long duration of CPB.
- Multiple extracardiac suture lines.
- Deep hypothermic circulatory arrest.

Aprotinin

As described earlier, aprotinin was taken off the market in 2007 after adult studies reported increased renal failure and death. Until then, aprotinin was used frequently in children undergoing congenital heart operations. The reason for this wider use was based on the generally beneficial effects observed with aprotinin in paediatric cardiac surgery. Some of these studies demonstrated benefits in terms of significant reduction in chest tube drainage, time to skin closure, and transfusion requirement,[141-143] while others showed substantial savings in cost in addition to decreased requirement of banked blood and donor exposures.[143,144] In addition, benefits were also shown in patients undergoing reoperation[143-145] and patients undergoing complex

surgical interventions.[146] In one of the largest reports by Chauhan et al,[141] low dose aprotinin (10,000 KIU/Kg after induction, 10,000 KIU/Kg in the CPB pump prime, and 10,000 KIU/hour for 2 hours after weaning from CPB) was used in 100 children. Their results showed that the time for sternal closure, maximum blood loss at 24 hours, and the requirement for packed red blood cells and platelets were decreased significantly as compared to the control group.

One important consideration in the use of aprotinin has been the selection of an appropriate dose regime. Doses used in children varied widely from a single bolus dose to a bolus dose with continuous infusion until the end of operation. In order to avoid excessive dilution of the drug due to inverse relationship between the blood volume and the large pump prime, additional aprotinin was added to the prime to achieve sufficient plasma levels to inhibit activation of coagulation cascade. One study showed that administration of a bolus dose of 30,000 KIU/Kg before CPB and addition of 50,000 KIU/Kg to the pump prime (instead of 30,000 KIU/Kg that is traditionally added to the prime) led to levels of aprotinin of > 200 KIU/mL throughout the operation.[147] A significant reduction in thrombin generation and suppression of fibrinolysis were also observed.

The anti-inflammatory effects of aprotinin were considered particularly important in paediatric patients in attenuating the whole body inflammatory reaction.[148] A review concluded that the use of high-dose aprotinin seems to be a rational approach for suppressing activation and amplification of systemic inflammatory response.[149] Thus, although all these reports suggested that aprotinin use is justified in children, (especially those undergoing complex surgical procedures), it has been discontinued. One study has evaluated the safety of aprotinin in a large multicentre cohort of children undergoing congenital heart operations. The study included 30, 372 children from 35 children's hospitals from 2003 to 2007. Overall 44 percent received aprotinin. Multivariate analysis found no difference in postoperative mortality, dialysis, or length of stay between aprotinin recipients and non-recipients.[150] Aprotinin recipients in the reoperation subgroup had significantly reduced length of stay. The authors concluded that aprotinin is not associated with increased mortality or dialysis and that further evaluation of aprotinin could be undertaken in children without undue risk.[150] Whether this happens or not remains to be seen. As of now, TA and EACA have

replaced aprotinin.

Epsilon aminocaproic acid

During the aprotinin era, there were a few studies describing its use in paediatric cardiac surgical patients. In one of the earlier reports, it was shown that the effect of EACA was more pronounced in children with CCHD (in whom bleeding was more profuse) and in children subjected to prolonged CPB.[151] In a study, EACA was dosed using 100 mg/Kg in CPB pump prime and 100 mg/Kg on weaning from CPB over 3 hours.[152] The authors documented that EACA significantly decreased postoperative blood loss (23.7 ± 5.8 mL/Kg in EACA group and 42.6 ± 6.9 mL/Kg in control group) and requirements of packed red blood cells and platelet concentrate. The same group also showed that these results are comparable to those obtained in patients receiving low-dose aprotinin.[141] In another study, EACA decreased intraoperative blood loss but did not significantly decrease postoperative blood loss or blood transfusion requirements.[153] This variability in results may be related to the different types of patients and the different dosing techniques used. A simple, more practical approach of using an initial loading dose of 75 mg/Kg over 10 min. and a maintenance infusion rate of 75 mg/Kg/hour with 75 mg/Kg placed in the prime has been suggested to maintain serum concentration more than the therapeutic level (assumed to be 130 μg/mL).[154] In the post-aprotinin era, many institutions updated the antifibrinolytic protocol and switched to EACA. In one study, the results of children during the period when they were receiving aprotinin were compared with those who were switched to EACA.[155] The results indicated that in neonates, the switch to EACA treatment led to a higher postoperative blood loss, but there were no differences in the transfusion requirements or major clinical outcomes. Another similar study observed a higher odds of acute kidney injury for aprotinin usage compared with EACA, suggesting that the known concern for adults with adverse kidney effects with aprotinin is also appropriate for paediatric patients.[156] It seems that EACA may offer an alternative to aprotinin, but more studies are necessary to define the most effective dose of EACA in children.

Tranexamic acid

Similar to EACA, TA was also not studied extensively in children during the

aprotinin era. In a prospective, randomized, double blind study, a single dose of TA (50 mg/Kg) was administered intravenously before skin incision.[157] It was shown that the postoperative blood loss was reduced to more than half that of the control group and blood product requirements were decreased significantly in children with CCHD. However, a subsequent study by the same group failed to show any beneficial effect in patients undergoing surgery for CCHD.[158] In another study, TA in the dose of 100 mg/Kg was used before skin incision followed by 10 mg/Kg/hour.[159] This study showed that the postoperative blood loss was reduced by 24 percent and the total transfusion requirements, total donor unit exposure, and the financial cost of blood components were less in the TA group. At some institutions, aprotinin has been replaced with TA. In a study that evaluated the results of patients during two different periods, receiving either aprotinin (n = 70) or TA (n = 70), it was found that there was no difference in terms of blood loss on blood and blood product transfusion (except platelet concentrate that were transfused more in TA group), length of stay in ICU, renal function values or in the rate of reexplorations.[160] The authors concluded that TA represents an adequate alternative to aprotinin in congenital heart surgery.

Since the place of aprotinin has been taken by EACA or TA, it will be useful to compare these two antifibrinolytics. However, there is sparse data on this issue. In neonates and children weighing less than 20 Kg, it has been shown that EACA and TA are equally effective with respect to perioperative blood loss and transfusion requirements.[160,161] In addition, the incidence of postoperative complications such as seizures and other neurological complications, renal injury, renal failure, low cardiac output syndrome, vascular thrombosis, and in-hospital mortality did not show any statistically significant difference.[161] However, the incidence of seizures in this study was four-fold higher in the TA group as compared with EACA (3.5 percent vs 0.8 percent, P = 0.203). Therefore, some may prefer to use EACA over TA.

It is evident that more trials are necessary to address the choice of antifibrinolytics in the absence of aprotinin. Further, the novel antiinflammatory effect of aprotinin is absent with EACA and TA. How important this effect is, will be proven in times to come.

Autologous blood transfusion

The safety and efficacy of autologous blood donation in children has not been

well studied. In one report preoperative autologous blood donation has been shown to be a safe and effective method to avoid homologous blood transfusion in paediatric cardiac operations.[162] It has been suggested that phlebotomised units of blood obtained from the patients with CCHD can be used for autologous transfusion. However, this blood is deficient in coagulation by many ways, such as alteration in coagulation factors, increased fibrinolysis, and platelet dysfunction.[158] Therefore, the practice of autologous transfusion in these patients is questionable. Nevertheless, some Japanese reports have shown that blood transfusion requirement can be decreased[163] or totally eliminated[164] by using bloodless prime and autologous blood donation immediately after induction of anaesthesia. Further studies are required to evaluate the efficacy of this technique.

Fresh whole blood

It has been shown that the fresh whole blood substantially reduced blood loss in children less than 2 years old undergoing complex surgical procedures.[165] Such a benefit is presumably due to a better preservation of platelet function. In contrast to adults,[166] these authors were unable to show additional advantages of fresh whole blood of less than 6 hours since donation over donation less than 48 hours. However, some centres still prefer to transfuse fresh warm blood that is less than 6 hours old.

Ultrafiltration during cardiopulmonary bypass

Ultrafiltration of the extracorporeal circuit volume after termination of the CPB with reinfusion of the salvaged concentrate in paediatric patients has been used as a means of blood conservation.[167] The technique is an effective method of salvaging red blood cells and reducing homologous transfusions and perioperative morbidity.[168] Ultrafiltration is also useful in attenuating the inflammatory response to CPB that leads to tissue oedema and multiple organ dysfunction.[169] It therefore, seems that ultrafiltration is an attractive method of conserving blood with the added advantage of attenuating the inflammatory response to CPB.

Modified Ultrafiltration

As already pointed out, modified ultrafiltration may be more beneficial in children. Animal experiments have suggested that modified ultrafiltration removes circulating inflammatory mediators, lessens pulmonary hypertension and reduces pulmonary-derived inflammatory markers, thus ameliorating pulmonary-based inflammation.[170] A meta-analysis, which included 8 studies has revealed that modified ultrafiltration resulted in significantly higher post-bypass haematocrit and higher mean arterial blood pressure, but benefits in postoperative blood loss, ventilator time, and ICU stay was not apparent.[171] However, there was significant heterogeneity among the studies surveyed.

Currently, ultrafiltration, modified ultrafiltration or combination of the two is utilized in cardiac surgery in children. The relative risks associated with each of the ultrafiltration strategies may influence the choice of technique in a given centre.[172]

Modification in cardiopulmonary bypass circuits

In an attempt to decrease the transfusion requirements in paediatric cardiac surgery, considerable progress has been made in the CPB circuitry. In this respect, the novel low-prime, surface-coated CPB circuits with vacuum assisted venous drainage are prominent.[173] It is also noteworthy that the perfusionist plays an important role in implementing these strategies. It has been shown that it is feasible to perform congential heart surgery safely without transfusion for patients weighting more than 10 Kg by using combined blood management strategies along with low-prime surface-coated circuits.[174]

In addition to above methods, sufficient haemodilution during CPB has also been used as a method of blood conservation in children. For more details, the reader is referred to the review on this subject.[140]

In conclusion, the advances in blood conservation techniques have reduced the load on the blood banks. A large number of elective open-heart surgical procedures can now be performed without transfusing any bank blood to the patient. Although, a variety of techniques are available (Table 11.1), no one technique can be labelled as the best. The choice should be made taking into

consideration the availability of funds, the manpower, and individual experience. In addition, the judicious use of rational transfusion guidelines should also be followed.

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Chapter 12: Perioperative Support of the Circulation

One of the anaesthesiologist's objectives when dealing with patients undergoing open-heart surgery is to sustain adequate oxygen balance in all tissues. Maintenance of cardiac output (CO) which is one of the major components of oxygen delivery becomes an important consideration during management of patients undergoing cardiac surgery. Myocardial dysfunction necessitating inotropic support is a typical complication following cardiac surgery. Acute cardiovascular dysfunction during the perioperative period occurs in more than 20 percent of patients undergoing cardiac surgery.[1] Some patients will have preoperative myocardial dysfunction due to cardiac disease and this fact will often be known to the anaesthesiologist based on the preoperative cardiac evaluation of the patient. More commonly, patients have left ventricular (LV) dysfunction leading to acute congestive heart failure (CHF) after cardiopulmonary bypass (CPB). Therefore, circulatory support by pharmacological or mechanical means is frequently required after CPB and sometimes preoperatively or following induction of anaesthesia. A wide variety of inotropic agents with different effects on peripheral vascular resistance are available. Physician's preference has been one of the major factors in deciding the choice of an agent.

In this chapter the various pharmacological and mechanical means that are used in the management of low CO state are discussed.

Pathophysiology

The heart has failed when it is unable to pump sufficient blood to meet the needs of the peripheral tissues. Heart failure can be defined as inability of the

heart to pump sufficient blood at normal end-diastolic pressure. This can occur after cardiac surgery and CPB in patients with either normal or poor preoperative ventricular function. The ischaemic insult of Aortic Cross Clamping, inadequate myocardial protection, inadequate surgical repair and reperfusion injury may all contribute to the acute myocardial dysfunction during the hours following cardiac surgery.

Reperfusion Injury

The myocardium is described as “stunned” when it fails to recover its contractility after an ischaemic episode, although coronary flow has returned to normal.[2] This is a transiently reversible condition. The mechanism for stunning is unknown. It has been hypothesised that stunning may be due to both generation of oxygen free radicals[3,4] and calcium injury during reperfusion of the ischaemic tissue. The contractile performance of a stunned myocardium may remain depressed for hours to weeks, with gradual recovery of viable myocytes. There is now considerable evidence that myocardial stunning occurs clinically in various situations in which the heart is exposed to transient ischaemia, such as unstable angina, acute myocardial infarction with early reperfusion, exercise induced ischaemia, cardiac surgery and cardiac transplantation.[5] Recognition of myocardial stunning is therefore, clinically important and may impact patient treatment.

Another factor contributing to myocardial dysfunction after CPB is the down-regulation of beta-adrenergic receptors so that there is a decreased inotropic response to beta-adrenergic stimulation. It has been suggested that this is due to decreased density of beta-1 receptors in the heart in response to elevated plasma catecholamine levels. Beta-2 receptors in the heart are not affected and are therefore, important in the treatment of heart failure. CPB is a potent stimulus for the release of endogenous catecholamines and it has been shown that beta-adrenergic receptor desensitisation occurs during CPB in canine myocardium.[6] Patients undergoing cardiac surgery may also be in chronic CHF before operation. Thus the myocardium may be exposed to high levels of catecholamines before and during CPB. This down-regulation of beta receptors may make the myocardium unresponsive to the exogenous beta agonists leading to difficulty in weaning from CPB.

LV dysfunction is common after cardiac surgery and is often treated with positive inotropic drugs. In general, the likelihood of a patient receiving these

drugs increases with advancing age and with more severe preoperative LV dysfunction. However, prolonged duration of CPB and aortic cross clamp, complex procedures, emergency surgery, and preoperative pulmonary hypertension are also contributory factors.

Some of these patients may require treatment for heart failure in the preoperative period, but more commonly, they need therapy during the weaning from CPB or in the postoperative period in the intensive care unit (ICU).

Frank Starling Relationship

The Frank Starling curve can be useful in understanding the basis of treatment of LV failure. The relationship between the LV filling pressure and cardiac index (CI) in the normal and failing heart is shown in Figure 12.1.

Based on this figure, the patients can be divided into 4 subsets. **Subset I:** The patient is maintaining essentially normal haemodynamics with normal CI at normal filling pressure. **Subset II:** Patients have normal CI but have excessive filling pressure which manifests as pulmonary congestion. These patients should be treated with diuretics and/or vasodilator. **Subset III:** Patients are mamtaining low CI due to hypovolaemia. These patients usually respond to volume replacement. **Subset IV:** These are the sickest patients with pulmonary congestion and low CI. They require therapy with inotropes and vasodilators. The intra-aortic balloon pump (IABP) counterpulsation may be required in these patients who are unresponsive to this therapy. Echocardiography and pulmonary artery catheter are useful monitoring tools and help to assess the volume status and contractility of the myocardium. The two primary goals of therapy in patients with CHF are : 1. to reduce pulmonary congestion by lowering the pulmonary capillary wedge pressure (PCWP); and 2. to improve the CI by improving the contractile function of the myocardium. Vasodilators can be used to lower the PCWP, and inotropic drugs with or without mechanical intervention (IABP) are utilised to improve the CI. In addition, establishment of sinus rhythm and a heart rate (HR) of 80 to 90 beats/min. is important in patients with cardiac failure. This may be accomplished with atrioventricular sequential pacing if necessary. The antiarrhythmic drugs with least ventricular depression should be preferred and sometimes, it may be necessary to reinstitute CPB and unload the heart while a normal or acceptable rhythm is being restored.

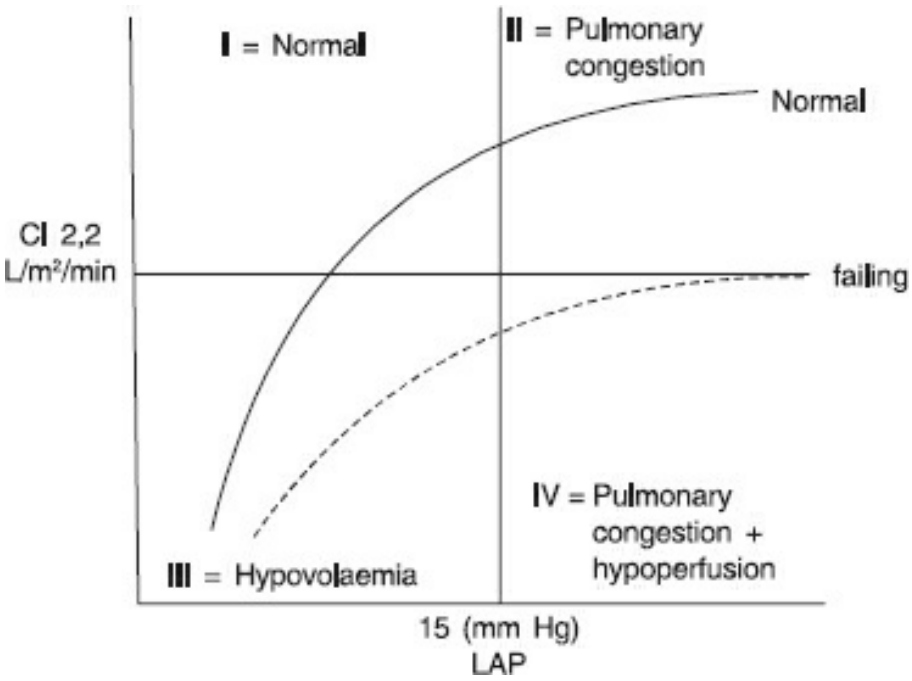

Figure 12.1: Diagram illustrating the relationship between cardiac index (CI) and left atrial pressure (LAP) in the normal and failing heart. For details refer to the text.

Inotropic Drugs

The number of inotropes available has increased from the time when we only had epinephrine, norepmephrine and isoprenaline. There is a wide variation in the number of patients in whom the inotropes are administered during cardiac surgery. To a large extent the indication for inotrope usage is clinician driven rather than the patient driven. The inotropic drugs can be divided into two main groups; adrenergic and non-adrenergic. The adrenergic group includes the familiar catecholamines and non-catecho-lamines. The non-adrenergic group includes phosphodiesterase inhibitors, levosimendan, calcium, and digoxin (Table 12.1).

Catecholamines

The effects of the adrenergic nervous system are mediated by both alpha and beta adrenoceptors. These have been subdivided into alpha-1 and alpha-2, and beta-1 and beta-2 respectively. Beta-1 receptors predominate in the myocardium and cause increased contractility and HR while beta-2 receptors predominate in the skeletal muscles and bronchi and cause muscle vasodilatation and bronchodilatation. Alpha-1 adrenergic receptors cause

peripheral vasoconstriction and increased myocardial contractility. Table 12.2 shows the effects of stimulating various adrenoceptors and Table 12.3 shows the effects of commonly used inotropes on them.

Table 12.1: Various inotropic agents.

Adrenergic		
Catecholamines		
	Natural	- Epinephrine - Norepinephrine - Dopamine
	Synthetic	- Isoproterenol - Dobutamine - Dopexamine
Non-catecholamines (All Synthetic)		
	Direct acting	- Phenylephrine - Methoxamine
Indirect acting		- Ephedrine - Mephentermine
Non-adrenergic		
PDE Inhibitors		
		- Amrinone - Milrinone - Enoximone - Piroximone
Calcium Sensitizer		Levosimendan
Miscellaneous		- Calcium - Digoxin

(PDE = Phosphodiesterase)

Epinephrine

Epinephrine stimulates the beta-1 receptors and therefore, is a powerful cardiac stimulant. It increases the force of systolic contraction, thereby shortening the systole. It also increases the HR. These actions markedly increase the cardiac work and myocardial oxygen consumption (MVO_2). It also improves the conduction through atrioventricular (AV) node and therefore, reduces the degree of AV block, if present.[7] Epinephrine in a dose of 0.02 to 0.08 µg/Kg/min. is predominantly a beta agonist and it is only with a higher dosage that peripheral constriction occurs. A number of units still consider epinephrine as the inotrope of choice for maximal effect at the termination of CPB, if needed. A recent survey performed in Germany has revealed that 41.8 percent of cardiac anaesthetists considered epinephrine as the first choice for the treatment of low cardiac output syndrome.[8] Its strong inotropic action and low cost may be the reasons for its preference, at the termination of CPB. It improves the myocardial contractility, minimises cardiac distention, optimises coronary perfusion and diminishes arrhythmias. Although all these effects are achieved at the cost of increased myocardial oxygen demand, it may still be necessary to use the drug at this stage to provide the patient with good coronary perfusion and quickly terminate the low CO state.

Table 12.2: Adrenoceptors

Alpha-1	Peripheral vasoconstriction, arteries (most)
	Increased contractility
Alpha-2	Coronary vasoconstriction
Beta-1	Coronary vasoconstriction
	Increased contractility
	Increased heart rate
Beta-2	Renin release
	Increased myocardial contractility and heart rate
Dopaminergic	Relax vascular smooth muscle
	Potassium uptake
	Bronchodilatation Renal and mesenteric

Table 12.3: Effect of sympathomimetic drugs on various receptors

Drugs	Alpha (α)	Beta (β_1)	Beta (β_2)	Dopaminergic (DA_1 & DA_2)
Epinephrine	+	++	++	0
Norepinephrine	+++	++	0	0
Dopamine	++	++	+	+ (only DA_1)
Dobutamine	0	++	+	0
Dopexamine	0	0	++	+
Phenylephrine	+++	0	0	0
Methoxamine	+++	0	0	0
Ephedrine	++	+	+	0
Mephentermine	++	0	0	0

0 = none, + = minimal increase, ++ = moderate increase, +++ = marked increase

Epinephrine is an extremely useful drug for the treatment of acute heart failure, peripheral vascular collapse or anaphylaxis. A bolus dose of 2 to 10 µg is very helpful in improving the haemodynamic status of the patient. It is useful for treating sudden episodes of hypotension during cardiac surgery that may be related to surgical manipulation, extreme vasodilatation or protamine administration. A dose of 5–10 µg/Kg is necessary for the treatment of anaphylactic shock. A study has demonstrated that a bolus of 5 µg of epinephrine produces an initial increase in the systemic vascular resistance (SVR), followed by a more prolonged reduction.[9] CO showed a small initial reduction coincident with the increase in SVR, followed by a substantial increase.[9] Epinephrine bolus dose has been recommended for the treatment of cardiac arrest, and animal experiments have shown that epinephrine bolus in combination with vasopressin[10] or levosimendan[11] can drastically improve the haemodynamic parameters (improved coronary perfusion pressure) and initial resuscitation success following ventricular fibrillation. However, some authors suggest that a bolus of epinephrine (1 mg) should not be used for resuscitation if a patient suffers a cardiac arrest shortly after cardiac surgery.[12] The authors believe that in a situation of cardiac arrest soon after

cardiac surgery, the chances of restoring sinus rhythm either by defibrillation or by an emergency resternotomy are high and epinephrine could be dangerous in this situation, if sinus rhythm is restored. Further, the evidence for adrninistering a bolus of epinephrine in this scenario is weak.

The usefulness of epmephine in cardiac surgical patients after CPB has been shown in the dose of 0.04 μg/Kg/min.[13] Epinephrine improved CI in all patients with increases in mean arterial pressure (MAP), HR and LV stroke work index and no change in SVR. In addition, no arrhythmias occurred with its use. Epinephrine infusion can cause hyperglycaemia and increased serum lactate levels due to metabolic actions of beta-2 stimulation.[14]

Due to its powerful cardiotonic effects, it is considered a drug of choice for the treatment of depressed inotropic function at the end of CPB.[15] In higher doses, peripheral vascular effects predominate and arrhythmias may develop. Vasodilators can be used concomitantly during such times.

Epinephrine can be safely used in patients in whom internal mammary artery (IMA) has been used during coronary artery bypass graft (CABG) surgery. It has been shown to increase the flow in the IMA proportional to the increases in systolic blood pressure (BP) and the patency of IMA graft is maintained.[16]

Epinephrine has also been administered via a left atrial (LA) catheter instead of the usual central venous catheter. The LA administration of epinephrine has an advantage with its immediate effect on the coronary circulation, while avoiding the associated pulmonary vasoconstriction by passing through the systemic circulation before reaching the pulmonary circulation. It has been shown that the LA administration of epinephrine increased CO and systemic BP more than the administration via central venous catheter, but the pulmonary arterial pressure was less elevated.[17] Such a practice can be useful in patients with right ventricular (RV) failure, but systemic air embolism may occur and appropriate care should be exercised.

Norepinephrine

Norepinephrine is a naturally occurring catecholamine. It is a potent beta-1 agonist and therefore increases myocardial inotropy. It also has pronounced effects on peripheral alpha receptors; this effect differentiates it from the epinephrine. It thus, produces arteriolar vasoconstriction causing profound increase in SVR. In normal individuals, the increase in BP leads to reflex

bradycardia and CO may decrease. The drug is indicated primarily to maintain BP in the setting of marked decreases in SVR. This may be during or after CPB in the operation theatre (OT) or ICU. The increased BP that it produces must be balanced against increased MVO_2 and reduced renal, mesenteric, and peripheral perfusion that may ensue, especially in higher doses. The increase in BP can induce a loss of plasma volume, particularly under increased microvascular permeability. A study has shown that norepinephrine causes pressure-dependent decrease in the plasma volume in patients with vasodilatory shock.[18] Plasma volume decreased by 6.5 percent and 9.4 percent when blood pressure was increased from 60 to 75 and 90 mm Hg, respectively in this study. It is frequently used during normo-thermic bypass and off-pump CABG to maintain satisfactory MAP. It can be used as a bolus of 2 to 5 μg followed by an infusion (0.02 to 0.08 μg/Kg/min.), if necessary. In off-pump CABG, it has been shown that norepinephrine increased the flow significantly in the grafted IMA.[19] Once the MAP has risen to a satisfactory level, it can be discontinued and some other inotrope such as dopamine can be substituted.

One of the concerns with norepinephrine use after cardiac surgery has been the fear that it might decrease kidney function through regional vasoconstriction. However, one study has demonstrated that continuous norepinephrine infusion in the postoperative period to treat hypotension (MAP less than 70 mm Hg) did not increase the postoperative serum creatinine concentrations.[20] The authors of the study concluded that concerns related to potential adverse effects on kidney function in this setting appear unjustified. It has been used effectively in combination with levosimendan in a patient with end-stage renal disease (on chronic haemodialysis) with poor LV function undergoing off-pump CABG.[21] Combined continuous levosimendan and norepinephrine infusion started soon after anaesthetic induction and continued for 24 hours maintained haemodynamic stability and allowed uneventful completion of surgery in this patient. It has also been shown that vasopressor therapy with norepinephrine after cardiac surgery did not jeopardise intestinal mucosal perfusion.[22] Norepinephrine has also been administered via LA in combination with prostaglandin Ea in central vein to wean from CPB, patients with refractory postoperative pulmonary hypertension.[23] This has been an effective means to wean patients from CPB. Thus, norepinephrine can be a useful inotrope, especially in the setting of

severe hypotension accompanied by low SVR.

Isoprenaline

Isoprenaline is a synthetic catecholamine with pure beta-adrenergic receptor activity. It stimulates both beta-1 and beta-2 receptors leading to profound cardiac stimulation that is accompanied by significant dilatation of vascular smooth muscle beds. It increases HR, and myocardial contractility. The CO, however, may not be increased due to impairment in cardiac filling resulting from tachycardia and peripheral vasodilatation. The MVO_2 is also markedly increased by this drug. Due to these effects, it is not considered a suitable choice in the presence of coronary artery disease (CAD), which has been demonstrated by some studies.[24,25] Nevertheless, it is very useful as a potent chronotropic agent in the presence of profound beta blockade that may be found in some patients with CAD. In addition, it is very effective in the management of acute bradyarrhythmias or AV block. It can be administered as a bolus of 5 to 10 μg followed by an infusion (0.02 to 0.04 μg/Kg/min.), if necessary.

Another area where it can be useful, is in patients with pulmonary hypertension. The pulmonary vasodilator property can be useful in the management of increased pulmonary vascular resistance (PVR) due to any cause thus, helping to control right ventricular (RV) failure. With the availability of newer inotropes such as milrinone with pulmonary vasodilator properties, isoprenaline is rarely used for this purpose. It has been used in the catheterization laboratory to provoke left ventricular outflow tract gradient in patients in whom hypertrophic cardiomyopathy was suspected, but not diagnosed using Doppler echocardiography. The isoprenaline challenge helped to diagnose hypertrophic cardiomyopathy by inducing a gradient of $\geq$ 50 mm Hg in these patients.[26] Extreme caution should be exercised during such a use of isoprenaline, as severe decrease in CO may occur.

Dobutamine

Dobutamine is a synthetic catecholamine that has powerful beta-1 stimulating effects. It causes improved ventricular contractility, stroke volume (SV) and CO.[27] It also causes beta-2 receptor stimulation leading to peripheral vasodilatation. Due to these effects of improved myocardial contractility and a degree of peripheral vasodilatation, dobutamine has achieved wide

acceptance in clinical practice. It has no effect on the dopaminergic receptors in the kidney, so it does not produce specific renal vasodilatation. However, renal blood flow is improved by increasing CO.

It has been used successfully in the treatment of low CO states associated with chronic CHF, myocardial infarction and cardiac surgery. It improves myocardial contractility, SV, CO and systemic pressures. It has been shown to have favourable effects on coronary blood flow and MVO_2. It also decreases wall stress by reducing diastolic and systolic ventricular volumes while increasing MAP and mamtairiing HR relatively unchanged.[28]

The beneficial haemodynamic effects have been proven by many studies.[24,29] It has also been shown to increase splanchnic blood flow without a concomitant increase in hepatosplanchnic metabolism.[30] In paediatric cardiac surgery, following CPB, dobutamine increased the CI and maintained a higher MAP and SVR as compared with dopexamine.[31] In animal experiments in early, endotoxaemic shock, dobutamine in combination with norepinephrine maintained systemic as well as portal blood flow leading to preservation of splanchnic and hepatic oxygen homeostasis and stable lactate concentration.[32] It can be administered in the dosage of 2.5 to 5 μg/Kg/min. that can be increased up to 10 μg/Kg/min.

A combination of positive inotropic drugs is often used with the assumption that there will be an additive effect of the two drugs. However, combining epinephrine with dobutamine does not cause an additional increase in CI, suggesting that combining dobutamine with epinephrine is not useful.[33] This may be related to the fact that dobutamine is also a partial agonist with the potential for inhibiting the response to other beta-adrenergic agonists.[33] Dobutamine is often used in cardiac surgery and in some centres an infusion of 5 μg/Kg/min. initiated at the time of separation from CPB is routinely used in all patients. However, dobutamine has a tendency to produce tachycardia, much more than epmephrine.[34] One study has shown that the increase in MVO_2 produced by dobutamine is matched by a proportionate increase in coronary blood flow.[35] In another recent study, the outcome after CABG was compared in patients, who either did or did not receive an inotrope (nearly always dobutamine).[36] The authors concluded that, all other things being the same, patients had worse outcome when they received dobutamine. Therefore, it seem that it is important to use dobutamine in patients in whom it can provide benefit and not just as a matter

of routine practice.[37]

Dopamine

Dopamine is the naturally occurring catecholamine. It is an intermediate compound in the synthesis of epinephrine and norepinephrine. It produces inotropic effect by stimulating beta-1 receptors. It also stimulates alpha-1 receptors by releasing endogenous norepinephrine to produce considerable vasoconstriction. It has a unique action of stimulating dopaminergic receptors in the renal, mesenteric and coronary arterial beds. This leads to smooth muscle relaxation and vasodilatation. The maximal dopaminergic receptor stimulation is observed in the dose of 2 to 3 μg/Kg/min. In the intermediate dose range of 2 to 6 μg/Kg/min., cardiac beta-1 receptors are stimulated leading to increase in CO. This further improves renal blood flow. Alpha adrenergic stimulation begins at the dose of 5 μg/Kg/min. producing vasoconstriction. In critically ill patients, dopamine is combined with more potent inotropic drugs to improve renal blood flow.[38,39]

It causes greater increases in SVR as compared with dobutamine. It does not stimulate vascular beta-2 receptors and therefore, its unopposed stimulation of alpha-1 receptors is responsible for overall vasoconstriction. It may, therefore, be necessary to combine vasodilators along with dopamine infusion.[35,40] Dopamine also increases pulmonary artery (PA) pressure, PVR and LV filling pressure.[41] The higher doses should be avoided as they cause increase in HR and vasoconstriction.

Dopamine is frequently administered in combination with other inotropes for its beneficial effect on renal function at a low dose (2 to 4 μg/Kg/min.). It has often been advocated for prophylactic ‘renal protection’. However, there is little objective evidence of such a benefit, especially in a patient who is potentially hypovolemic and hypothermic with coexisting ischaemic heart disease, hypertension or diabetes. Indeed, doubts regarding direct beneficial effect on renal function have been raised.[42-44] In one report, urinary excretion of retinol-binding protein, which is a sensitive and accurate marker of early renal tubular injury was used to assess the renal effects of dopamine in patients undergoing CABG.[45] The authors concluded that renal dose of dopamine appears to offer no renal protection in patients with normal heart and kidney function. On the contrary, it exacerbates the severity of renal tubular injury during the early postoperative period. Therefore, the use of

dopamine for routine renal prophylaxis is not recommended.

Dopexamine

The quest for the discovery of an “ideal” inotropic agent has resulted in the development of many new agents. A new synthetic catecholamine, dopexamine is one amongst them. It is structurally related to dopamine and dobutamine. It stimulates DA1 and DA2 receptors as well as beta-2 receptors, but has little effect on beta-1 and no effect on alpha receptors. It also has an inhibitory action in the neuronal catecholamine uptake mechanism that is most probably responsible for the positive inotropic action of this drug. Continuous infusion of dopexamine has been shown to result in systemic and preferential renal vasodilatation, causing after-load reduction, increases in CO and improved renal perfusion in animals and normal volunteers.[46] Haemodynamic studies in patients with severe chronic heart failure have indicated that dopexamine reduces afterload through systemic arterial vasodilatation, increases renal perfusion by selective renal vasodilatation, and causes mild cardiac stimulation. The cardiac stimulation is achieved through direct and indirect (i.e. inhibition of catecholamine uptake) positive inotropic mechanism. The haemodynamic effects in patients following cardiac surgery have been similar to those seen in patients with chronic CHF, and may be useful in this setting.[47,48] The effects are most pronounced when used as a continuous infusion of 1 to 4 μg/Kg/min. However, HR can be substantially increased at higher doses leading to increase in MVO_2. It has a short plasma half-life (6 min. in healthy volunteers and 11 min. in patients with low CO) that allows a rapid return to pretreatment status at discontinuation of the infusion.[49]

Dopexamine has also been employed in the management of patients with septic shock. A preferential increase in splanchnic blood flow with dopexamine has been demonstrated.[50] It has been shown to be useful in the management of congestive heart failure in the dose range of 1 to 6 μg/Kg/min.[51,52], but its use may be limited by the tachycardia at doses more than 4 μg/Kg/min.[53] In paediatric cardiac surgery, following CPB, dopexamine increased CI similar, to dobutamine, but not the MAP and SVR.[31]

Thus, dopexamine is a useful inotrope (although not widely used), which also reduces peripheral vascular resistance and has beneficial effects on

splanchnic blood flow when administered after cardiac surgery.

Phosphodiesterase Inhibitors

This class of drugs acts through inhibition of phosphodiesterase type III (PDE-III) that is found predominantly in cardiac muscle and results in increased levels of cAMP. This leads to an increase in calcium channel entry into the cell. Due to the mechanism of action, these drugs do not rely upon beta receptor stimulation for their positive inotropic activity and can be useful in a situation, where the beta receptors are down-regulated. These drugs have a potent positive inotropic effect as well as arterial vasodilatory activity and hence, have also been named as “inodilators”. The classification of these drugs is based on their biochemical properties. They are either bypiri-dines; amrinone and milrinone, or imidazoles; enoximone and piroximone.

Amrinone

As already pointed out, amrinone is non-cate-cholamine and non-adrenergic. Therefore, it does not rely upon beta receptor stimulation for its positive inotropic activity. The vasodilator activity of amrinone is also due to PDE-III inhibition directly in the vascular tissue.

Amrinone has been used for the treatment of low CO state and in weaning patients from CPB.[54-57] The drug has been shown to increase CI, while decreasing PCWP, SVR and PVR. HR and BP generally remain stable. The hemodynamic effects of amrinone have been compared with dopamine and dobutamine.[58,59] Amrinone and dobutamine both have been shown to consistently increase CO while simultaneously decreasing SVR, right atrial pressure and PCWP. However, with prolonged infusion, amrinone produced a sustained improvement. Dopamine increases CO without decreasing PCWP and also produces a significant increase in HR. Combined use of dobutamine and amrinone in patients with severe heart failure[60] and amrinone and epinephrine in stable patients just weaned from CPB[56] has also been reported. The combined administration produced greater improvements in haemodynamic response. It can be used in combination with other catecholamines, vasodilators and IABP in treating patients with low CO following cardiac surgery. Amrinone has also been used prophylactically before separation of a patient from CPB and has been shown to improve weaning success regardless of LV ejection fraction.[61] In addition, it also

ameliorates postoperative deterioration in cardiac function and oxygen transport and reduces dopamine requirement.[62]

It has a prolonged half-life (3.5 hours) and is administered as an intravenous loading dose followed by an infusion to maintain adequate plasma concentration of the drug. A loading dose of 1 to 2 mg/Kg followed by a maintenance infusion of 5 to 10 μg/Kg/min. has been used in clinical practice.

By the nature of its action, amrinone can be useful in a situation where the heart has a reduction in beta-1 receptors (prolonged sympathetic stimulation in heart failure). It would also be useful in diastolic LV failure due to its property of improving the compliance of the ventricle. However, due to its vasodilator property, it can produce a precipitous decrease in BP after the bolus loading dose, especially, if the cardiac filling pressures are normal or low. Coronary perfusion pressure is particularly important soon after CPB and although, amrinone would be expected to affect myocardial oxygen demand less than sympamomimetics, this may not be of prime importance at this stage. Therefore, the anaesthesiologist must learn to use new drugs from his own clinical experience.

Milrinone

It is a second generation PDE-III inhibitor and has a similar haemodynamic profile to amrinone.[63,64] However, its positive inotropic action is much more than that of amrinone. It produces increase in CO, decrease in PCWP and SVR without any significant increase in HR or MVO_2. The changes in systemic arterial pressure occur indirectly from an increased CO. It also improves myocardial relaxation (positive lusitropic effect) and improves coronary perfusion. Its ability to improve myocardial performance in patients undergoing cardiac surgery has been demonstrated[65-68] and has also been administered prophylactically before the termination of CPB in patients undergoing CABG.[62] Using haemodynamic parameters and transthoracic echocardiacgraphic measurements, it has been shown that milrinone is beneficial in patients with poor LV function undergoing CABG.[69] It also improves the diastolic LV function soon after aortic unclamping in patients undergoing CABG.[70]

In patients with dilated cardiomyopathy with poor LV function undergoing LV restoration surgery, milrinone helped to maintain stable haemodynamics

and reduced the postoperative doses of dobutamine and epinephrine.[71] It can be administered in a loading dose of 50 μg/Kg followed by an infusion of 0.3 to 0.75 μg/Kg/min. It has been shown to be effective in the treatment of cardiogenic, haemorrhagic or septic shock following cardiac surgery, in the dose of 0.5 μg/Kg/min. infusion without bolus loading dose.[72] Milrinone has been compared with amrinone following cardiac surgery. It has been shown that they had similar beneficial haemodynamic effects after CPB with the exception of blood pressure (no change in blood pressure with milrinone).[73]

Of particular interest is the ability of milrinone to decrease PVR. It has been shown to progressively decrease the PVR with greatest change occurring in patients undergoing mitral valve replacement with a high baseline PVR (>200 dynes/sec/min.$^{-5}$).[74] However, the accompanying decrease in SVR may necessitate use of norepinephrine. Therefore, use of inhaled milrinone as a possible therapeutic option has been tried. It was shown that inhaled milrinone caused a decrease in mean pulmonary artery pressure (MPAP) and PVR comparable to intravenous milrinone, but MAP and SVR were significantly higher.[75] Further, inhaled milrinone improved the arterial oxygen tension/fraction of inspired oxygen (PaO_2/FiO_2) ratio.[75]A combination of intravenous as well as inhaled milrinone has also been used effectively in two patients with severe PAH after valve surgery.[76] The inhaled milrinone can be delivered by means of a nebulizer attached to the inspiratory limb of the ventilator circuit, just before the Y piece. Milrinone can be dissolved in normal saline to get a final concentration of 0.5 mg/ml. The major advantage of inhaled milrinone is its pulmonary selectivity, thus avoiding the systemic side effects and ventilation-perfusion mismatch. Inhaled milrinone appears to be an alternative promising approach to treat severe PAH with RV dysfunction following CPB.

It has been compared with another potent pulmonary vasodilator, inhaled nitric oxide, in adult patients with pulmonary hypertension undergoing cardiac surgery. It was shown that the improvement in RV ejection fraction with milrinone was similar to that produced by nitric oxide in the dose of 20 parts per million (ppm), but was less as compared with 40 ppm dose of nitric oxide.[77]

Milrinone has also been used in infants and children after corrective surgery for congenital heart disease. Low cardiac output syndrome (LCOS) affects up to 25 percent of neonates and young children after cardiac surgery

and contributes to postoperative morbidity and mortality. Milrinone administered prophylactically in the dose of 75 µg/Kg bolus followed by a 0.75 µg/Kg/min. infusion, significantly reduces the risk of development of LCOS.[78]

Milrinone, thus appears to be a very useful inotrope during cardiac surgery and can be utilised in a variety of clinical situations. However, two recent publications have reported some adverse effects with rnilrinone. The first one has suggested that milrinone use is an independent risk factor for postoperative atrial fibrillation after cardiac surgery[79] and another one, a meta-analysis has suggested that milrinone might increase mortality in adult patients undergoing cardiac surgery.[80] However, one should await further evaluation of these aspects before changing the practice.

Enoximone

Enoximone is an imidazole and its haemodyna-mic effects are similar to other PDE-III inhibitors. Its ability to augment ventricular function in low CO states following CPB has been demonstrated.[81,82]

It can be administered in a bolus of 1 mg/Kg before weaning from CPB to improve the overall cardiac function and reduced need of catecholamines after CPB.[83,84] It has also been shown to increase CO and decrease PA pressure in patients with mitral regurgitation and pulmonary hypertension.[85] In combination with epinephrine, it can potentiate the effect of epinephrine, a fact that can be useful in patients with severe heart failure.[86] Its prophylactic use in the elderly patients undergoing cardiac surgery has demonstrated attenuation of the inflammatory response.[87] However, it failed to improve diastolic function after valve replacement for aortic stenosis as assessed by Doppler echocardiographic examination.[88] It is usually administered as a bolus (1 mg/Kg) followed by a continuous infusion of 10 µg/Kg/min.

Other Inotropic Drugs

Levosimendan

Levosimendan is a calcium sensitizing inodilator. The positive inotropic effect is exerted through sensitisation of myofilaments to calcium, and vasodilatation through opening of ATP sensitive potassium channels on vascular smooth muscle. The haemodynamic effects include, a reduction in

PCWP and SVR with an increase in CO. These effects occur without increasing the myocardial oxygen demand.[89] It has an intermediate metabolite OR-1855, which is further acetylated to the active metabolite OR-1896. The OR-1896 has haemodynamic and pharmacological properties similar to the parent drug.[90] Since, the active metabolites have a longer half-life (up to 80 hours), the haemodynamic improvements can be observed for a prolonged period. It has been shown to improve 6-month survival in patients with acute myocardial infarction and LV dysfunction.[91] It also improves the contractile function of the stunned myocardium in patients with acute coronary syndromes.[92]

In cardiac surgery, it has been used preoperatively, during weaning from CPB, and in the postoperative period. A study performed on 11 patients with severely impaired CO after cardiac surgery revealed that levosimendan improved haemodynamics with significant increase in CI and SV, and a decrease in MAP, SVR, MPAP, right atrial pressure and PCWP.[93] It is also described as a myocardial protective agent, the effect is mediated via opening of ATP sensitive potassium channels. The postoperative cardiac troponin release is reduced by it following CPB.[94] It can be administered as a bolus dose of 12 μg/Kg as a 10 min. loading dose, followed by an infusion of 0.1 μg/Kg/min. The infusion can be continued for 24 hours to a maximum of 48 hours. Starting the levosimendan treatment before CPB, rather than after aortic clamp release may provide higher initial postoperative stroke volume and a lower incidence of atrial fibrillation.[95]

It has been compared with IABP in patients with cardiogenic shock complicating acute myocardial infarction. Levosimendan or IABP was added when standard therapy failed. Infusion of levosimendan resulted in early and sustained haemodynamic improvement that was comparable to IABP.[96] In patients with poor LV function undergoing CABG, it enhances the primary weaning from CPB with reduction in the need for additional inotropic or mechanical support.[97]

Levosimendan has been mostly used in combination with other conventional inotropes. It is a promising new inotrope and is a safe and efficient choice in the management of LCOS during and after open-heart surgery.[98] It leads to improvement in haemodynamic status, deescalation of traditional inotropes, weaning from IABP, and reduction in brain natriuretic peptide levels.[98] Thus, levosimendan has emerged as an important option of

pharmacological inotropic support in patients with cardiogenic shock. Several controlled studies have suggested that levosimendan is efficacious in improving haemodynamics after cardiac surgery and its use as an adjunct to catecholamines instead of PDE inhibitors has been recommended in patients with post-cardiotomy heart failure and cardiogenic shock.[99] Its prophylactic use before CPB in patients with compromised ventricular function may also be considered rational.[99] The utility of levosimendan has been confirmed by a recent meta-analysis that has revealed that it may reduce mortality in cardiac surgery and cardiology settings of adult patients.[100]

Calcium

Many clinicians believe that intravenous adrninistration of calcium during termination of CPB is helpful. This belief is based on the consideration that infants, young children and adults are often hypocalcaemic during and shortly after CPB. In addition, it has been shown in-vitro, that increasing the concentrations of extracellular calcium ions improves the contractility of the cardiac muscle. However, studies performed on patients undergoing CABG have shown that calcium chloride (5 to 10 mg/Kg) increased MAP and blood ionised calcium concentration but had no effect on CI.[101-103] In addition, calcium may blunt the response to catecholamines[104] (such as epinephrine and dobutamine) and calcium influx during ischaemia-reperfusion contributes to myocardial dysfunction after CPB. Therefore, routine administration of large doses of calcium salts to adult patients after CPB appears to be unjustified.[105]

Nevertheless, calcium salts are used to improve myocardial performance in some situations such as rapid transfusion of large quantities of citrate preserved blood products,[106] and sometimes with large doses of protamine. It can also be administered during severe hyperkalaemia or with calcium channel blocker overdose. A major concern with the use of calcium chloride is the precipitation of coronary artery spasm after CPB.[107] However, it has been suggested that judicious administration of calcium salts to restore concentrations of ionised calcium to physiological level can be practised for the benefit of the patient.[108]

Digoxin

There is little evidence that digoxin provides effective inotropic support in

cardiac surgical patients emerging from CPB. It is primarily used in the preoperative period to treat disturbances of cardiac rhythm. Digitalis is more useful in the treatment of chronic CHF and is routinely administered in patients suffering from valvular heart disease. Digitalis inhibits the enzyme Na^+/K^+ activated ATPase and thus inhibits the transport of sodium and potassium ions across the cell membrane.[109] This results in a net potassium exit from the myocardium and an increase in the calcium released to the contractile element at the time of excitation-contraction coupling.[110]

Digoxin increases myocardial contractility. In patients with acute CHF, digoxin improves CO and decreases SVR and venous tone. However, its inotropic effects are relatively mild[111] and also the half-life is quite long. Due to these drawbacks, it is rarely used during cardiac surgery. Its main use continues to be the control of tachyarrhythmias, especially atrial fibrillation during preoperative period.

In summary, there is a wide choice of inotropes at present. Both beta-adrenergic agonists and PDE inhibitors have advantages and disadvantages related to their pharmacological side effects and cost. Dopamine, dobutamine and now the inodilators are quoted commonly in the literature. However, during the termination of CPB, particularly in patients with poor LV, a strong cardiotonic drug is preferable. In this respect, epinephrine is still regarded as an inotrope of choice for maximal effect by many units, if needed. In the dose range of 0.02 to 0.08 µg/Kg/min., it is predominantly a beta-agonist and it is only with a higher dosage that peripheral constriction occurs. Some may prefer dobutamine or levosimendan and yet others, a combination of inotrope and vasodilator or an inodilator. Norepinephrine may seem to be a suitable agent to raise SVR in some patients (septicaemia). However, PDE inhibitors and levosimendan may find a place in certain situations such as patients with pre-existing ventricular dysfunction or when stunning of the myocardium is suspected with down-regulation of the beta receptors. Dopamine in the renal vasodilating dose is still used by some to improve renal perfusion and urine output. The doses and concentrations of commonly used inotropes are shown in Table 12.4.

Arginine-vasopressin

CPB can be associated with vasodilatory hypotension, which requires pressor support. At times the hypotension can be severe that is nonresponsive to

usual inotropes such as epinephrine, norepinephrine, dobutamine, etc. It has been shown that arginine-vasopressin can be effective in the treatment of such a refractory hypotension,[112,113] and reduces the catecholamine pressor requirements. Low ejection fraction (< 0.35) and angiotensin-converting enzyme inhibitor use have been identified as the risk factors for the post-bypass vasodilatory shock, which is associated with vasopressin deficiency.[112] It has been used in different doses, but an infusion of up to 6 units/hour is generally sufficient and increasing the dose further provides little added vasopressor effect. In children, it has been used in the range between 0.0003 to 0.002 units/Kg/min.[113] It has also been shown to be effective in the treatment of vasodilatory shock following off-pump CABG.[114]

Vasodilators

The addition of vasodilator drugs to the inotropic therapy of patients with CHF is one of the important advances in the management of heart disease. It has been shown that vasodilators can be used to shift the Starling curve up and to the left, thereby reducing the pulmonary congestion and improving the CO. This improvement in cardiac performance is associated with a decrease in MVO_2. In a patient with moderate to severe ventricular dysfunction, SVR is elevated because of increased catecholamine levels. In this situation, addition of a vasodilator helps to decrease the outflow resistance, thereby increasing the SV and CO. Simultaneous infusion of volume may be necessary to avoid preload and afterload mismatch as concomitant venodilatation may lead to reduction of intracardiac volume.

Table 12.4: Concentration of various inotropes used in clinical practice. Please note that the concentration can be increased if patient needs fluid restriction.

Drug	*in 500 mL*	*in 1 mL*	*Dose (µg/Kg/min)*
Epinephrine	4 mg	8 µg	0.025 to 0.15
Dopamine	400 mg	800 µg	2 to 10
Dobutamine	500 mg	1000 µg	2.5 to 10
Isoprenaline	4 mg	8 µg	0.025 to 0.1
Amrinone	200 mg	400 µg	5 to 10
Milrinone	10 mg	20 µg	0.3 to 0.75

The vasodilators can be classified according to the site of action. Those that predominantly affect the venous system (venodilators), increase the

venous capacitance and lead to a decrease in preload. The CO is generally not affected, but may decrease if hypovolemia already exists. The venodilatation leads to an increase in the capacity of the vascular bed causing redistribution of blood from the cardiac chambers and pulmonary circuit to the periphery.[115] Therefore, venodilators are most useful in patients with markedly elevated venous filling pressure where they do not affect the CO.

Drugs which predominantly cause arterial vasodilatation, decrease the SVR and increase the CO. They should be used when SVR is markedly elevated and venous filling pressures are relatively normal. Drugs having mixed action (both arteriolar and venodilatation), decrease the LV end-diastolic volume along with MVO_2 and SVR, while increasing the CO. They can, therefore, be used in a situation where both filling pressures and afterload are elevated.

The vasodilators that are freely available and commonly used are sodium nitroprusside and nitroglycerin. They are frequently used during cardiac surgery along with inotropic agents for the treatment of low output states as well as pulmonary hypertension. In addition, they are also used to control perioperative hypertension.

Sodium Nitroprusside

Sodium nitroprusside is a very rapidly acting and potent arterial and venous dilator. It is the most thoroughly studied and widely used agent for reducing afterload in low output states. It acts by direct relaxation of arteriolar and venular smooth muscle, thus decreasing both preload and afterload.[116] The haemodynamic effects of nitroprusside in patients with low CO include, decrease in SVR and increase in CO with little or no decrease in BP. In addition, PA pressure, PCWP, central venous pressure (CVP) and PVR are also decreased. In patients with elevated MAP, nitroprusside causes decrease in MAP and can be used for the treatment of postoperative hypertension after CABG.[117] It also improves the splanchnic blood flow and has no adverse effects on splanchnic tissue oxygenation.[118] It is generally administered as an infusion in a starting dose of 0.5 µg/Kg/min. The dose can be increased further depending upon the haemodynamic response (Table 12.5). Reflex tachycardia that is commonly observed in patients with normal CI during nitroprusside infusion for induced hypotension, is rarely a problem in patients receiving nitroprusside for afterload reduction in low CO states. In fact, HR

may sometimes decrease due to improvement in SV and CO.[119]

It can be used during cardiac surgery to lower systemic and pulmonary hypertension, and for the treatment of low output state along with inotropes. It has been investigated whether SNP, as a nitric oxide donor, can reduce the incidence of atrial fibrillation (AF) following CABG. In a randomized, placebo-controlled trial, it has been shown that SNP in a dose of 0.5 µg/Kg/min. significantly reduced the incidence of AF.[120] It has also been used by intracoronary route in the setting of percutaneous intervention (PCI) for acute myocardial infarction. One study has shown that selective intracoronary administration of SNP prior to PCI was well tolerated and prevented no or slow reflows, and improved reperfusion of the infarcted myocardium.[121], while another failed to show any improvement in coronary flow and myocardial tissue perfusion, but improved clinical outcome at 6 months.[122] The adverse effects of SNP include increased intracranial pressure, decreased cerebral blood flow, and the accummulation of cyanide and thiocyanate.[123,124] It has been shown that elevated cyanide levels were best predicted by a mean dose of 1.8 µg/Kg/min. in paediatric cardiac surgical patients.[125]

Nitroglycerin

Nitroglycerin is another vasodilator that is used commonly during cardiac surgery. It predominantly affects the venous system with less effect on arteries. It therefore, decreases preload with little or no effect on the afterload. In patients with CHF, it causes reduction in the PA pressure, PCWP, CVP and PVR. The CO may remain unchanged or even decrease, if decrease in preload is significant.[126] Due to its property of coronary artery dilatation,[127] it may be preferred over nitroprusside in patients undergoing CABG. It is administered as an intravenous infusion in the dose of 0.5 to 5 µg/Kg/min. Like nitroprusside, it can be used for the treatment of systemic as well as pulmonary hypertension and in combination with an inotrope for the treatment of low output state. However, due to its predominant venodilating effect, it may not be an effective antihypertensive agent. It has been shown that nitroglycerin should not be considered as the primary agent for urgent control of BP because it has poor efficacy and may lead to hypotension and reflex tachycardia.[128,129] Another important use of nitroglycerin is its antispasmodic property for arterial grafts used during CABG. Its topical use

along with verapamil has shown promise in reducing the incidence of radial artery graft occlusion.[130] Its infra-arterial administration has been used to treat the IMA graft spasm[131] and a cocktail of nitroglycerin and nicardipine has been shown to provide a new antispastic protocol for radial artery and IMA grafts to be used in CABG.[132]

Table 12.5: Concentrations of vasodilators.

Drug	*in 500 mL*	*in 1 mL*	*dose (µg/Kg/min.)*
Nitroglycerin	50 mg	100 µg	0.5 to 5
Nitroprusside	50 mg	100 µg	0.5 to 5

Both nitroglycerin and sodium nitroprusside can worsen the ventilation-perfusion mismatch and it has been shown that stopping their infusion in the post-cardiac surgical patients requiring a high inspired oxygen concentration improves the arterial oxygen tension and venous admixture facilitating the weaning from mechanical ventilation.[133]

Calcium Channel Blockers

Calcium channel blockers (CCB) are potent vasodilators and can be useful in the perioperative setting. The first generation CCBs (verapamil, diltiazem, and nifedipine), the second generation, (nicardipine) and the third generation (clevidi-pine) can all be used. In a meta-analysis it was concluded that calcium antagonists during cardiac surgery significantly reduce the rates of myocardial infarction, ischaemia, and supra-ventricular tachycardia.[134] Nifedipine, diltiazem and nicardipine are the commonly used drugs. However, the negative inotropic effect of some of these agents (nifedipine, diltiazem) may make them undesirable unless ischaemia is the cause of myocardial depression, which can be reversed by calcium antagonists.[135] The safety and efficacy of clevidine, nitroglycerin, sodium nitroprusside, and nicardipine have been compared in the treatment of perioperative acute hypertension in patients undergoing cardiac surgery.[128] Results showed that mortality was significantly lower with clevidipine versus sodium nitroprusside, (1.7 percent versus 4.7 percent), but not clevidipine versus either nitroglycerin or nicardipine. It was also shown that clevidipine was more effective compared with nitroglycerin or sodium nitroprusside and equivalent to nicardipine in control of the blood pressure.

Prostacyclin

Prostacyclin is an effective vasodilator that also has a pronounced pulmonary vasodilator effect. It increases the CO and SV associated with decreases in SVR and PVR. These effects have been shown to be more pronounced as compared with sodium nitroprusside.[136] It thus appears to be a useful agent in the treatment of postoperative heart failure with elevated cardiac filling pressures, where vasodilator treatment is indicated. It is especially useful in the treatment of pulmonary hypertension and RV failure. It has also been used successfully in an inhaled form for the treatment of refractory pulmonary hypertension after cardiac surgery.[137]

Fenoldopam

Fenoldopam is a selective DA_1, agonist with potent vasodilator effect, and enhances natriuresis, diuresis and renal blood flow.[138,139] It may have hepato-protective effect following CPB.[140] It is an alternative to sodium nitroprusside with fewer side effects and improved renal function. A meta-analysis has shown that fenoldopam significantly decreased the risk for in-hospital death and the requirement for renal replacement therapy in patients undergoing cardiovascular surgery.[141] Preservation of renal blood flow in the setting of decrease in blood pressure is the feature of this drug. Further trials are necessary to confirm the utility of the agent in patients undergoing cardiac surgery.

Nesiritide

Nesiritide is a human recombinant brain natriuretic peptide that increases cyclic guanosine monophosphate and causes venous, arterial and coronary vasodilatory effects.[142] It is a unique medicine used to manage heart failure in the sense, it mediates natriuresis and vasodilatation and suppresses the renin-angiotensin-aldosterone axis. In patients with acute heart failure, nesiritide improves the clinical status by decreasing cardiac filling pressures and increasing the CI.[143] The Nesiritide Administered Peri-Anesthesia in Patients Undergoing Cardiac Surgery (NAPA) trial has evaluated the impact of perioperative nesiritide treatment on postoperative renal function, systemic haemodynamics, clinical outcome and safety in patients undergoing CABG.[144] In patients receiving nesiritide, there was improved renal function,

shorter hospital stay, and reduced 180- day mortality. Another study performed on patients with LV dysfunction undergoing CABG failed to show any benefit with nesiritide in comparison to milrinone.[145] Some studies have also demonstrated impaired renal function[146] and increased risk of death[147] with nesiritide treatment. Therefore, the role of nesiritide in the treatment of acute heart failure needs to be evaluated further.

Phenoxybenzamine

Phenoxybenzamine is the alpha-1 antagonist that irreversibly binds the receptors. It is used in intravenous doses in cardiac surgery and has a half-life of about 24 hours. It decreases the SVR and increases CO, and blood flow to the skin and viscera is increased. In cardiac surgery, it is used in children with congenital heart defects (especially lesions with left-to-right shunt) during the periopertive period.

It is commonly administered before the onset of CPB in the dose of 1 mg/Kg as an infusion over 5 to 10 min. at the time of aortic cannulation. Alternatively, half the dose can be administered in the prime and the remaining half intravenously. The maximal dilatation of the systemic circulation permits higher flows on CPB ($\overline{>}$ 150 mL/Kg/min.) thereby maintaining organ perfusion and peripheral circulation. In a comparison with sodium nitroprusside in infants undergoing cardiac surgery, it has been shown that phenoxybenzamine was better in terms of organ perfusion and peripheral circulation.[148] Phenoxybenzamine has also been used in combination with sodium nitroprusside and nitroglycerin.[149, 150] Addition of sodium nitroprusside can be useful in patients where full dose of phenoxybenzamine cannot be used due to concerns of excessive vasodilatation, and nitroglycerin helps to decrease the pulmonary artery pressure. The dose of phenoxybenzamine can be repeated every 8 to 12 hours in the ICU.

Hydralazine and phentolamine are some other agents that can be used to treat hypertension, but are not preferred.

Mechanical Support of Circulation

Intra-aortic balloon counterpulsation

The principle and concept of counterpulsation was known in early 1960s. However, the first clinical use of IABP was reported by Kantrowitz et al[151] in 1968. Initially, insertion of the IABP required surgical exposure of the femoral artery, attachment of a vascular prosthesis and then passage of the balloon through the prosthesis. With the improvements in technology, the insertion of balloon is now possible percuta-neously by Seldinger technique, so that the balloon insertion can be performed as a bedside procedure.

Mechanism of Intra-aortic Balloon Counterpulsation

Basically, IABP is designed with the purpose of augmenting myocardial perfusion by increasing coronary blood flow during diastole and unloading the LV during systole. The percutaneous intra-aortic balloon that is used is shown in Figure 12.2. The balloon is positioned in the proximal segment of the descending aorta (Fig. 12.3) and is alternately inflated and deflated by carbon dioxide or helium. The inflation and deflation of the balloon leads to mass displacement of generally 30 to 50 mL of blood. The inflation and deflation are synchronised to the cardiac cycle so that the balloon is inflated rapidly during diastole (triggered by the ECG 'R' wave) and then deflated during systole. The ratio of the inflation and deflation sequence to the pulse rate can be set at various levels, such as 1:1,1:2, etc. The balloon inflation during diastole causes increased aortic pressure which improves the coronary, cerebral, and renal perfusion (Fig. 12.4). During subsequent rapid deflation of the balloon in systole, the impedance to LV emptying decreases, LV wall tension is lowered and hence, oxygen demand is less. Improvement in CO, brain and coronary blood flows and MAP are frequently seen with the use of IABP.

Indications and Contraindications

Although the indications for IABP have grown rapidly over the years, the most common use of IABP is for the treatment of cardiogenic shock. Inside the cardiac OT, such a situation frequently arises at the time of separation of the patient from CPB, as more and more sick patients are being subjected to surgery. The general tendency is to insert the IABP catheter at the slightest indication or suspicion of LV failure in order to avoid subjecting the heart to high inotropic support. The IABP is now the most commonly used

mechanical assist device in cardiac operative procedure. Amultivariate analysis has shown that age greater than 70 years, moderate and poor LV dysfunction, previous cardiac surgery, emergency operation, left main disease, Canadian Cardiovascular Society 3–4 class and recent myocardial infarction are independent risk factors for the need of IABP insertion.[152] Sometimes, IABP may be inserted preoperatively to stabilise the haemodynamics in a sick patient before subjecting him to surgery.[153] This can be done in patients with left main CAD with unstable angina or patients who are in pulmonary oedema due to LV failure. A multicentre study performed on high-risk patients (Euroscore > 8) revealed that prophylactic IABP support in the preoperative period significantly decreased in-hospital mortality, 30-day mortality, perioperative myocardial infarction, perioperative low output syndrome, and ICU and hospital length of stay as compared with those who did not receive IABP preoperatively.[154] A recent Cochrane Database review has concluded that preoperative IABP may have beneficial effect on mortality and morbidity in specific high-risk patient groups undergoing CABG. However, the precise patient groups that may benefit remains to be defined.[155] Similar benefits in mortality and morbidity have been shown with preoperative IABP in patients with severe LV dysfunction undergoing off-pump CABG.[156]

Figure 12.2: A percutaneous intra-aortic balloon catheter.

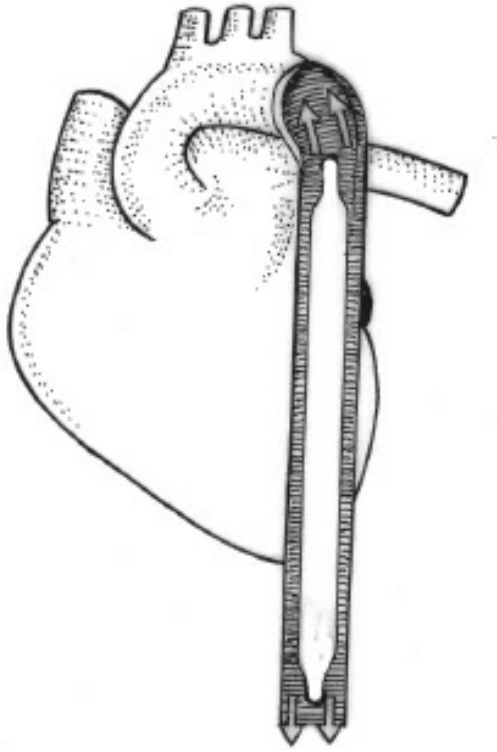

Figure 12.3: Correctly positioned balloon in the descending thoracic aorta.

If the patient comes to the OT with an IABP, whether to turn it off or keep it on while on CPB needs to be answered. The general practice is to stop IABP on commencement of CPB. However, the literature search revealed that IABP induced pulsatile perfusion during CPB improves perfusion to vital organs, better lung function in chronic obstructive pulmonary disease patients, ameliorates the coagulative system and lowers endothelial activation.[157] Therefore, in patients who already have IABP in-situ while going on CPB, it should be turned on to internal trigger mode. IABP is also being increasingly used inside the cardiac catheterisation laboratory as a device to support the circulation in high risk patients undergoing coronary angioplasty.[158] The use of IABP in the setting of a failing RV after CPB is controversial. Boeken and colleagues have shown that IABP can be beneficial in low CO syndrome caused by predominantly RV failure, particularly after CABG.[159] Therefore, it may be an additional indication for IABP.

Despite the use of IABP support in complex cardiac surgical patients, morbidity and mortality rates are high. Attempts have been made to identify early, readily available prognostic markers for patients receiving IABP support. It has been shown that mortality can be predicted by the presence of

elevated serum lactate, elevated base deficit, hypotension, oliguria and large vasopressor doses. Serum lactate more than 10 mmol/L in the first 8 hours of IABP support predicted a 100 percent mortality.[160] One paper has shown that the overall operative mortality was 35 percent. The mortality as per time of balloon insertion was: preoperative 18 percent, intraoperative 33 percent, and postoperative 58 percent.[161] The incremental risk factors for death were: female gender, smoking, preoperative creatinine more than 120, cross-clamp time more than 80 min, and IABP insertion postoperatively.[161]

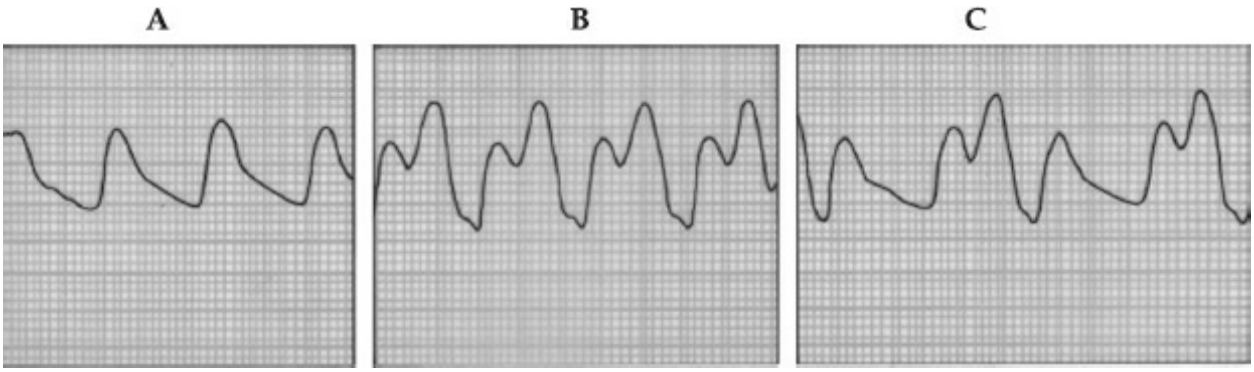

Figure 12.4: Augmentation of arterial pressure with intra-aortic balloon pump (IABP). A: arterial pressure waveform without IABP support, B: with 1:1 augmentation, C: with 2:1 augmentation.

Contraindications to IABP are relatively few (Table 12.6). Presence of aortic regurgitation (AR) or aortic dissection is considered to be an absolute contraindication for IABP, as IABP can lead to worsening of the haemodynamic condition of the patient. In AR, the blood displaced from aorta during diastole is pushed into the LV leading to LV distention. In addition, as there is no augmentation of pressure during diastole, the coronary perfusion is also not improved. In aortic dissection, the dissection can increase due to an increased pressure during diastole.

Technical Aspects

The most common method of balloon insertion that is currently used is percutaneous insertion by Seldinger technique. Occasionally, when the femoral pulses are feeble (due to low output), or in the OT when the patient is on CPB and pulsatile flow is not possible due to poor ventricular ejection, direct surgical exploration of the femoral artery may be performed. The percutaneous insertion can be rapidly performed with the commercially available kits. In the OT, the insertion is performed by the surgeon, most

commonly at the time of separation from CPB. Sometimes, the anaesthesiologist may perform it before induction of anaesthesia in a sick patient to support the circulation. In other areas, such as ICU, coronary care unit or catheterisation laboratory, it can be performed by any trained personnel. Strict aseptic precautions with adequate haemodynamic monitoring are essential for accurate placement of the balloon.

Table 12.6: Indications and contraindications for Intra-aortic balloon counterpulsation.

Indications
1. Cardiogenic shock
myocardial infarction
cardiomyopathy
valvular disease (except AR)
2. Difficulty or failure to separate from CPB
3. Stabilisation of a patient preoperatively
4. Haemodynamic support during angiography/ angioplasty
5. Bridge to transplant
Contraindications
1. Aortic regurgitation
2. Aortic disease: dissection, aneurysm
3. Severe peripheral vascular disease

AR: aortic regurgitation, CPB: cardiopulmonary bypass

The length of the balloon to be inserted is estimated by laying the catheter on the chest with the tip positioned at the angle of Louis. The distal point is marked that corresponds to the point of insertion at the femoral artery. The manufacturer's instructions for removal of the balloon from its package must be strictly followed so as not to cause any damage to the balloon. Most currently available balloons come already wrapped and need only to be properly deflated before removal from the package.

The femoral artery is punctured with the supplied needle and the J-tipped guide wire is inserted up to the aortic arch. The needle is then removed and the arterial puncture site is enlarged successively with 8F dilator followed by 10 or 12F dilator/sheath combination. The dilator is removed, leaving the sheath and the guide wire in the artery. The balloon is threaded over the guide wire into the aorta up to the previously estimated length. To minimise the risk of ischaemic complications to the distal extremity, the sheath should be pulled back so that the entire sheath is out of the arterial lumen. This also

ensures that the balloon is completely out of the sheath and inflates freely in the aorta. “Sheathless” balloons are also available that can be inserted without a sheath. The distal end of the balloon is connected to the console via a tubing that is provided. The lumen provided for the measurement of pressure is connected to the console via a pressure transducer to measure the aortic pressure.

The correct placement of the balloon can be verified by fluoroscopy, if available (catheterisation laboratory) or more commonly by monitoring the left radial arterial pressure waveform. A reasonable estimate of position may be made by watching the diastolic augmentation produced during balloon inflation. If the balloon is placed too far in (occluding the flow to left subclavian artery), the radial arterial pressures will decrease with balloon inflation. Good diastolic augmentation is produced if the balloon is placed appropriately. The position may also be checked by transoesophageal echocardiography (TOE) or radiography. After appropriate positioning and timing of the balloon, counterpulsation at the desired ratio (1:1 or more) is initiated.

Some other routes of insertion of the balloon that can be used are subclavian, axillary or iliac arteries. In patients, in whom extreme peripheral vascular disease exists, the ascending aorta or aortic arch may be used as the routes of insertion. These approaches, however, require median sternotomy for insertion as well as removal of the catheter.

IABP Timing

For optimal effect of the IABP, inflation and deflation of the balloon must be correctly timed to the cardiac cycle. The basic console design of the currently available IABP systems includes, electrocardiograph, and arterial BP waveform monitoring, triggering selection switches, adjustments for the timing of inflation/deflation, gas reservoir, adjustment for degree of augmentation and battery back-up (Fig. 12.5). The balloon inflation should be timed during early diastole to correspond with aortic valve closure. Early balloon inflation can result in aortic insufficiency, whereas late inflation will result in inadequate augmentation of pressure during diastole, thereby not helping the coronary perfusion. Early deflation can cause inappropriate loss of afterload reduction while late deflation can lead to increased afterload. The present day machines are fairly sophisticated with microprocessor controls that have several safety features that avoid accidents from happening. Once

the balloon is inserted and operational, the timing adjustments can be made by using the markers on the arterial tracing.

The common reasons for failure to achieve optimum augmentation are: inappropriate position of the balloon, inappropriate timing of inflation/deflation, and choosing inappropriate balloon volumes for inflation.

Weaning from IABP is determined by the sustained improvement in the haemodynamic condition of the patient. The IABP support should be withdrawn in stages with careful haemodynamic monitoring. In addition, adjustments in the doses of inotropes and vasodilators may be necessary. In the postoperative cardiac surgical ICU, it is often debated whether extubation of the patient should be delayed until the patient is off the IABP support. There is no contraindication for extubation, if the patient is on IABP support and the support can continue even after extubation in a conscious and awake patient, if necessary. Ventilation of the patient need not be prolonged (if other parameters of extubation are achieved) just because he is on IABP support.

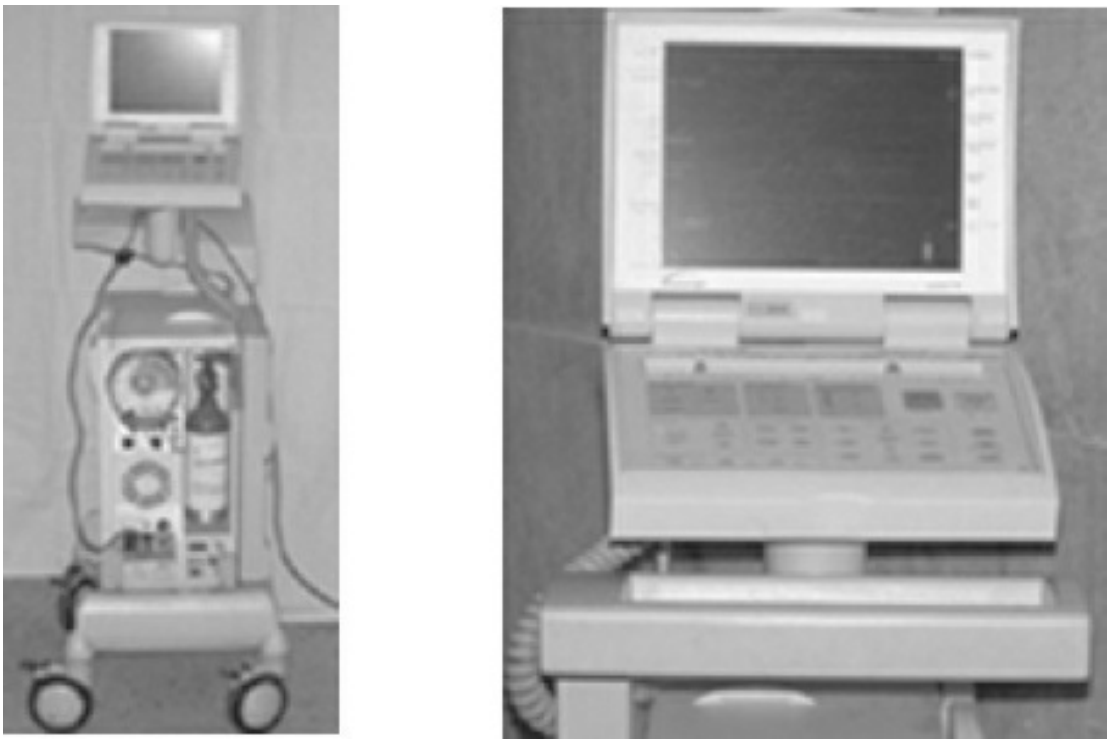

Figure 12.5: Intra-aortic balloon pump console (Datascope system 98, Datascope Corp, Paramus, NJ).

Complications

The complications of IABP are related to the vascular system and involve the insertion vessels. Lower limb ischaemia is the commonest complication.

Perforation and dissection of the femoral artery or aorta, the femoral artery thrombosis, and pseudoaneurysm of the femoral artery are some other vascular complications. Infection, haemolysis and thrombocytopaenia may occur. One study has shown that sheathed catheterization increases the risk of vascular complications. Therefore, sheathless catheterisation is recommended for IABP application.[162]

Ventricular Assist Devices

These are the devices that are connected to the heart or placed within the heart (right or left) to unload it and pump the blood into the aorta (left ventricular assist device, LVAD) or pulmonary artery (right ventricular assist device, RVAD). They may be used when there is inability to wean the patient from CPB despite inotropes and IABP support. This may help to reverse the ventricular dysfunction. The other applications include, bridging patients to heart transplantation, and serving as destination therapy for those who are not fit to undergo transplant. The pulsatile assists devices provide a pulsatile flow, the examples are Abiomed BVS 5000, the Thoratec VAD system, the Novacor and the HeartMate. The nonpulsatile devices generate a continuous flow (centrifugal or axial flow pattern) and are relatively small, silent, valveless and fully implantable. The examples are Jarvic 2000, and the HeartMate II. The Jarvic 2000 is implanted at the LV apex and the outflow cannula is placed in the descending thoracic aorta. In HeartMate II, an inflow graft placed in the LV delivers blood to the pump, and an outflow graft delivers blood from the pump to the ascending aorta. Both Jarvic 2000 and the HeartMate II are used for long-term ventricular support as a bridge to heart transplantation.

Contraindications to LVAD placement include active infection, irreversible renal dysfunction, severe liver impairment, stroke, severe pulmonary hypertension, incurable malignancy, and for the larger LVADs, a small body surface area (< $1.5m^2$).[163] However, smaller size devices that can be used is patients with smaller body surface area (women and children) are now available.[164]

The patients needing LVAD are generally quite sick since they have decompensated heart failure refractory to medical management. A varying degree of end-organ dysfunction caused by low-output is present in them.

Coagulopathy is common and a high incidence of heparin induced thrombocytopenia (HIT) is present, as prolonged or intermittent heparin is administered to them.[165] Therefore, the patients should be tested for HIT antibodies and alternative plans for anticoagulation should be made. In addition, adequate measures to tackle excessive bleeding in these patients are necessary. These include antifibrinolytic agents, large bore intravenous lines for rapid transfusion, and sufficient stock of blood and blood products.

Etomidate can be used for induction of anaesthesia and fentanyl for analgesia. Monitoring should include PA catheter and TOE. TOE is especially desirable to diagnose RV dysfunction, AR, tricuspid regurgitation (TR), patent foramen ovale, ventricular septal defect, ascending aortic plaques and ventricular thrombi. Significantly decreased RV function should prompt the use of biventricular support device. Mild TR may become severe after LVAD implantation as the LV decompression leads to distraction of the tricuspid subvalvular apparatus to the left causing failure of apposition of the tricuspid leaflets. Tricuspid annuloplasty should be considered in presence of TR.

Presence of moderate to severe AR will lead to LV distension once the LVAD is activated. Thus the LV cannot be decompressed and also the forward flow is decreased. Presence of patent foramen ovale can result in right-to-left shunt leading to desaturation, as the left atrial pressure can decrease after the LV is decompressed by the LVAD, hence, it should be closed.

During surgery, TOE can help to ensure appropriate placement of the inflow and outflow cannula and adequate de-airing of the LV before termination of the CPB. In the postbypass period, adequate reversal of anticoagulation and haemostasis should be achieved. The requirement of blood and blood products may be high. The chest closure may not be possible for 24 to 48 hours, until the cardiac function is stabilised and bleeding is under control.

The early results of LVAD implantation have been reported to be good. In a series of 11 patients who underwent HeartMate-II implantation, eight patients were successfully bridged to heart transplantation after median 155 days (range, 65 to 316 days) and one was ongoing for 748 days, intended for destination therapy.[166] Ten of the eleven patients were discharged after median 64 days (range, 40 to 105 days) and one patient died.

Percutaneous left ventricular assist devices

The recent development of percutaneous extracorporeal circulatory support systems has revolutionised the care of patients in whom IABP and inotropes are not sufficient to reverse or prevent cardiogenic shock. The devices are, Tandem Heart (Cardiac Assist Inc. Pittsburgh, PA, left atrial-femoral arterial bypass), and Impella Systems (Abiomed Inc, Danvers, MA, transvalvular aortic axial flow devices). The therapeutic goals of these systems are to restore or maintain normal haemodynamics and organ perfusion in cardiogenic shock (bridge to recovery), serve as support for a procedure in complex high-risk percutaneous interventions (bridge to procedure), or bridge to surgery for the implantation of a long-term ventricular assist device as destination therapy or a bridge to transplantation.

The Tandem Heart provides left heart bypass. The cannulae are placed percutaneously into the LA (by trans-septal puncture), and the femoral artery. The device uses a low-speed centrifugal continuous flow pump that can deliver a flow up to 4 L/min. The trans-septal puncture can lead to right-to-left shunt and the risk of paradoxical air embolism. The Impella system has a different mechanism of ventricular unloading and circulatory assistance. A miniature axial rotary blood pump is positioned across the aortic valve. The system unloads the ventricle by drawing blood through the distal port in the ventricular cavity and pumping it into the ascending aorta through the proximal port of the device. The device is inserted via the femoral artery and advanced past the aortic valve under fluoroscopic guidance. There is no need for concomitant venous access and transseptal puncture is not required. Although these devices have shown beneficial physiological effects, there have been limited human studies. For further details, the reader is refered to the review article by Pulido and coworkers.[167]

Extracorporeal membrane oxygenation

The extracorporeal membrane oxygenation (ECMO) consists of a blood pump (centrifugal) and a circuit with a built-in oxygenator providing full cardiopulmonary support. In adults, a 16F to 18F arterial cannula is inserted via a femoral artery into the descending aorta, and an 18F to 20F venous cannula is inserted via the femoral vein into the right atrium. The cannulae are de-aired and connected to the centrifugal pump (suitably primed) and the membrane oxygenator. Blood is withdrawn from the right atrium and pumped

through the heat exchanger and membrane oxygenator to the aorta via femoral artery. ACT of 200 to 300 seconds is maintained.

Cardiogenic shock develops whenever there is failure to wean CPB despite the use of inotropes and IABP. ECMO can be utilised to provide temporary assisted circulation in order to prevent multiple organ failure and death. The term extracorporeal life support has been used to describe the use of ECMO as a temporary support. ECMO has been used for this purpose during cardiac surgery in adults as well as children. In adults, it has been shown to provide viable temporary support after CPB, although the mortality is reported to be high (more than 50 percent).[168-170] The preoperative risk factors for mortality are identified as, poor LV ejection fraction, refractory severe metabolic acidosis, systolic blood pressure less than 90 mm Hg, and a peak lactate level more than 12 mmol/L before ECMO imitation.[169,171] The peri-ECMO predictors of mortality include low serum albumin, level, low platelet count, low oxygen pressure of venous tube of ECMO and poor cardiac systolic function.[171] In children also it has been used after corrective surgery to support the circulation. It carries a high mortality, but remains the ultimate chance for children and acceptable proportion of children who are weaned from ECMO survive to leave the hospital.[172,173] ECMO has been used in children during the preoperative period as a bridge to surgery, especially those with complex heart defects and failing circulation.[174]

With the growing progress, more and more sick patients are being subjected to cardiac surgery. The haemodynamic management of such patients requires understanding of the pathophysiology and pharmacology of the inotropes and dilators. With the availability of newer pharmacological agents that have more selective properties, more precise control of the haemodynamics is possible. This has enabled more efficient management of the right, left and a combination of right and left heart failure. The cardiac anaesthesiologist, therefore, feels more confident in handling such patients.

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Chapter 13: Myocardial Protection during Cardiopulmonary Bypass

It is well recognised that ischaemic myocardial damage frequently occurs during cardiopulmonary bypass (CPB). As the extent of damage can influence the outcome of patient, methods to protect the myocardium from suffering damage during CPB have been described. Arresting the electromechanical activity of the heart by potassium-enriched cardioplegia solution is the single most important step in reducing the heart's metabolism. The reduction in oxygen consumption so produced, is further augmented by hypothermia (cold cardioplegia solution). Over the years, the methods of myocardial protection have improved considerably. Indeed, the improvement has been evident in the markedly better cardiac contractility at the termination of CPB as well as the reduced need for inotropic drugs. More recently, the techniques of retrograde cardioplegia[1] and normothermic cardioplegia[2] have been described. The overall improvement in cardiac surgery has been possible due to optimal preservation of the viable myocardium during surgery.

Amongst the several factors and events during CPB that predispose to myocardial injury, aortic cross clamping is the most important event. Use of cardioplegia solutions during the period of aortic cross clamping is the mainstay of myocardial preservation. In this chapter, various cardioplegia techniques that are used for myocardial preservation will be discussed. In addition, other supportive measures that can be used to prevent or rninimise the myocardial damage will also be discussed.

Almost all patients undergoing cardiac surgery suffer some degree of

myocardial injury. The injury can be subclinical with mild elevation of cardiac enzymes, but can frequently manifest with significant cardiac failure and substantial elevation in cardiac enzyme levels. It has been shown that creatine kinase isoenzyme (CK-MB) values more than 10 times the upper limit of normal during the initial 48 hours after coronary artery bypass grafting (CABG) were significantly associated with 6 month mortality.[3] Appropriate myocardial protection measures are important in today's practice, as more and more older and sicker patients having more severe and diffuse disease, potentially requiring longer ischaemia times are being subjected to cardiac surgery.

Myocardial Ischaemia

Myocardial preservation involves maintenance of oxygen supply and demand. In the event of myocardial oxygen demand not being met by oxygen supply, anaerobic metabolism sets in and results ultimately in infarction. The major factors that determine myocardial oxygen demand are heart rate (HR), preload, afterload and the inotropic state of the myocardium. The oxygen supply is determined by the sufficiency of regional coronary blood flow that is well oxygenated. The oxygen content of the blood is determined by oxygen saturation, oxygen tension and haemoglobin concentration. At this stage, it may be worthwhile considering two important basic mechanisms of myocardial damage, i.e. hypoxia and ischaemia. Hypoxia means a reduction in oxygen supply due to decrease in the oxygen content of the coronary blood without any change in the coronary blood flow, whereas myocardial ischaemia means a reduction in oxygen supply due to an inadequate coronary blood flow in the presence of adequate oxygen content. In clinical practice, hypoxia is a relatively rare cause of myocardial damage during CPB. Ischaemia on the other hand, is likely to occur more frequently during CPB. Various metabolic and functional changes occur with ischaemia. First of all, the myocardial oxygen supply is rapidly depleted that is followed by a brief acceleration of glycolysis that decreases rapidly to below control levels. Adenosine triphosphate (ATP) levels rapidly decrease. Due to anaerobic metabolism, lactic acid accumulates resulting in intracellular acidosis. This further depresses glycolysis by interfering with enzymes that are necessary in the glycolytic pathway. The net result is depletion of ATP. The levels of ATP are restored after establishment of the perfusion. However, the time required

to do so is directly related to the period of ischaemia.

The myocardium can suffer structural damage during the period of ischaemia. This structural damage can manifest as functional impairment that is observed as a low cardiac output (CO) state following CPB. Sometimes atrial and ventricular dysrrhythmias are also suggestive of subtle manifestation of myocardial damage.[4,5] Occasionally, a transient and reversible myocardial dysfunction, “stunned myocardium” ensues. Inmyocardialstunning (usually following ischaemia of a limited duration), there is no structural or biochemical evidence of tissue injury. This insult is characterised functionally by depressed myocardial contractility, which eventually recovers completely over 48 to 72 hours. Reperfusion of myocardium following an extended period of ischaemia (usually > 45 min.) results in a phenomenon known as ischaemia-reper-fusion injury. This reperfusion that is essential for tissue survival, may lead to cell damage as a result of reperfusion itself. The major effect of this injury is stimulation of the endothelium of the coronary circulation that has an impact on vascular tone and the inflammatory response. Generation of oxygen derived free radicals and a disturbance in calcium homeostasis are believed to be responsible for the observed post-ischaemic contractile dysfunction. In addition to this inflammatory response generated due to tissue reperfusion injury, there is a significant systemic inflammatory response that is generated by the CPB. This could further worsen the myocardial injury, as surgery without CPB appears to be associated with reduced myocardial injury.[6] The net result is the requirement for postoperative inotropic support inspire of a technically correct operation. In high-risk patients with compromised cardiac reserve, this myocardial dysfunction may become a crucial factor determining the outcome.

There are many events during CPB that predispose the myocardium to ischaemic injury and prolonged functional impairment. Some of these are aortic cross clamping, ventricular fibrillation (VF), ventricular distention, coronary embolism, catecholamines, and reperfusion (Table 13.1). Amongst these, aortic cross clamping is the most important event and merits some discussion.

Table 13.1: Events during cardiopulmonary bypass that may lead to myocardial injury

1. Aortic cross clamping
2. Ventricular fibrillation
3. Ventricular distention
4. Coronary embolism
5. Low perfusion pressure
6. Catecholamines
7. Reperfusion

Aortic Cross damping

By cross clamping the aorta, the coronary perfusion is completely stopped. Therefore, it is an obvious and most important cause of myocardial damage during CPB. The cross clamping of the aorta is a surgical necessity. The surgeon requires a still and bloodless field to execute most cardiac operations. In the early days of cardiac surgery, continuous coronary artery perfusion was performed to protect the myocardium, and surgery was performed on an empty and beating heart. VF was also induced frequently to quieten the heart, which helped to improve the operating conditions considerably. Nevertheless, many complex repair procedures were difficult to perform on a beating or fibrillating perfused heart. In addition, myocardial damage commonly occurred and there were complications associated with direct coronary cannulation that was performed for coronary perfusion. Therefore, aortic cross clamping with intermittent periods of reperfusion was practised. VF was induced during aortic cross clamping to provide the surgeon with a quiet heart. The aorta was undamped and the heart was defibrillated during the periods of reperfusion. This, however, increased the risk of air embolism, particularly during open repairs. Therefore, this method was useful only in short surgical procedures such as atrial septal defect closure. Subsequently, the techniques of chemically induced cardioplegia were introduced that provided myocardial protection during the periods of aortic cross clamping and also provided the surgeon with an absolutely quiet heart and bloodless surgical field. The surgical procedure could be completed in a single uninterrupted period of cross clamping.

Intermittent Cross Clamping with Periods of Reperfusion

In this technique, the aorta is cross clamped and VF is induced with the help

of a fibrillator. The fibrillation is continued for a period of about 10 min., which is followed by a period of reperfusion when the aortic clamp is released. The heart is defibrillated and reperfusion is continued for 3 to 5 min. The reperfusion period allows the partial regeneration of high energy metabolites and also allows the washout of metabolic end products. The operative procedure is performed during the period when the aorta is cross clamped.

Currently, this method is used by some surgeons to perform CABG. The distal anastomosis of each graft is performed when the aorta is cross clamped with the heart fibrillating and the proximal anastomosis is performed when the aorta is undamped and the heart is beating. The same sequence is repeated to complete the anastomosis of subsequent grafts. Despite the changing trend towards the use of blood cardioplegia, this method is used as a strategy to manage the myocardium with impressive results.[7] It has been found to be comparable with the conventional cold crystalloid cardioplegia in terms of myocardial preservation[8] and inddence of postoperative atrial fibrillation.[9] When compared with cold blood cardioplegia, however, it was shown that the use of intra-aortic balloon pump was higher with fibrillation and aortic cross clamping.[10] A recent review based on 13 studies (eight of which were randomised prospective trials) has shown that intermittent cross-clamp fibrillation is a versatile and cost-effective method of myocardial protection, with the immediate postoperative outcome comparable to cardioplegic arrest in first time CABG.[11] The shorter ischaemic duration with this technique as compared with cardioplegic arrest may offer an explanation for comparable outcomes. In addition, the preconditioning effect of intermittent cross clamp may also be responsible. The incidence of perioperative microembolic and postoperative neuropsychological disturbances were also comparable in patients with no clinical evidence of aortic or cerebrovascular disease.[11] It has also been suggested that arrest, rather than fibrillation during intermittent cross clamping may be beneficial. It has been shown in animal experiments that arrest produced by multiple doses of esmolol (every 10 min.) may be a beneficial alternative to intermittent cross clamping with fibrillation.[12]

Cardioplegia

Institution of CPB, empties the heart and significantly reduces the contractile

work and myocardial oxygen consumption (MVO_2). Chemically induced cardiac standstill during the periods of aortic cross clamping results in minimal oxygen consumption and thus provides effective myocardial protection. The MVO_2 can be further decreased by inducing hypothermia (Table 13.2).[13,14] Thus, the idea of stopping the heart to provide ideal surgical conditions and then restart it after the operation, was conceived. The cardioplegia is used to eliminate electromechanical activity and hypothermia to reduce basal metabolism so that the myocardium can be protected from an ischaemic insult. Aortic cross clamping with cardioplegic arrest is the most prevalent method of myocardial preservation.

Table 13.2: Myocardial oxygen consumption (mL O_2/100 gm/min.) at different conditions of myocardial temperatures.[14]

Temperature	*Empty beating*	*Fibrillating*	*Arrested heart*
37°C	5.59	6.5	1.1
32°C	4.93	3.84	0.83
28°C	3.93	2.93	0.59
22°C	2.87	1.95	0.31

It was suggested by Hooker[15] in 1929 that potassium chloride solutions can be used to stop the heart during VF and Melrose et at[16] introduced potassium cardioplegia into clinical practice in 1955. In the early 1970s, there was a revival in the interest in potassium induced arrest. It was shown in animals that 12 to 15 mEq/L of potassium containing iso-osmotic solution produced arrest at normothermia and that left ventricular (LV) function was only mildly depressed after 60 min. of such arrest.[17] It was also determined that 10 to 50 mEq/L of potassium was the safe range of cardioplegia.[18]

Subsequently, many studies demonstrated the superiority of cardioplegia in terms of better protection of LV function and preservation of high energy compounds than with hypomermia alone or with intermittent cross clamping and hypothermia.[19,20] It was also shown that intermittent infusion of cardioplegia solution every 15 min. during the ischaemic period provided better protection than single dose cardioplegia.[20] Cold crystalloid solutions were employed to initiate and maintain intraoperative cardiac arrest. The cardioplegia facilitated adequate visualisation of the anastomotic site as well as provided the presumed advantage of inhibiting myocardial enzymatic activity during the period when perfusion to the heart was suboptimal.

Although, several methods of producing cardioplegic arrest have been described, the most common agent used to produce electrical and mechanical quiescence is potassium. Several types of cardioplegia solutions containing high levels of potassium are available. The composition of a typical cardioplegia solution is shown in Table 13.3.

Table 13.3: Cardioplegia solution

Component	*Approximate concentration (mmol/L)*
Potassium	20 to 30
Sodium	109
Chloride	114
Calcium	1
Bicarbonate	27
Glucose	28
Mannitol	54

The principles underlying the composition of cardioplegia solution have been reviewed by Buckberg[21] and Hearse et al.[22] In general, the cardioplegia solution should produce immediate arrest. It should be cold, hyperosmolar and provide substrate for continued metabolism during aortic cross clamping. In addition, it should also have membrane stabilising property and buffering capacity to counteract anaerobic acidosis.

The safe limit of aortic cross clamping using cold cardioplegia protection is difficult to predict for an individual patient. It probably should vary with the vulnerability of the myocardium to ischaemic damage. The extent of the preexisting myocardial disease that the patient has, should also be considered to determine this safe limit. It was generally agreed that the outcome is adversely affected when the cross clamping time exceeds 120 min.[23,24] The current thinking is that the postoperative myocardial damage is determined more by how the heart is protected, than how long the aorta is clamped.[25]

Mechanism of Potassium Arrest and Composition of Cardioplegia

The resting membrane potential of the myocardial cell is determined by the potassium transmembrane gradient. The elevation of extracellular potassium lowers the transmembrane gradient and the membrane potential is lowered to a less negative value. When the membrane potential reaches –50 mV, the fast inward movement of sodium current during the initial part of the action potential is inactivated so that the action potential is not generated.[26] Maintenance of the membrane potential at this value of –50 mV causes diastolic arrest. It has also been shown that high potassium concentrations increased the energy utilisation that is associated with an increase in the myocardial wall tension and intracellular calcium accumulation.[27] It is, therefore, necessary to achieve an optimal concentration of extracellular potassium that is sufficient to inactivate sodium influx, thereby preventing generation of the action potential without causing intracellular calcium accumulation. This optimum concentration of potassium is not well defined and in clinical practice, the concentration of potassium varies from 15 to 40 mEq/L in the commonly used cardioplegia solutions.

The concentration of potassium also varies with the vehicle used for cardioplegia. For instance, 28 to 30 mEq/L of potassium is required if blood cardioplegia is used[21] and 20 mEq/L of potassium is required if crystalloid cardioplegia is used.[28] The oxygenated blood cardioplegia is used with the hope of maximising intraoperative myocardial protection. It was shown that blood cardioplegia improved oxygen carrying capacity, enhanced myocardial oxygen consumption and preserved high energy phosphate stores.[29,30] Cardioplegia solutions with increasingly higher concentrations of blood have been used and the blood crystalloid composition has ranged between 2:1 to 8:1. Blood cardioplegia is the preferred mode of cardioplegia in current practice. It provides improved outcome in patients with sicker hearts, e.g. cardiogenic shock, acute myocardial infarction.[31]

Cold blood cardioplegia has also been used in paediatric surgery. In a study performed on paediatric patients undergoing ventricular septal defect repair, it has been shown that cold blood cardioplegia is associated with less metabolic myocardial ischaemic stress and reperfusion injury when compared with cold crystalloid cardioplegia.[32]

The effectiveness of cardioplegia solution is also influenced by other ions such as sodium, calcium and magnesium. Generally a sodium concentration in the range of 100 to 120 mEq/L and calcium concentration of 1 mEq/L is used. The role of magnesium is not clear but may have a beneficial effect by controlling the calcium influx.[33]

The buffering capacity, the osmolarity, the membrane stabilising properties and the delivery vehicle of cardioplegia solutions are other important considerations. Bicarbonate is commonly added to the cardioplegia solution to counter acidosis during aortic cross clamping. Hypertonic solutions are used to counteract the oedema formation. The use of buffered and hyperosmolar cardioplegia solutions has been shown to provide an effective means of controlling acidosis and oedema formation during aortic cross clamping.[34,35] Steroids and prostaglandins have also been used as adjuncts to myocardial preservation, although their role is controversial. Blood and crystalloids are the two vehicles used to deliver cardioplegia and the merits of the two are debatable.[36,37] Blood is considered as a more physiological substrate capable of providing better oxygenation and buffering capabilities, whereas crystalloid solution is easy to prepare and has a homogenous distribution due to decreased viscosity. Nevertheless, more recent approaches have included blood-only formulations associated with appropriate electrolyte supplementation.[38]

The debate regarding oxygenated crystalloid or blood cardioplegia (either cold or warm) and the use of free radical scavengers and other additives to minimise the consequences of ischaemia, continues. The analysis of the published papers is complex, as several variable factors (such as warm or cold blood cardioplegia, antegrade and retrograde administration, systemic hypothermia or normothermia, topical heart cooling, high and low potassium solutions, ‘hot shots’, warm induction, volume of cardioplegia, patient factors and bypass times) could be present.[39] A survey of UK practice found that 56 percent of surgeons use cold blood cardioplegia, 14 percent use warm blood cardioplegia, 14 percent use crystalloid cardioplegia, 21 percent use retrograde infusion and 16 percent do not use any cardioplegia.[39]

The addition of beta adrenergic blocking agents[40] and administration of calcium channel blocking agents prior to or immediately following the onset of global ischaemia[41-13] have also been found to be beneficial.

Administration of cardioplegia

In addition to the chemical composition, rapid initiation of cardioplegic arrest and uniform distribution of cardioplegia solution are important supportive measures of myocardial preservation. This is especially important in patients who have a myocardium vulnerable to ischaemic damage, such as severe ventricular hypertrophy and severe coronary artery disease (CAD). It is a common practice to administer the cardioplegia solution via a 14 gauge cannula into the clamped ascending aorta (Fig. 13.1). The initial 1 litre of ice-cold cardioplegia solution in an adult (20 mL/Kg in small adults) at a pressure of 150 mm Hg applied to the bag is delivered into the ascending aorta, where it should generate a pressure of 80 to 100 mm Hg. Alternatively, one of the pump heads of the heart-lung machine can be used to deliver the cardioplegia solution. The cardioplegia drains into the CPB circuit via the coronary sinus and venous cannula. In patients having aortic regurgitation (AR), the aorta is opened and the cardioplegia is delivered directly into the coronary ostia with the help of a cannula. The myocardial temperature can be monitored by using special temperature probes and it is desirable to attain a temperature of less than 10°C. Occasionally, additional quantity of cardioplegia solution may be infused, if cessation of electromechanical activity or temperature of less than 10°C is not attained. During the infusion of cardioplegia, the surgeon should ensure by direct palpation of the LV, that the LV is not distending due to aortic valve incompetence. This ensures that cardioplegia is properly reaching the coronary circulation and not entering the LV via the regurgitant aortic valve.

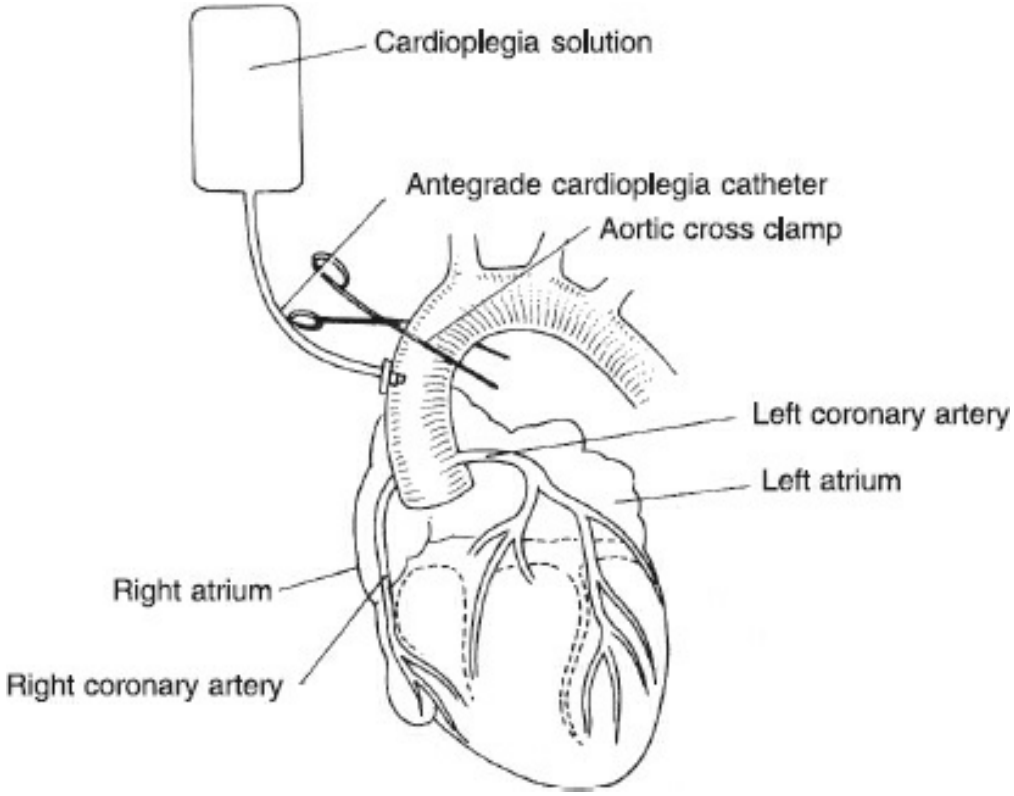

Figure 13.1: Diagram showing administration of antegrade cardioplegia.

The presence of noncoronary collateral flow via mediastinal and bronchial vessels tends to counter the cooling of the myocardium. This effect may be minimised by effective venting, reducing systemic perfusate temperature and cold saline irrigation of the pericardial cavity.

Supplemental infusions of cardioplegia are administered every 20 to 30 min. during the period of cross clamping. However, this can be done earlier, if the myocardium shows electrical/mechanical activity. Usually half the initial dose is administered or until the myocardial temperature of 10°C is attained. In patients undergoing CABG, antegrade cardioplegia via vein or free arterial grafts after completion of each distal anastomosis may improve myocardial protection.[44] In patients undergoing reoperation with patent internal mammary artery (IMA) graft, it is believed that clamping of the graft will provide optimal myocardial protection. However, it has been shown that leaving the mammary graft undamped did not change the mortality and the risk of injury to the patent graft may be reduced (if it were to be dissected for clamping).[45]

Other Events Causing Myocardial Damage

No doubt, aortic cross clamping is the most obvious and important event leading to myocardial ischaemia, but the anaesthesiologist should be aware of some other events that may contribute to ischaemia.

Ventricular Fibrillation

VF may result in increased myocardial wall tension, increased MVO_2 and impaired subendocardial blood flow.[46,47] The damaging effects of VF can be potentiated by ventricular distention, low perfusion pressure and ventricular hypertrophy. It is, therefore, important to prevent VF or correct it as soon as possible by cardiac defibrillation during the surgical procedure. If the therapy fails and VF persists, it should be ensured that the heart is empty and the systemic perfusion pressure is adequate until defibrillation is achieved. VF before the CPB is instituted can occur in sick patients during the manipulation of heart by the surgeon. It can also occur during the early stage of CPB, if the myocardium is rapidly cooled. If the VF does not respond to defibrillation, aortic cross clamping and the infusion of cardioplegia solution should be accomplished as quickly as possible to achieve cardiac standstill. Following surgical repair and unclamping of the aorta, VF is corrected by direct cardiac defibrillation. Myocardial damage due to direct defibrillation can be avoided by using lower energy settings (less than 30J).[48] Alternatively, biphasic defibrillation can be used.[49] The other important measures at this stage are to ensure normal acid-base and electrolyte status, and near normal temperature.

Inadequate Myocardial Perfusion

Maintenance of adequate systemic perfusion pressure throughout the CPB is important. However, the pressure is particularly important for coronary perfusion during the periods when aorta is not cross clamped. Clinically, myocardial perfusion pressure is related to the mean radial arterial pressure minus mean left atrial (LA) pressure. If the LA pressure is maintained at zero (as it should be during CPB), the mean radial artery pressure determines the

coronary perfusion pressure. Aperfusion pressure of 50 to 70 mm Hg is adequate in most circumstances.[50] However, a higher perfusion pressure may be required in the presence of CAD or concentric ventricular hypertrophy.[51] The perfusion pressure is known to decrease at two stages; 1. At the initiation of CPB, and 2. When the aorta is undamped. These two stages are therefore, important, particularly in patients who have CAD. At the initiation of CPB, the perfusion pressure decreases due to loss of pulsatile flow, venous drainage and haemodilution. As the hypothermia is gradually induced, the perfusion pressure is restored. It has also been shown that there is a significant decrease in mean arterial pressure (MAP) after the aortic cross clamp is released.[52] At this stage, the coronary circulation is re-established, however, in patients undergoing CABG, the proximal anastomosis is still to be performed. Therefore, the coronary circulation is taking place via diseased coronary arteries. Adequate perfusion pressure at these stages or any other stage during CPB can be maintained with the use of alpha-agonist such as phenylephrine or norepmephrine.

In addition to the perfusion pressure, some other factors that may contribute to inadequate myocardial perfusion are coronary emboli, myocardial oedema, ventricular distention or VF.

Ventricular Distention

There are many occasions during CPB when ventricular distention could occur. This is not desirable as it increases myocardial wall tension and MVO_2, and decreases subendocardial perfusion. Some of the important reasons of ventricular distention during CPB are inadequate venous drainage, AR, VF, infusion of cardioplegia solution and post-repair cardiac failure. It is best detected by palpation or by monitoring the LA or pulmonary artery (PA) pressure and nowadays, by transoesophageal echocardiography (TOE). Treatment should be aimed at correcting the cause of distention while the surgeon gently decompresses the ventricle manually, or ensures that there is a properly functioning LA or PA vent. Occasionally, it may be necessary to place a vent directly into the LV apex in order to achieve adequate decompression.[53]

Coronary Embolism

Gaseous or particulate coronary emboli jeopardise the coronary perfusion

leading to ischaemia. Gas emboli are common in open-heart procedures. Careful and appropriate de-airing manoeuvres are important in all open-heart procedures.

Retrograde Cardioplegia

Retrograde delivery of cardioplegia solution via a cannula inserted into the coronary sinus has been described. It was introduced with the objective of ensuring homogeneous distribution of cardioplegia beyond coronary artery occlusion. In addition, in aortic valve surgery, the need to cannulate coronary arteries for the delivery of cardioplegia is prevented. This avoids the perfusion related coronary artery complications such as dissection of the left main coronary artery[54] and also offers the opportunity to repeat cardioplegia administration without interrupting the operative procedure.

Complete occlusion of a coronary artery represents a challenge for adequate delivery of cardioplegia to the myocardial area distal to the occlusion. The resulting maldistribution of cooling and cardioplegia is a recognised cause of inadequate myocardial preservation.[55,56] The coronary venous system is an extensive and unobstructed network that offers an effective conduit for delivering cardioplegia throughout the thickness of the myocardium. Therefore, retrograde administration of cardioplegia solution through the coronary sinus has emerged as an attractive option.[57,58] Animal experiments have shown that near infrared imaging can be used for real-time visualisation of cardioplegia distribution.[52a] This technology may prove useful is guiding intraoperative decisions pertaining to when retrograde cardioplegia is mandated.[59]

Technique

A balloon tipped catheter is placed into the coronary sinus. In the early days, the catheter was inserted under direct vision after clamping the ascending aorta and snaring the vena-cavae. A small atriotomy was made on the anterior aspect of right atrium (RA) and the coronary sinus was cannulated. Foley's urinary catheter was used initially, but later-on was replaced by a catheter having a pear shaped balloon that nicely fitted the coronary sinus orifice. The right atriotomy necessitated the separate cannulation and snaring of the two vena-cavae to avoid air getting sucked into the venous cannulae. As this

technique was found to be cumbersome by many surgeons, new coronary perfusion cannulae have been developed that can be inserted trans-atrially in a blind fashion. These have a flexible introducer placed in the coronary sinus cannula. The introducer is shaped into a hockey stick formation and then passed into the coronary sinus with the patient either on bypass or off bypass. The correct placement of the cannula can be guided by the TOE.

This method is less cumbersome and permits the use of a single venous cannula. The catheter has three lumens. One for the delivery of cardioplegia, second for the balloon inflation and the third for monitoring the pressure in the coronary sinus.

Before the delivery of cardioplegia, the balloon is gently inflated with saline solution until it occludes the coronary sinus orifice and infusion of cardioplegia solution is initiated. Catheters with self inflating balloon tips that inflate with the infusion of cardioplegia are now available. The self inflating balloon is in fluid communication with the infusion lumen of the cathether and is filled by a flow of cardioplegia solution. During administration of cardioplegia, the coronary sinus pressure is measured via the pressure monitoring line and is maintained around 40 mm Hg. The rate of administration is generally maintained around 100 mL/min. The cardioplegia returns to the root of aorta and it must be vented by an aortic root vent. In patients undergoing aortic valve replacement (AVR), aortic root vent is not necessary as the aorta is opened for the sake of replacing the valve. The catheter can be kept secured in the coronary sinus by means of balloon inflation throughout the period of aortic cross clamping. Ridges on the surface of balloon enhance the self maintenance of catheter in a proper position. Alternatively, the catheter can be anchored in the sinus by means of a purse-string suture placed along the rim of the coronary sinus ostium.

Retrograde cardioplegia can be used as the sole method of cardioplegia. In this method, one litre of crystalloid cardioplegia solution at 4°C is initially given over a period of 10 to 15 min. Additional doses of 500 mL of solution are reinfused in the same way every 20 to 30 min. Systemic cooling and topical hypothermia are also used to be able to maintain desirable myocardial temperature. On completion of the surgical procedure, the balloon is deflated and the catheter is removed. The disadvantage of this technique is the delay in the onset of arrest as the solution can be infused at a relatively slower rate. Therefore, a combined method of cardioplegia delivery has been described in which the initial dose of antegrade cardioplegia is delivered through the

aortic root which ensures a rapid arrest.[60] However, excellent clinical results have been reported with the exclusive use of coronary sinus route in both valve[61] and CABG[62-64] procedures. When the combined method is used, it must be ensured that the balloon of the retrograde cardioplegia catheter is deflated during antegrade infusion of cardioplegia to allow its free return into the coronary sinus. This is not necessary with the self inflating balloon catheters. The retrograde cardioplegia can also be administered continuously.

The precautions that should be taken during the administration of retrograde cardioplegia are: (1) Gentle inflation of the balloon and avoidance of excessively tight fit; (2) Adjustment of flow rate to about 100 mL/min. and prevention of perfusion pressure rising above 40 mm Hg, and 3. Aortic root should be vented during the infusion of retrograde cardioplegia.

The clinical efficacy of retrograde cardioplegia in patients having critically obstructive multivessel coronary artery disease has been shown.[65,66]

Advantages of retrograde cardioplegia

1. It is more effective than aortic root perfusion for ensuring uniform distribution of cardioplegia with even cooling in myocardial areas distal to coronary artery obstruction. This fact has been clinically documented in patients having critically obstructive multi-vessel coronary artery disease.[66]
2. Retrograde cardioplegia improves the preservation of hypertrophied myocardium subjected to global ischaemia. This advantage could be of special relevance in patients having severely hypertrophied hearts. The retrograde cardioplegia is likely to be distributed throughout the thickness of the myocardium and achieve effective core cooling and cardioplegic arrest. It has been shown that retrograde cold blood cardioplegia that is administered continuously is associated with lower hospital mortality in heart valve operations.[67]
3. It may retard atrial rewarming during the ischaemic period[68] probably due to topical endocardial cooling resulting from spillage of cold cardioplegia solution into the right atrium. This may reduce the incidence of postoperative supraventricular arrhythmias.[61]
4. In patients undergoing aortic valve surgery, it avoids the risk of

coronary artery complications associated with direct ostial cannulation such as late stenosis. Retrograde approach is especially helpful in patient with heavily calcified aortic roots.[61]

5. In valve operations, there is no need to interrupt the surgical procedure to deliver antegrade cardioplegia. The surgery can proceed in an uninterrupted fashion, while the retrograde cardioplegia is being delivered via the coronary sinus catheter that remains in-situ throughout the period of aortic cross clamp.
6. It is also beneficial in CAD patients undergoing reoperations. The native coronary arteries of these patients are usually occluded so that retrograde cardioplegia can perfuse the myocardium adequately. In addition, the risk of antegrade cardioplegia causing embolisation of atheromatous material from still patent saphenous vein grafts is avoided.

Disadvantages

Like any technique, retrograde cardioplegia suffers from some limitations.

1. **Coronary sinus injury**
   The catheter placement in the coronary sinus can injure it, resulting in bleeding from the area.[69] Although, coronary sinus rupture occurring during retrograde cardioplegia is rare, it can be fatal.[70] The injury should be recognised before termination of the CPB. This is necessary as the surgical repair on this relatively inaccessible area becomes easier to perform on CPB. By taking simple precautions such as not advancing the balloon too far and avoiding excessive inflation of the balloon, the rupture of the venous wall can be prevented. In a large series, the incidence of coronary sinus injury has been reported to be 0.6 percent.[61]
2. **Delay in cardiac arrest**
   Due to its slow rate of administration, it takes a longer time to arrest the heart. This may be important in patients having severely hypertrophied hearts. Nevertheless, this drawback can be countered by giving the first dose of cardioplegia solution antegradely through the aortic root or direct coronary cannulation.
3. **Inadequate preservation of right ventricle**

Since anterior region of the right ventricle (RV) is not drained by the coronary sinus, inadequate preservation of RV has been a matter of concern with retrograde cardioplegia. However, reports demonstrating adequate preservation of RV function after retrograde cardioplegia in patients undergoing AVR and CABG are available.[62,71] There are numerous variations of the coronary veins, coronary sinus, valves and systemic/pulmonary venous return systems, all of which may affect the degree of myocardial protection provided by retrograde cardioplegia. Accordingly, when there is evidence of a compromised cardiac vasculature, the use of both antegrade and retrograde cardioplegia is recommended.[72]

4. **Need for bicaval cannulation**
   If right atriotomy is performed for direct coronary sinus cannulation, bicaval cannulation is required. This is considered as quite cumbersome by some surgeons who prefer to use single venous cannulation. However, this problem can be solved by the stylet-guided catheters that are advanced blindly into the coronary sinus through a stab wound in the right atrial wall. TOE can also help to confirm accurate placement.

Warm Blood Cardioplegia

There have been major advances in the field of myocardial preservation during last few years. Hypothermia was considered to be the single most important component of myocardial protection. The intermittent cold cardioplegia (crystalloid/blood) that is administered constitutes the cold anaerobic arrest. The rationale underlying this approach is based on the fact that myocardial hypothermia significantly diminishes cardiac metabolism. Hence, during the anaerobic arrest, oxygen consumption is decreased and postoperative cardiac impairment is minimised. Although this technique allows for a dry and quiet operating field, it leaves the myocardium anaerobic for the duration of aortic cross clamp. In addition, hypothermia is considered to have many other disadvantages such as its effect on enzyme function, membrane stability and tissue oxygen uptake. The heart function continues to deteriorate (at a slower rate) than if the heart were maintained normothermic.[73] Furthermore, the reperfusion after ischaemic arrest can lead

to an extension of the ischaemic damage resulting from “reperfusion injury”. Therefore, continuous warm blood cardioplegia that constitutes warm aerobic arrest has been introduced.[73,74] Since electromechanical work is the major determinant of myocardial oxygen consumption, it has been hypothesized that the ideal state of the heart during an operative procedure would be electromechanically arrested and perfused with blood, that is, aerobic arrest.[73] This has mostly been tried in patients undergoing CABG.

In this technique, the heart is maintained at 37°C with continuous warm blood cardioplegia. This eliminates the period of ischaemia and also the effects of hypothermia and reperfusion injury. Since the heart is normothermic, systemic hypothermia is not considered necessary and the body temperature is also maintained at 37°C. There is a considerable debate regarding the best perfusion temperature, but it has been shown that it is better to allow the temperature to drift to a tepid level (32 to 33°C).[75] Therefore, many centres practice this approach.

Technique

The CPB is established and the temperature of the patient is allowed to drift to a lower value (32 to 33°C). With the heart empty and beating, the aorta is cross clamped and a high potassium (20 to 30 mEq/L) blood cardioplegia solution is administered into the root of the aorta. After delivery of the calculated dose, a low potassiumblood cardioplegia that is identical to the high potassium solution (except for a potassium concentration of 6 mEq/L) is delivered at a rate of 50 to 150 mL/ min. This low potassium solution at 37°C is perfused throughout the procedure. Occasionally, perfusion of high potassium cardioplegic solution may be necessary, if myocardial electrical activity returns. The surgical procedure is performed during this period and at its completion, the aortic clamp is released and patients are weaned off CPB after rewarming to 37°C. The warm cardioplegia can also be delivered retrogradely via coronary sinus. Many studies have established the efficacy of the technique in terms of better myocardial preservation in patients undergoing CABG.[73,76,77] The improved myocardial preservation leads to decreased incidence of perioperative myocardial infarction (MI), use of intra-aortic balloon pump and prevalence of low CO syndrome. A recent meta-analysis of 41 randomized controlled trials including 5879 patients has revealed that although, warm cardioplegia was associated with improved

cardiac index, and decreased CK-MB and cardiac troponin concentrations postoperatively, the incidence of postoperative clinical events was similar to the cold cardioplegia groups.[78]

Drawbacks

1. Due to continuous infusion of cardioplegia during the surgical procedure, visualisation may be difficult due to blood in the operating field. It has been suggested by Lichtenstein[73] that during construction of distal anastomosis (in CABG), a soft probe may be used to occlude the artery or the arteriotomy can be irrigated with room temperature saline. Alternatively, the cardioplegia infusion is interrupted for periods up to 10 to 15 min. This, however, may expose the myocardium to the risk of ischaemia especially when the protection provided by the hypothermia is not there. Although continuous flooding of the operating field may be considered as a minor surgical inconvenience by some,[73] others may not agree with it.
2. Due to continuous infusion of the cardioplegia solution, patients can be hyperkalaemic after the aortic cross clamp is released. The anaesthesiologist should, therefore, be aggressive in the management of hyperkalaemia before the cross clamp is released. Treatment with glucose and insulin or diuretics should be instituted if potassium levels are elevated.
3. The systemic vascular resistance is lowered during and in the early hours after normothermic CPB. This may result in increased use of vasopressors during normothermic CPB to maintain optimal MAP.[79,80] Some centres use higher perfusion flow rates during normothermic CPB (2.5 L/min./m^2) to maintain adequate MAP.[81-83] If phenylephrine is used during normothermic CPB to maintain adequate MAP, it might result in vasoconstriction of the engrafted IMA conduit and may compromise myocardial blood flow in the immediate post-CPB period.[80] The clinical and experimental data on this issue is controversial with some showing reduction in the IMA graft flow with phenylephrine,[84,85] whereas others showing that even large doses of phenylephrine do not produce

clinically significant IMA vasoconstriction.[86]

4. In the absence of systemic hypothermia, the major organs such as brain may be susceptible to suffer from ischaemic damage, thereby increasing the incidence of neurological injury in the postoperative period. There is conflicting opinion on this particular aspect of normothermic bypass.[87,88] A more detailed discussion on this aspect can be found in chapter 14.

Some other issues regarding this technique that need to be clarified are:

a. Is haemodilution wise during normothermia?
b. What should be the heparin repeat dose and optimum activated clotting time?
c. Is awareness more likely? If yes, how it should be countered.
d. Do these patients need more narcotic and less relaxant due to less risk of shivering?
e. Is postoperative period more stable and extubation earlier?

Advantages

The major advantage of warm blood cardioplegia (if it can be run continuously) is in patients, who require prolonged cross clamp times. This is so because continuous warm blood cardioplegia constitutes warm aerobic arrest and the cross clamp time has no relation to the true ischaemic times. Therefore, it is particularly useful in complex high risk procedures such as patients with recent MI or procedures requiring very long aortic cross clamp times.

Antegrade warm blood cardioplegia

It was suggested that the delay in metabolic and functional cardiac recovery was secondary to the hypothermic inhibition of myocardial enzymes, which would remain inactive for hours following cold cardioplegic arrest. It was shown that warm induction of cardioplegic arrest improved myocardial metabolic and functional recovery following CABG.[89] Subsequent studies have indicated that intermittent antegrade warm blood cardioplegia provides an improved myocardial protection with less myocardial injury as compared

with intermittent cold blood cardioplegia[90,91] as well as cold crystalloid cardioplegia[92] in patients undergoing CABG. More recently, in a comparison with intermittent cold blood cardioplegia in patients requiring prolonged aortic cross clamp times, it was shown that patients with cold cardioplegia needed more intraoperative defibrillations, had more postoperative blood transfusions, and a prolonged hospital stay.[93] However, the myocardial injury was more pronounced in the intermittent warm cardioplegia group with a significantly higher incidence of major adverse cardiac events. Multivariate analysis revealed intermittent warm cardioplegia to be an independent predictor of 30-days all-cause mortality, cardiac death, major adverse cardiac events, and perioperative myocardial injury.[93] Magnesium is cardioprotective, and some authors have added it to the cardioplegia to increase the interval between the administration of intermittent warm-blood cardioplegia from 15 min. to 25 min.[94]

Intermittent warm blood cardioplegia has also been used in children. A study has demonstrated that the technique is not deleterious in comparison to conventional intermittent cold blood cardioplegia.[95] Another study has revealed that intermittent warm blood cardioplegia led to spontaneous resumption of sinus rhythm in more patients, shorter duration of ventilatory support, smaller increase in troponin levels and shorter duration of ICU stay, but no improvement in early mortality.[96] It seems that intermittent warm blood cardioplegia should be used cautiously until results of larger trials are available. Effective cardioprotection with normothermic cardioplegia requires higher flow rates of 80 mL/min. or greater and haemoglobin concentration of at least 8 gm percent.[38]

Retrograde warm blood cardioplegia

Retrograde warm blood cardioplegia can be administered intermittently or continuously, but more commonly is administered continuously. This results in fewer cardioplegic interruptions and also enables distribution of cardioplegia to regions of myocardium supplied by occluded or stenosed vessels. In a comparison with retrograde continuous cold blood cardioplegia, it was shown that warm blood cardioplegia provides better protection of the myocardium from ischaemia-reperfusion injury.[97] In addition, it has also been shown to provide adequate protection of the right heart, when used as the exclusive mode of myocardial preservation.[98] Retrograde perfusion flow

rates ranging from 100 mL/min. to 300 mL/min. (with coronary sinus pressure measuring 40 mm Hg) have been used and flow rates of 200 mL/min. or more (but less than 300 mL/min.) have been shown to minimise lactate production and maintain coronary venous pH within physiological limits.[38]

Combination of antegrade and retrograde cardioplegia

In order to overcome the inherent limitations of both antegrade and retrograde cardioplegia techniques, a combined antegrade and retrograde approach has been proposed. It has been shown that the viability of myocardium measured with oxygen utilisation and functional recovery is better preserved with simultaneous antegrade and retrograde cardioplegia as compared to retrograde alone.[99] Likewise, in comparison to antegrade alone, this technique has shown decreased inotrope use, RV dysfunction and postoperative balloon pump use in patients undergoing CABG.[100,101]

Optimal cardioplegia temperature

Due to detrimental effects of both cold (8°C) and warm (37°C) cardioplegia, use of tepid (27°C to 30°C) blood cardioplegia delivered in either an antegrade or retrograde fashion has been investigated. Although, both warm and tepid cardioplegia are useful, tepid cardioplegia offers additional protection during cardioplegic interruptions. Furthermore, by preventing cold related injury, myocardial functional recovery with tepid techniques is immediate.[38] In comparison to cold cardioplegia, tepid or warm cardioplegia may be associated with better early and late event-free survivals.[102,103] An intermediate lukewarm (20°C) antegrade intermittent blood cardioplegia has also been studied and has been found to be superior to cold cardioplegia, but less effective than warm cardioplegia.[104]

Adenosine

Adenosine is a potent coronary vasodilator and arresting agent. It has the potential to reduce potassium concentration required for arrest and to improve distribution of cardioplegia. In addition, it also attenuates neutrophil-

mediated reperfusion injury. Experimental evidence shows that adenosine reduces post-ischaemic injury when administered before ischaemia and at the onset of reperfusion. However, clinical studies show cardioprotective trends, but the effects are not as dramatic as those reported by experimental studies.[105] In animal experiments, it has been used continuously with an in-line micropump system during administration of cardioplegia.[106] It can be administered in the dose of 400 μmol/L along with blood cardioplegia or can also be infused as a pretreatment in the dose of 250 to 350 μg/Kg, 10 min. before CPB. A recent clinical trial using adenosine in cold blood cardioplegia failed to show any cardioprotective effects in patients undergoing aortic valve replacement.[107]

Nitric Oxide/L-Arginine Supplemented Cardioplegia

Experimental studies have revealed that nitric oxide (NO), an endogenously produced labile gas reduces post-ischaemic reperfusion damage.[108] L-arginine has been suggested to improve myocardial protection through an increase in NO production. L-arginine enriched blood cardioplegia solutions have been used in CABG patients, and have been shown to be associated with reduced release of biochemical markers of myocardial damage suggesting improved myocardial protection.[109]

Some other techniques have included addition of magnesium to cardioplegia and substrate enriched (glutamate, aspartate, with and without insulin) cardioplegia solutions. All these developments have shown improved myocardial preservation, but large scale trials are awaited.

Warm Body Cold Heart

Despite the theoretical advantages of warm blood cardioplegia and favourable clinical experiences, some surgeons are reluctant to abandon the familiar and time tested hypothermic technique. The technical difficulty due to continued presence of blood in the operating held has been the main concern. This along with the absence of any convincing evidence that myocardial hypothermia is significantly harmful and alters the outcome,

some clinicians have combined normothermic CPB with intermittent cold cardioplegia, a technique termed as “warm body cold heart”. In this technique normothermic CPB with multi-dose cold blood cardioplegic arrest is used. Consequently, there is greater rewarming of all the areas of heart as compared to the hypothermic CPB. However, no detrimental effect on RV function has been shown.[110] Some other studies also concluded that normothermic CPB when combined with myocardial hypothermia and cardioplegic arrest can provide similarly effective myocardial preservation as systemic hypothermia.[111,112] Currently, body temperature allowed to drift to around 34°C with cold cardioplegia (antegrade or retrograde) is the most commonly used technique for myocardial protection.

Secondary Cardioplegia

Despite all attempts to protect the myocardium, ischaemic damage may occur intraoperatively. This may result in varied degree of depressed ventricular performance depending upon the extent of ischaemic damage. Temporary support with total vented bypass improves the myocardial recovery in such a situation. However, it is not possible to achieve complete reversal of ischaemic damage by this method. It has, therefore, been hypothesised that using a cardioplegia solution after the ischaemic damage (i.e. just before the aorta is undamped), would allow the oxygen to be utilised towards cellular repair, rather than expending it on electromechanical work. This brief continuous infusion of cardioplegia solution just before the release of aortic cross clamp is called as secondary cardioplegia. It has been shown in animals that an infusion of blood cardioplegia at 37°C after an ischaemic injury results in more complete reversal of ischaemic damage.[113] Use of crystalloid cardioplegia at 28°C in a similar fashion (just before removal of the aortic clamp) has also been shown to improve the rate and extent of the post-ischaemic functional recovery in a group of patients undergoing valve surgery.[114]

In clinical practice, warm (37°C) blood cardioplegia is infused immediately before the removal of the aortic clamp (“hot-shot”). The hot-shot cardioplegia has also been administered via retrograde route in patients with left ventricular hypertrophy undergoing aortic valve replacement. Although, it did not add any extra benefit in preventing myocardial injury, it

appeared to reduce the ischaemic stress on the right ventricle.[115] A combination of terminal non-cardioplegic warm blood retrograde perfusion after terminal warm-blood cardioplegia perfusion prior to aortic unclamping has also been used and shown to increase the incidence of spontaneous heart beat recovery, shorten the CPB duration following aortic unclamping, and lower postoperative CPK-MB.[116] This may be after a normothermic or hypothermic CPB. Presumably normothermia enables the early resumption of temperature dependent mitochondrial enzymatic function with a return to aerobic metabolism and ATP generation.[38] Terminal warm blood cardioplegia has also been shown to be beneficial in paediatric cardiac surgery by way of reducing the myocardial injury or necrosis.[117] Modifying the normothermic reperfusate with glutamate and aspartate has however, not been shown to provide any additional benefit.[118] The various types of cardioplegia used in clinical practice are summarised in table 13.4.

Ischaemic Preconditioning

Ischaemic preconditioning is the endogenously mediated form of myocardial protection and accounts for the heart's inherent ability to tolerate brief episodes of cardioplegic interruption during CABG. It was first described in 1986 by Murry et al, when they demonstrated a 75 percent reduction in the infarct size caused by a 40-min. coronary artery occlusion when the occlusion was preceded by four episodes of 5 min. of ischaemia and 5 min. of reperfusion.[119] Ischaemic preconditioning can be produced with 5 min. of ischaemia and 5 min. of reoxy-genation before the long ischaemic insult. Adenosine is believed to be a mediator of ischaemic preconditioning. It has been shown that ischaemic preconditioning is protective in patients undergoing CABG surgery on beating heart without the use of cardiopulmonary bypass, but it offers no additional benefit when associated with bypass regardless of the mode of cardioprotection used.[120]

Table 13.4: Various types of cardioplegia used in clinical practice

Antegrade (cold/warm)
- Intermittent crystalloid (only cold)
- Intermittent blood
- Continuous blood

Retrograde (cold/warm)
- Intermittent crystalloid (only cold)
- Intermittent blood
- Continuous blood
- Continuous crystalloid (only cold).

Combined antegrade and retrograde (cold/warm)
- Initial antegrade crystalloid + continuous retrograde crystalloid (only cold)
- Initial antegrade blood + continuous retrograde blood

Hot shot
- Following cold crystalloid or blood cardioplegia

Tepid cardioplegia (29°C)

Substrate enriched cardioplegia
- Adenosine
- L–arginine
- Magnesium
- Insulin

Cardiac surgeons, however, have not incorporated this technique in the clinical practice. The research then focused on identifying agents that could pharmacologically mimic the cardioprotective effects of ischaemic preconditioning. Inhalational anaesthetic agents have been shown to have a preconditioning effect. Freedman et al reported an improvement in the post-ischaemic myocardial recovery with enflurane in the isolated rat heart.[121] The technique has a clear advantage of not requiring ischaemia to produce the effect. Furthermore several experimental and clinical studies have shown that in addition to a preconditioning effect, volatile anaesthetic agents may afford myocardial protection by minimising ischaemia-reperfusion injury, improving the myocardial oxygen balance and free radical scavenging.[122,123] Thus, inhalational agents in addition to providing anaesthesia, can be utilized to provide myocardial protection.

Belhomme et al performed preconditioning by exposing the patients to

isoflurane for a period of 15 min. versus the patients in the control group who underwent an equivalent period of pre-arrest isoflurane free CPB.[124] The authors showed that postoperative release of CPK-MB and troponin-I was consistently smaller in the isoflurane group. De Hert et al compared sevoflurane and propofol during CABG with CPB and showed that the cardioprotective effects of volatile anaesthetics were most apparent clinically when the agent was administered throughout the surgical procedure.[125] These findings were confirmed with sevoflurane and desflurane in elderly, high-risk patients undergoing on-pump CABG.[126] Similar beneficial results have been shown in patients undergoing off-pump CABG[127-129], and a metaanalysis has suggested that volatile anaesthetics may reduce mortality in cardiac surgery.[130] It appears that inhalational agents should form a part of the anaesthetic regime in cardiac surgery. The agent of choice, the dosage and the timing of administration to derive the best myocardial protection needs to be investigated.

Post-conditioning and remote preconditioning

Ischaemic post-conditioning consists of repeated brief cycles of ischaemia-reperfusion performed immediately after reperfusion following a prolonged ischaemic insult. It has been shown to diminish the infarct size in experimental model. A clinical study has shown that repeated brief episodes of inflation and deflation of the angioplasty balloon performed immediately after re-opening of the occluded coronary artery significantly reduced the infarct size in patients with acute MI.[131] Postconditioning represents a novel method of improving the outcome in patients with acute ML It has been applied in patients with hypertrophic myocardium undergoing valve surgery[132] and support the need for further clinical trials.

Remote ischaemic preconditioning is a technique in which brief ischaemia of one organ or tissue (e.g. arm or leg) provides protection of another organ or tissue (e.g. heart) against a more sustained ischaemic insult. Three cycles of 4/4 min. ischaemia/reperfusion of one of the limbs can be given after induction of anaesthesia. Some studies on patients undergoing CABG have confirmed the cardioprotective efficacy of this technique.[133,134], but another

study could not demonstrate any benefit in terms of troponin release, haemodynamics or renal or lung protection.[135]

Myocardial Preservation during Off-pump Coronary Artery Bypass Grafting

With the advent of coronary stabilisers, CABG on beating heart is being increasingly performed. It is often believed that since the heart is beating during surgery, myocardial preservation is not necessary. However, haemodynamic deterioration occurs frequently and is almost inevitable during off-pump CABG, especially during the placement of stabiliser. The MAP may decrease to as low as 60 mm Hg and cardiac index to less than 2 L/min./m^2. This is often accompanied by an increase in the left ventricular end-diastolic pressure as reflected by an increase in the pulmonary capillary wedge pressure, which may further decrease the coronary perfusion pressure. Although, intra-coronary shunts are used to maintain coronary blood flow distal to the anastomotic site, the blood flow across the diseased coronary artery in the presence of compromised coronary perfusion pressure is questionable. Therefore, the period of anastomosis may be considered as an ischaemic period. Several measures can be followed in order to minimise myocardial injury during off-pump CABG.

Maintenance of perfusion pressure

This is especially important during the anastomosis of vessels on the lateral aspects of the myocardium. Patients should be adequately preloaded before manipulating the heart. This can be achieved by administration of fluid and giving the Trendelenburg position to the patient. If this is not sufficient, alpha agonist such as phenylephrine should be administered.[136] Other inotropes such as dopamine, epinephrine, norepmephrine or dobutamine can also be used.

Active coronary perfusion

To avoid myocardial ischaemia completely during anastomosis in off-pump

CABG in any situation, coronary active perfusion system has been devised.[137,138] This system perfuses arterial blood to the coronary artery at the diastolic phase of the cardiac cycle, similar to native coronary flow. The arterial blood removed from the femoral artery is perfused to the coronary artery with the help of a pump. Blood injection is controlled to provide pulsatile flow synchronised with an electrocardiogram. It has been shown that active coronary perfusion provides adequate oxygen supply independent of systemic blood pressure.[138] This method has been used in animal experiments only and clinical trials on humans are not available.

Temperature

A mild to moderate decrease in temperature occurs during off-pump CABG in most patients, but in a few patients, it may be severe. This may increase circulatory catecholamine levels leading to an elevated systemic vascular resistance, which causes deterioration in CO. Cardiac troponin levels were found to be higher in hypothermic patients, signifying increased myocardial damage.[139] Active warming measures such as warming blankets, warm intravenous fluids and warm operation theatres, should be followed.

Noncoronary Beating Heart Surgery

Noncoronary beating heart surgery, especially mitral valve surgery with continuous coronary perfusion has been revived at some centres. Normothermic CPB and continuous coronary perfusion (antegrade or retrograde) is used after aortic cross clamp to keep the heart beating. The technique offers an alternative to cardioplegia for performing complex valvular surgery in sick patients. Furthermore, in mitral valve repair surgery, it offers an opportunity to the surgeon to visualise the efficacy of the repair while the heart is beating. The available evidence for the efficacy of this technique is controversial.[140] In one study using retrograde coronary sinus perfusion for aortic valve replacement, it was shown that the CPB and aortic cross clamp times were shorter, but the troponin-I release was more.[141] Another study showed no difference in clinical outcome between on-pump beating heart and hypothermic arrested heart valve replacement surgery.[142] A technique of simultaneous antegrade/retrograde warm blood perfusion with a beating heart has been used as a method of protecting hypertrophied hearts in

valve surgery.[143] The results of this paper showed that the technique is comparable, if not superior to conventional techniques of intermittent cold blood cardioplegia. Further studies are necessary, especially in sicker patients with LV dysfunction to fully evaluate the benefits of this technique.

In summary, techniques of myocardial preservation are constantly evolving. Changes in cardioplegia composition, temperature and mode of delivery have shown improved myocardial protection. However, stable patients presenting for elective CABG surgery face a relatively low risk of perioperative morbidity and mortality. Therefore, such patients are likely to have little benefit from these additional protective measures. Myocardial preservation is an even more pressing problem when the LV has already been damaged (e.g. acute MI) or hypertroptried, and in some complex procedures requiring prolonged cross clamp times. Newer techniques of myocardial preservation can be useful and likely to benefit such patients.

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Chapter 14: Neurological Dysfunction following Cardiac Surgery

During open-heart surgery, there may be injury of the central nervous system (CNS), affecting the brain or spinal cord. In addition, peripheral neurological injury affecting the cranial or spinal nerves may also occur. Neurological complications have an impact on the duration of hospitalization, mortality, health care costs and quality of life. In addition, they constitute a financial burden.

A prospective data of 16,184 patients between 1996 and 2001 have revealed an overall incidence of stroke to be 4.6 percent, and in patients undergoing coronary artery bypass grafting (CABG) 3.8 percent, aortic valve 4.8 percent, mitral valve 8.8 percent, double/triple valve 9.7 percent, and CABG and valve 7.4 percent.[1] There is a growing concern regarding neurological morbidity including subtle neurological changes associated with open-heart surgery. Such a concern is justifiable, especially in view of the acceptable mortality, that has now been achieved with this procedure. It is generally believed that patients undergoing operations involving an open cardiac chamber (valves and congenital defects) are more likely to suffer from neurological damage as compared with those that do not require an open cardiac chamber (CABG). This needs to be reviewed, as more and more older and sicker patients are being subjected to CABG surgery. These patients have a high incidence of risk factors such as hypertension, atherosclerosis, diabetes and carotid artery disease that may expose them to the risk of neurological injury.

A resurgence of interest in off-pump surgery has been seen in recent times. However, cardiopulmonary bypass (CPB) is still used in majority of patients undergoing CABG, and for all open chamber procedures. Some other procedures not requiring CPB, such as those performed on descending

thoracic aorta (coarctation repair, aneurysm or dissection) can also be complicated by neurological damage. In this chapter, pathophysiology, causative factors, the preventive strategies and management of neurological complications, following cardiac surgery will be discussed

Incidence

Despite significant advances in CPB technology, surgical techniques, and anaesthetic management, CNS complications occur in a large percentage of patients undergoing surgery requiring CPB. The incidence of neurological injury after open-heart surgery depends on the diagnostic methods used and has been reported to be as high as 79 percent.[2] The cardiac surgeons have reported the incidence of neurological complications to be as little as 1 percent[3] whereas the neurologists have reported it to be as much as 61 percent.[4] Such a wide variation in the incidence is due to the fact that surgeons have considered only the “obvious cerebral deficits”, whereas the neurologists have included “minor cerebral dysfunction” in the neurological assessment.

The neurological injury has been classified into two broad categories, type I (focal injury, stupor or coma at discharge) and type JJ (deterioration in intellectual function, memory deficit, or seizures).[5] Another way of classification could be stroke, encephalopathy, and cognitive dysfunction. The most obvious and serious neurological complication is stroke and most series have reported an incidence of 1 to 3 percent.[5,6-8]

Most of the studies of the epidemiology of stroke are based on patients undergoing CABG. Anyanwu et al have analysed 5085 patients undergoing CABG, isolated valve, valve + CABG, thoracic aorta, transplant/assist device, adult congenital and other surgical procedures at a single institution over a six year period (1998-2004).[9] They reported an overall incidence of stroke in 2.6 percent patients (CABG 1.7 percent, isolated valve 1.8 percent, valve/CABG 4.4 percent, and ascending aorta 4.6 percent). They further reported that patients who had a stroke had a higher perioperative mortality rate than that of patients who did not (32.8 percent versus 4.9 percent, $P < 0.0001$) and a longer period of hospitalization (median 30 days versus 7 days, $P < 0.0001$). Cognitive dysfunction is much more common neurological complication and affects 30 to 65 percent of patients one month

postoperatively[10,11] A recent paper has reported an incidence of 43 percent 5-days after surgery.[12]

Newman and colleagues evaluated long-term cognitive outcomes in 261 patients who underwent CABG using neurocognitive tests performed preoperatively, before discharge, and six weeks, six months and five years after surgery.[13] They demonstrated that the incidence of cognitive decline was 53 percent at discharge, 36 percent at six weeks, 24 percent at six months, and 42 percent at five years. Cognitive function at discharge was shown to be a significant predictor of long-term cognitive function.

The incidence of neurological complications has remained almost static during the last few years despite increasing number of elderly patients with co-morbidities being subjected to surgery. This maybe attributed to improvement in technical approaches.

It must be remembered that neurological deficits also occur in patients undergoing other major surgery and anaesthesia and it has been shown that 31 percent of patients having non-cardiac operations developed neurological abnormalities postoperatively.[2] Thus, factors unrelated to CPB are also responsible for the adverse neurological outcomes seen in cardiac patients.

Pathophysiology

The basic reasons involved in brain damage are disturbances of blood flow (ischaemia), oxygen content (hypoxia), and metabolic rate.

Brain Ischaemia

Brain ischaemia can occur before, during or after CPB. This may be due to either global or local reduction in blood flow or no flow at all. During CPB, the brain blood flow is usually nonpulsatile and it may be interrupted altogether [as in Deep Hypothermic Circulatory Arrest (DHCA)], or reduced intermittently by the surgeon for short periods of time during surgery. Macroemboli (> 200 μm) consisting of thrombus, tumour, atheroma, valve debris or air can arise during the surgical procedure and may compromise the cerebral circulation. Amongst these, atheromas arising from the atheromatous aorta in patients undergoing CABG are common and important considerations. Aortic atheromatosis is being recognised as a significant cause of stroke independent of cardiac surgery, with noncalcific plaque

representing the greatest risk.[14] Disruption of the aortic atherosclerotic plaque account for a large portion of the CNS injury occurring in patients undergoing CABG.

In a series of 1200 patients in whom intraoperative epiaortic ultrasound scanning was employed, moderate or severe ascending aortic atherosclerotic disease was found in 231 (19.3 percent) patients.[15] The clinical manifestations will depend on the location of brain injury, whether the ischaemia is regional or global, and whether it is transient or permanent. Microemboli (< 200 μm) consisting of aggregates of red cells, platelets or microgas bubbles and lipids can arise during CPB and contribute to the embolic load of the brain. They embolise mainly in border zones between cerebral arteries, spine and basal ganglia, and are more frequently associated with cognitive dysfunction. Cerebral microembolism as a cause of cognitive dysfunction is supported by the finding of a relationship between cerebral microembolic load during CPB and cognitive dysfunction after CABG.[8] Such a relationship has not been observed following valve surgery where the embolic load is higher.[16] This suggests that vulnerability to cognitive dysfunction is determined more by the composition than by absolute number of microemboli.[17]

Brain Hypoxia

Brain hypoxia occurs due to a reduction in the oxygen content of blood that can be caused by desaturated or an inadequate level of haemoglobin. In addition, marked leftward shift of the haemoglobin dissociation curve due to hypothermia or blood pH changes can lead to reduced availability of oxygen. In clinical practice, brain hypoxia is relatively rare and is usually due to mishaps related to oxygenation by the anaesthesiologist or the perfusionist. Marked haemodilution used during CPB can decrease the oxygen content, but is compensated by increases in cerebral blood flow. Although, increases in cerebral blood flow do not match the decrease in arterial oxygen content, marked haemodilution during CPB is well tolerated by normal brain.[18]

The Metabolic Rate

The cerebral metabolic rate ($CMRO_2$) may be relevant in neurological injury, particularly if cerebral blood flow or oxygen content is abnormally low. The

$CMRO_2$ is decreased after induction of anaesthesia and a further decrease occurs during hypothermic CPB. For every 1°C decrease in brain temperature, the $CMRO_2$ decreases by 7 percent.[19,20] Hypothermia may also be harmful as it displaces the haemoglobin dissociation curve to the left leading to decrease in tissue oxygen transfer and it increases the systemic vascular resistance. These effects may be compensated by haemodilution that decreases blood viscosity and promotes microcirculation. Further, the cerebral blood flow is autoregulated, meaning thereby, that it is proportional to the CMR02. The autoregulation is reported to be maintained during hypothermic CPB using alpha-stat method of acid-base management.[21] Mild hypothermia (33°C to 35°C) during CPB decreases the cerebral risk of early neuropsychological dysfunction after cardiac surgery,[22] but the ideal temperature for non-complex cardiac surgery procedures remains undertermined.[23] Nevertheless, the importance of hypothermia in reducing the $CMRO_2$ must be appreciated. Similarly, it should be remembered that hyperthermia increases the metabolic rate and is undesirable especially in the presence of cerebral injury.

Systemic Inflammatory Response

The systemic inflammatory response associated with CPB, characterized by the release of cytokines in response to the activation of coagulation, fibrinolytic, and complement cascade has been the subject of recent discussion. With exposure of blood to foreign surface of the bypass circuit, not only does contact activation occur but serine proteases act on precursor to form bradykinin and kallikrein. In a complex series of cascades, kallikrein and bradykinin are now identified as being among the most potent enzymes responsible for changes in microvascular permeability. Haemolysis and damage to the erythrocyte membrane is also encouraged. These mechanisms produce a significant increase in permeability and/or blood-brain barrier disruption.[24]

Risk Factors

The various risk factors that may cause neurological dysfunction are listed in table 14.1.

Patient related

Age

We are now operating on older and sicker patients. In one report from the USA, 20 percent of patients were more than 70 years of age, 33 percent had poor left ventricular function (ejection fraction < 40 percent) and 1 in 4 suffered from diabetes.[25] These figures represented a substantial increase as compared with data collected in 1981. The authors also noted that the stroke rate in their institution increased from 1.5 to 2.8 percent. Similar findings demonstrating a greater burden of comorbidity in elderly patients were reported by Ferguson et al.[26] A direct correlation between patient age and associated neurological morbidity has been demonstrated with stroke rate rising significantly over 65 years of age.[27] However, some other authors did not consider age as a risk factor.[28] A strong correlation between the age of the patient, the presence of peripheral vascular disease or concomitant diabetes, and atheroemboli has been reported.[29,30] In addition, the elderly are more likely to have reduced baseline cognitive function, so that a relatively small deterioration may have a significant impact on the patient's life. Thus, age is an important risk factor, mainly due to associated comorbidities.

Table 14.1: The risk factors leading to neurological dysfunction

Patient related
Age
Sex
Peripheral vascular disease
Hypertension
Diabetes and hyperglycaemia
Heart disease
Preoperative intracranial pathology
Anaesthesia related
Cannulation of vessels
Hypocapnoea before CPB
Ventilatory mishaps
Nitrous oxide
Surgery related
Dislodgement of the atheromatous emboli
– aortic cannulation
– aortic cross clamping
Dislodgement of LA/LV thrombi/tumour
CPB related
Major disasters
Oxygenator
Priming fluid
Optimal pressure and flow
Methods of acid-base management
Normothermic bypass
Arterial line filters
Cerebral hyperthermia
DHCA

CPB: cardiopulmonary bypass, LA: left atrium, LV: left ventricle, DHCA: deep hypothermic circulatory arrest.

Sex

Few studies have examined the influence of sex on neurological outcome after cardiac surgery. The examination of the US Society of Thoracic Surgery, National Cardiac Surgery database for the years 1996 and 1997 has revealed that new neurological events after surgery were higher for women than for men. (3.8 versus 2.4 percent).[31] The 30-day mortality was also higher when these complications occurred in women. Female sex was found to be independently associated with significantly higher risk of suffering new neurological events after cardiac surgery.

Peripheral Vascular Disease

It has been regarded as a neurological risk factor. The incidence of atheroemboli to various organs such as brain, kidneys and heart is increased in patients having peripheral vascular disease. Presence of aortic atheromatous disease is an important consideration. The severity increases with age and postmortem studies indicate a prevalence of 20 percent in the fifth decade increasing to 80 percent in the eighth decade.[32] Its presence increases the risk of perioperative cerebrovascular disease by 4.5 fold and is considered an incremental risk factor for future stroke and mortality.[30,33] Surgical manipulations of the proximal aorta, cannulation through an atheromatous plaque or dislodgement of the plaque during reperfusion may cause atheroembolism. High velocity flow patterns may be generated at the orifice of the aortic cannula that might lead to “sand blasting” effect promoting disruption of atheroma.[34] Due to these concerns, the ultrasonic assessment prior to cannulation and cross clamping is increasingly being employed. An epiaortic probe is used to scan the aorta before cannulation to detect atheroemboli, so that an appropriate site of cannulation may be chosen.

The transoesophageal echocardiography (TOE) is another way of detecting the aortic atheromas and is being routinely employed in many centres. However, it is unable to detect atherosclerosis in the distal ascending aorta due to the ‘blind spot’ created by the interposed air-filled bronchus between aorta and oesophagus. A new method of aortic view (A view) that uses a fluid-filled catheter inserted into the left bronchus via the endotracheal tube to enhance the visualisation of distal ascending aorta has been described. It has been shown that the A-view method allows visualisation of distal ascending aorta in all patients and offers a rrunimally invasive and safe approach to resolve the blind spot of the TOE.[35] However, it is not widely used in clinical practice. The comparison between epiaortic ultrasound and TOE has shown that TOE underestimated the presence and severity of aortic atherosclerosis.[36] A metaanalysis has revealed that the TOE has a low sensitivity to detect ascending aortic atherosclerosis in comparison to epiaortic scanning.[33] Therefore, a negative test result by TOE requires verification by additional testing using epiaortic scanning.[37] Epiaortic ultrasound scanning of the ascending aorta is the current ‘gold standard’ for detecting ascending aortic atherosclerosis. A high-frequency, linear-array probe is used. A large series has shown that epiaortic scanning has a

significant impact on the surgical decision making in cardiac surgical patients and might result in improved perioperative neurological outcome.[38] In many centres, the surgeon palpates the aorta manually before cannulation to determine the optimal place for cannulation and cross clamping, but, this technique misses a large number of atheromatous lesions. Surgical techniques without instrumenting or manipulating the aorta, and replacing the diseased aorta have been described to minimise the neurological complications following surgery.[39-41]

The carotid artery plaques or asymptomatic carotid stenosis are not considered as the predictors of an adverse neurological outcome.[42] However, in symptomatic carotid stenosis, carotid endarterectomy along with CABG may be performed. Studies have shown that stroke and mortality are higher in combined procedures as compared with CABG alone[43,44] suggesting a need for randomized trials to provide evidence in support of efficacy and safety of combined CABG and carotid endarterectomy. Carotid artery stenting may offer an alternative.

Transient ischaemic attacks and preoperative strokes have been correlated with an increase in postoperative neurological deficits.[27] The incidence of perioperative stroke is reported to be 13–15 percent in patients with previous stroke.[30,45] The patients with prior stroke are at particular risk of cerebral hypoperfusion. In one study magnetic resonance imaging (MRI) was obtained before cardiac surgery, and it revealed brain infarction in 40 percent of patients.[46] The infarcts are usually clinically asymptomatic and pose an increased risk of stroke and cognitive dysfunction. A retrospective study has revealed that the patients who had had a stroke in the 3 months before surgery were more likely to have worsening of a prior deficit, whereas those with a more remote history of stroke were more likely to have a stroke in a different brain region.[45]

Hypertension

Hypertension has been labelled as a risk factor because it is a risk factor for atherosclerosis. In addition, cerebral autoregulation disorders are commonly present in hypertensive patients and may increase during CPB.[47]

Diabetes and Hyperglycaemia

Diabetes is also considered an adverse factor. This is perhaps due to a higher

incidence of hypertension, peripheral vascular disease and the loss of cerebral autoregulation.[30,47,48] In addition, the effects of high or low plasma glucose after brain injury has been sustained, may also be important. Consequently, outcome of stroke can be worse in diabetics and some reports have suggested that diabetes mellitus is a risk factor for poor neurological outcome after CPB.[49-51] In a study evaluating electrolyte versus dextrose prime, the neuropsychological outcome was found to be worse in dextrose prime patients.[52] On the basis that hyperglycaemia may worsen neurological outcome, some investigators claim that hyperglycaemia during cardiac surgery should be avoided,[53] while others suggest that glucose administration may be beneficial.[54] In clinical practice most centres treat intraoperative hyperglycaemia with insulin, but critical glucose concentration at which treatment should be instituted is unknown.

Heart Disease

Congenital heart disease (CHD) particularly cyanotic disease, may cause brain damage pre-operatively from paradoxical emboli causing cerebral infarct or cerebral abscesses. This factor along with mental retardation as well as preoperative hypoxia and cyanotic attacks may influence the cerebral outcome after surgery in patients with CHD.

Patent foramen ovale (PFO) constitutes the risk of a paradoxical air embolism before or during surgery. In addition, the shunting of blood from right-to-left that may be produced before CPB can produce hypoxaemia.[55]

Some manifestations of heart disease may be associated with an increased incidence of CNS abnormalities. These include atrial fibrillation, cardiac failure or infarction, that carry the risks of clot emboli or inadequate cerebral perfusion. However, the Multicentre Study of Perioperative Ischemia (McSPI) Research Group found that neither congestive cardiac failure nor arrhythmia on the day of surgery were associated with adverse neurological outcome.[50] The improvements in the care of these conditions may have reduced the impact of poor cardiac function on the neurological outcome. Severe left ventricular dysfunction with sustained hypotension and low cardiac output favour perioperative neurological side effects.[30] Endocarditis vegetations from the native or prosthetic valve as well as thrombi are important risk factors. The incidence of neurological complications in patients undergoing valve surgery versus CABG has been reported to be

variable. Most authors have reported a higher incidence of neurological complications following valve surgery[1,56,57] with some reporting a higher incidence with CABG surgery.[58] However, as already pointed out this may be examined again in view of sicker elderly population (prone to develop neurological complications) being subjected to CABG surgery nowadays.

Preoperative Intracranial Pathology

Preoperative intracranial pathology may be present in some patients before cardiac surgery. This fact may not be recognised in many patients at the time of surgery. In one study, 35 percent of patients having CABG were found to have some type of neurological abnormality preoperatively.[4] Many patients may have MRI evidence of brain infarction before surgery,[46] and some patients have also been shown to have a psychiatric pathology before open-heart surgery.[59] These factors appear to be contributory in the ultimate outcome after surgery, but their correlation with an increase in postoperative neurological deficits is not known.

Anaesthesia Related Risks

For the sake of best outcome, the anaesthesiologist should be aware of all the risk factors, and as a member of the team, he is expected to actively participate in the management, in the event of an insult. However, he must be particularly aware of the anaesthesia related risk factors so that he does not overlook them.

In this respect, any drug causing anaphylactic or anaphylactoid reactions may lead to CNS morbidity. Also, haemodynamic compromise produced during anaesthetic induction can contribute towards brain damage.

Cannulation of Vessels

Cannulation of various vessels is performed by the anaesthesiologist for the purpose of fluid and drug administration or for monitoring. During internal jugular vein (IJV) cannulation, carotid artery plaques may be displaced or complications such as haemothorax or pneumothorax may cause respiratory problems leading to hypoxia, hypercarbia or both. In addition, excessive haemorrhage or accidental entry into spinal canal may occur.[60,61] Venous air can also be introduced unintentionally and may give rise to paradoxical air embolism, especially in the presence of a PFO. Air can be accidentally

introduced in the carotid artery (if inadvertently cannulated) or into the arterial monitoring line or the left atrial (LA) catheter. The air flushed into the radial artery can reach the vertebral artery retrogradely and that flushed into the LA catheter can reach the cerebral circulation.

Hypocapnoea before CPB

Hypocapnoea before CPB has been considered a hazard.[62] This is due to cerebral vasoconstriction produced by hypocapnoea leading to decrease in cerebral blood flow in the absence of reduced CMR02. This factor may be significant at the initiation of CPB when there is a tendency for the perfusion pressure to decrease with patients still being normothermic. Nevin et al[62] demonstrated a correlation between hypocapnoea before CPB and postoperative psychometric deficits. However, the data from this study revealed that the patients with most psychometric deficits were also hypercarbic during CPB. Thus increased cerebral perfusion (increased microemboli) produced by hypercarbia during CPB may also have been the causative factor.

Ventilatory Mishaps

Mishaps such as accidental disconnection of the ventilator in the operation theatre (OT) or when transferring the patient from OT to the intensive care unit (ICU) are not unknown and may lead to serious hypoxia. Such events are rare nowadays, as all the ventilators have disconnection alarms. However, in cardiac surgery, failure to switch on the ventilator when weaning from CPB could result in a serious degree of brain damage from hypoxia. Unfortunately, there are no alarms to remind the anaesthesiologist of this particular event and therefore, this important step must not be forgotten. Likewise, it is important to continue mechanical ventilation in a patient on partial CPB support before full flow is established.

Hypercarbia produced due to inadequate ventilatory management before CPB can be important, especially in patients with pulmonary artery hypertension. The increase in pulmonary vascular resistance can produce or increase the right-to-left intracardiac shunting, thus producing arterial hypoxia in patients with CHD.

Nitrous Oxide

Nitrous oxide has a solubility 20 times that of oxygen at 37°C and can cause

air emboli to increase in size, thus increasing the degree of vascular obstruction. Its use, is therefore, not recommended after CPB. In many centres it is not used at all.

Some other factors that may contribute towards neurological damage are; overlooking heparin administration or not giving it in error[63] before CPB, and protamine administration leading to profound haemodynamic disturbances sometimes requiring reinstitution of CPB.

Surgery related risks

Ascending aorta is an important source of atheromatous emboli. The aortic cannulation or cross clamping performed by the surgeon can dislodge these emboli into cerebral circulation. Also, the aortic cannula can be a source of air embolism, cause aortic dissection or may be malpositioned into the innominate or carotid artery.

The other cause of neurological threat during surgery is the compromised circulation produced by haemorrhage, mechanical manipulation or myocardial depression at a time when the temperature is near normal. The threat of excessive haemorrhage is always present during cardiac surgery, but it is especially there when the chest is reopened in a patient who has undergone previous cardiac surgery.

Air can be introduced into the left side of heart during venous cannulation in many forms of CHD. Air may also remain trapped in the LA or left ventricle (LV) after an open cardiac procedure despite meticulous de-airing techniques before releasing the aortic cross clamp.[64] This trapped air can be ejected into the aorta after the cardiac rhythm is restored.

Clots can be dislodged into systemic circulation from the LA or LV aneurysm during manipulation, unless the aorta has been clamped. Duration of CPB may be considered as a risk factor for CNS injury presuming that micro-embolisation can occur throughout the CPB. No relation between the number of retinal microemboli and CPB time has been found,[65] but longer duration of CPB has been shown to be associated with greater number of cerebral microemboli.[66] CPB time in increments of 30 min. has been shown to be an independent risk factor for mortality and morbidity including neurological complications.[67] It must be noted however, that factors responsible for prolongation of bypass may themselves contribute to cerebral injury, such as haemorrhage, aortic dissection and difficulty in weaning from

bypass.

CPB related risk factors

Major Disasters

Certain major disasters during CPB may result in profound brain damage. These include massive air embolism, failed venous return, oxygen supply failure, power failure and failure of oxygenator. These events that were not uncommon during the early days of cardiac surgery are rarely seen nowadays. However, as risk factors, they are always present and occasional reports of such incidents still appear.[68,69]

Oxygenator

The oxygenator can be a source of microemboli of gas or aggregates. Gas emboli can arise when there is low blood level in the oxygenator and the aggregates may be from blood components, fillers and antifoam. Although, the merits of bubble versus membrane oxygenators are widely discussed, as far as neurological outcome is concerned, no difference has been found between the two.[28,70] However, it has been shown that by using pulsatile flow and an arterial filter, membrane oxygenator resulted in significantly less incidence of retinal emboli.[71] Thus, if retinal emboli are considered a measure of cerebral emboli, membrane oxygenator appears to be a better choice. Presently, using the membrane oxygenator is a norm in all cardiac surgical units.

The priming fluid

It may influence the CNS outcome as haemodilution produced by crystalloid solutions affect oxygen delivery and perfusion pressure. Oxygen delivery is the product of oxygen content and blood flow. Therefore, with a fall in haematocrit, the cerebral blood flow should increase or metabolic demand fall in order to maintain normal cerebral oxygen balance. The haematocrit levels, therefore, appear to be relevant at the beginning, towards the end, and after CPB when the temperature is near normal and cerebral blood flow may not be optimal (as haemodynamics may not be optimal). The importance of oncotic pressure of the pump prime has not been defined although, it is known that crystalloid prime lowers the colloid osmotic pressure and is

associated with brain swelling soon after CABG.[72,73] Animal studies have shown that both higher haematocrit and higher colloid oncotic pressure improve cerebral recovery after deep hypothermic circulatory arrest.[74]

Optimal pressures and flows during CPB

Within a span of 50 years, cardiac surgery has become a sophisticated and routine procedure. However, questions regarding fundamental management of CPB such as optimal pressures and flows during CPB remain unanswered. Embolic phenomena and hypoperfusion during CPB are important causes of adverse neurological outcome. Ideal perfusion pressure during CPB is therefore, a very important consideration. Low flow and low pressure perfusion had its advocates,[56,75] but it has been shown that cerebral blood flow is determined by the arterial pressure and not CPB flow rate.[76] Mean arterial pressure (MAP) of 50 mm Hg has been widely considered as safe during CPB. There have been many reasons for the acceptability of this pressure, but mainly this has been due to the maintenance of cerebral autoregulation to MAP of 20 to 30 mm Hg during hypothermic CPB[21,77] (whereas it lies between 60 and 130 mm Hg MAP at normothermia).[78]

Application of MAP of 50 mm Hg to all patients may not be correct, especially in the current era of high-risk patients, who may have altered autoregulation (e.g. hypertension, diabetes, prior or acute stroke). One report suggested that higher MAP may reduce central nervous system complications during CPB.[79] The authors observed a better neurological as well as cardiovascular outcome in patients in whom MAP was maintained at 80 to 100 mm Hg compared with those managed at a conventional 50 to 60 mm Hg. Nevertheless, routine use of higher perfusion pressure (> 70 mm Hg) may not be desirable as it may worsen the neurological outcome, particularly if pH-stat acid-base management is employed. This is so because the increased cerebral blood flow (cerebral blood flow is pressure dependent with pH-stat management) can increase the embolic load. In addition, higher perfusion pressure may cause greater trauma to blood elements and exacerbate the inflammatory process associated with CPB. It therefore, appears that there is a need to define the subset of patients who are likely to be benefited by higher perfusion pressure. It has been suggested that patients with advanced atherosclerotic disease (cerebrovascular or aortic arch), the elderly, the diabetics and those with chronic hypertension are likely to be

benefited by this approach.[80] The optimal arterial pressure targets during CPB in such patients are not defined.[17]

It is apparent that the ideal perfusion pressure during CPB is undetermined, as is evident from a publication, where the authors were prepared to lower the perfusion pressure to 40 mm Hg.[81] Although, it seems that more evidence in support of MAP of 50 mm Hg is, perhaps necessary, it may be wiser to follow the guideline of Murkin; "by default, mamtaining pressures at the normal lower limit of cerebral autoregulation, 50 mm Hg or higher, appears judicious".[82] It is also likely that perfusion pressure is particularly important at times when the $CMRO_2$ has not been reduced substantially by hypothermia. This would be at the commencement and towards the termination of CPB, especially if extensive cerebrovascular disease is present. Likewise, cerebral perfusion pressure (CPP) rather than mean aortic pressure is important, when the arterial pressure is low. A raised pressure in the superior vena cava (SVC) during CPB (that can arise from technical difficulties) can markedly reduce the CPP, especially when aortic pressure is low.[83]

Pulsatile versus nonpulsatile flow

Nonpulsatile flow is the most widely used method of perfusion during CPB. Animal experiments have shown that pulsatile CPB perfusion increases cerebral blood flow and brain oxygenation compared with nonpulsatile flow.[84] However, clinical studies have failed to demonstrate any difference in the neurological outcome with pulsatile flow.[85] It needs to be evaluated, if pulsatile flow can be beneficial in patients at high risk of neurological complications.

Methods of acid-base management

As the blood is cooled, CO_2 becomes more soluble, arterial carbon dioxide tension ($PaCO_2$) falls and this results in the blood becoming less acidic. In alpha-stat management, the temperature of blood is not corrected (taken as 37°C) and CO_2 is not added. While in pH-stat management, CO_2 is added to the oxygenator gas supply so that the pH, if it was measured at the patient's hypothermic temperature, would be maintained at 7.35 to 7.45.[86] With alpha-stat acid-base management, the normal cerebral autoregulation is maintained

at moderate hypothermia, while with pH-stat management, the autoregulation is lost and cerebral blood flow becomes pressure dependent resulting in luxury perfusion at high pressure and hypoperfusion at low pressure.

The principal advantage of alpha-stat strategy is the theoretical preservation of intracellular electrochemical neutrality and maintenance of cerebral autoregulation, thereby limiting luxuriant cerebral blood flow during CPB. The excessive cerebral blood flow associated with pH-stat management may increase the cerebral embolic load and possibly aggravate cerebral oedema. It may however, provide a more uniform and quicker brain cooling. There are conflicting opinions regarding cerebral outcome when the two methods have been compared.[87,88] Bashein et al found no difference in the outcome with either pH- or alpha-stat strategies during mode rate hypothermic CPB in adults.[89] Whereas Stephan et al[90] and Murkin et al[91] found that neurological dysfunction occurred more often in patients undergoing CABG with pH-stat management. In patients at risk for impaired cerebral blood flow autoregulation, it has been shown that jugular venous desaturation (< 50 percent) occurred more frequently with alpha-stat as compared with pH-stat method signifying better cerebral oxygenation with pH-stat method.[92] More recently it has been shown that the neurological outcome using pH-stat acid base management is better in infants undergoing surgery with DHCA.[93-95] While in adult patients requiring DHCA, alpha-stat method provides better results.[95]

It has been suggested that blood gas management strategies are less important at moderate hypothermic temperatures. In procedures requiring DHCA, effective and rapid brain cooling is an important consideration and therefore, a cross-over strategy employing a combination of both alpha- and pH-stat strategies has been suggested.[96] A brief period of pH-stat, only during initial cooling is used in this technique. In conclusion, studies incorporating sensitive neurological outcome may be necessary to determine the best acid-base management strategy. However, it appears that in children undergoing DHCA, pH-stat and in adults undergoing routine cardiac surgery, alpha-stat strategy should be used.[97]

Haematocrit

Haemodilution during CPB is commonly practised. However, observational data indicate that profound haemodilution to a minimal haematocrit on CPB

of 15 to 17 percent is associated with greater cognitive decline at 6 weeks after CABG surgery, especially in elderly.[98] In infants, psychometric development at 1 year was superior in those with higher haemotocrit (28 percent) versus those with lower haemato-crits (21 percent).[99] It seems that extreme haemodilution (haematocrit $\leq$ 24 percent) should be avoided in high-risk elderly patients and in infants, haematocrit of $\geq$ 28 percent should be maintained.

Normothermic Bypass

In order to improve the myocardial preservation, the technique of continuous warm blood cardioplegia has been introduced.[100,101] As the heart is maintained at 37°C with this technique, systemic hypothermia is not considered necessary and the body temperature is also maintained at 37°C or allowed to drift to a tepid level (32–33°C). The efficacy of the technique in terms of better myocardial preservation has been shown.[102,103] However, it has evoked some controversy regarding the neurological outcome of the patient. This is so because the use of moderate (28° to 30°C) systemic hypothermia to facilitate cooling of the heart is considered to have added benefit of cerebral protection during periods of potential hypoperfusion and cerebral ischaemia. The reduction in $CMRO_2$ was believed to be the primary mechanism by which hypothermia improved ischaemic tolerance. Currently, its effects on mediators (extracellular and intracellular) of ischaemic injury are considered important.[104] In particular suppression of ischaemic release of excitatory amino acids, glutamate and aspartate, is considered to be of great consequence.

The Emroy study[105] and Warm Heart Investigators (WHI) trial[103] are the only randomised trials of warm versus cold heart surgery of sufficient size. The Emroy group observed a 3 fold increase in stroke rate (4.5 percent in warm and 1.4 percent in cold) that resulted in the termination of their study. In contrast, the WHI study found no difference in the incidence of strokes (warm-1.6 percent versus cold-1.5 per-cent). Differences in the management of perfusion temperature during warm CPB and different techniques for the delivery of warm cardioplegia between the two studies may have been responsible for the different results. Retrograde cardioplegia was used in a majority of patients in the normothermic group in the Emroy study while in WHI trial, few patients in either normothermic or hypothermic group

received retrograde cardioplegia. Retrograde cardioplegia may flush air or atherosclerotic debris out of the coronary circulation into the aortic root, which might be swept into cerebral circulation upon release of the aortic cross clamp. This might represent a significant mechanism of cerebral injury, however, further studies on neurological assessment following different routes of administration of cardioplegia are necessary to support such a conclusion.

Many studies have failed to demonstrate any beneficial effect of hypothermic CPB as far as neurological outcome is concerned.[106-108] However, these are not prospective randomized trials and have used historic controls. It has been shown that patients undergoing normothermic CPB are at greater risk for cerebral desaturation as defined by jugular bulb venous desaturation.[109] The clinical significance of this finding is yet to be proven, but in a study of 96 patients, it has been shown that patients managed at 37°C had a significantly greater incidence of deterioration on cognitive test scores than those managed at either 28°C or 32°C.[110] Cooling to 28°C did not offer any additional benefit in terms of cognitive function over cooling to 32°C. These findings suggest that employment of tepid CPB should be utilised for better myocardial preservation without increasing the cerebral risk associated with true normothermic perfusion.[111] Few other studies have also concluded that active warming during CPB to maintain systemic temperatures more than or equal to 35°C increases the risk of perioperative neurological deficit in patients undergoing elective CABG.[112,113] In contrast, some recent prospective randomised studies have shown that there are no differences in the neurological or neurocognitive outcomes between normothermic and hypothermic groups and that hypothermic CPB does not provide additional CNS protection in adult cardiac surgical patients[114] and may actually be harmful.[115]

Global hypoperfusion or focal occlusion of cerebral vasculature from emboli are important causes of cerebral ischaemia. Calcific or atheromatous emboli are likely to be dislodged from the ascending aorta at the time of aortic cannulation, clamping and unclamping or during proximal vein graft anastomosis. These periods are considered as periods of highest risk of embolisation of particulate matter. It is agreed that since the patients are normothermic at the time of these events (irrespective of the temperature at which systemic perfusion occurred during CPB), the protection provided by

hypothermia is not there. It is further argued that hypothermia offers negligible protection in the setting of a permanent focal or global ischaemia so that, if macroembolisation occurs during hypothermia, it would not be expected to offer substantial brain protection. However, the mechanism of neuropsychological dysfunction after CPB is less clear than that of frank strokes.

Normothermia and warm blood cardioplegia are frequently used in adults, but in children, hypothermic CPB remains the norm. In a prospective randomized study performed in children, it was shown that a more physiological ATP-steady state suggesting the absence of cellular ischaemic insult was observed in normothermic group.[116] Further, no significant difference was found between hypothermic and normothermic group as regards early and late neurodevelopmental status.

The neuroprotective effects of hypothermia during and after transient cerebral ischaemia are well known.[117] It has also been shown to be beneficial in comatose survivors of cardiac arrest with interval between collapse to return of spontaneous circulation of more than 15 min.[118] To say that transient ischaemic events during CPB are unknown is rather overambitious. In addition, there are many other factors that can lead to adverse complications. Roller pump can damage the cells and release free radicals, patients can receive cerebral emboli (gas or particulate), and ideal CPB pump flows and pressures are unknown and are set without the knowledge of the perfusion needed by the individual patient. The brain is likely, therefore, to suffer some insults during CPB and hypothermia has been advocated to provide cerebral protection. During normothermic perfusion, the patients are likely to maintain low MAP. It has been demonstrated that changes in MAP below the apparent cerebral autoregulatory range influence cerebral blood flow directly.[76] This finding may have some relevance in patients undergoing normothermic CPB. It appears that large scale prospective studies will be necessary to confirm if hypothermic CPB is better than normothermic CPB in terms of neuropsychological dysfunction.

In conclusion, the superiority of either normothermia or hypothermia in brain protection remains controversial. However, employment of normothermic rather than hypothermic or tepid CPB should be considered as one of the factors found to be associated with CNS dysfunction after CPB.

Cardiopulmonary bypass circuit and arterial line filters

It is known that cerebral microembolisation is associated with CPB and it has been shown that embolic load is directly related to the postoperative neurobehavioural dysfunction.[119] Using transcranial Doppler to quantify microemboli, these investigators demonstrated that patients having the lowest numbers of emboli evidenced a relatively low (< 10 percent) incidence of neurobehavioural dysfunction on postoperative psychometric testing. However, as the embolic load increased, over 40 percent of patients who had greater than 1000 emboli detected intra-operatively demonstrated postoperative cognitive impairment. The potential embolic material captured by the inline filters after uneventful cardiac surgery has been demonstrated.[17] Lipid emboli primarily arising from pericardial suction have been implicated for neurological complications. Lower transcranial Doppler (TCD) embolic signals and improved cognitive outcome occurs with the use of arterial line filters.[120] Leukocyte depleting filters remove inflammatory mediators during CPB and reduce the organ damage.[121] It was shown that during CABG surgery, leukocyte depleting filters led to reduced TCD microembolic signals, but no difference in cognitive dysfunction was observed.[122] Similar results have been observed by other authors.[123] It is possible that some commercially available arterial line filters perform better than others. Newer filters are being introduced and will need to be evaluated for their clinical utility. Any microemboli arising from aorta at any time will still reach the systemic circulation, despite the inclusion of an arterial line filter in the CPB circuit. In this respect, the retrograde cardioplegia delivery may be relevant. It has been shown that retrograde cardioplegia is associated with significantly more emboli upon release of the aortic cross clamp.[124] This implies that with retrograde cardioplegia there may be flushing of coronary atherosclerotic debris or air within the coronary circulation into the aortic root so that with the release of aortic cross clamp, these embolic particles are delivered into the cerebral circulation.

The systemic inflammatory response during cardiac surgery is initiated by the contact of blood with the foreign surfaces of the CPB circuit. The surfaces of the CPB circuit have been modified in many ways to improve their bio-compatility. Heparin bonded circuits have been most widely studied. Their use has been shown to reduce contact activation and inflammation that can

lead to improvements in postoperative cognitive function.[125,126] In another trial of low-risk patients undergoing CABG, heparin bonded circuits did not influence the postoperative memory impairment.[127] It seems that arterial line filters should be used in all patients, and use of heparin-bonded circuits should be strongly considered in high-risk patients.

Cerebral hyperthermia

Temperature of the brain has profound effect on cerebral metabolism and blood flow. In routine practice nasopharyngeal temperature is monitored, which has been found to be an unreliable measure of brain temperature[128] (brain temperature may be higher than nasopharyngeal temperature). At the time of aortic cannulation, aortic cross clamping and weaning from CPB (when the risk of cerebral emboli is maximum), the brain is more susceptible to damage from ischaemia because it is usually normothermic.[57] Likewise, cerebral hyperthermia during rewarming that is observed after hypothermic CPB[128,129] may have some relevance in terms of neurological outcome of the patient. In animal experiments, cerebral hyperthermia has been shown to increase neuronal damage.[130]

It would be expected that hyperthermia with its associated increase in metabolic rate would be dangerous, unless it is matched by an increase in oxygen delivery Therefore, it may be worthwhile considering maintaining the body at normothermia or mild hypothermia after the termination of CPB as transient cerebral hyperthermia is the rule rather than exception for most patients currently undergoing moderate hypothermic CPB.[82] Further, the hyperthermia is prevalent in the first 48 hours after CABG surgery using CPB, which may contribute to neurological dysfunction in these patients.[131,132] It has been reported that rewarming to 34°C is associated with fewer cognitive deficits at 1 week and 3 months after CABG as compared with rewarming to 37°C.[133,134] Therefore, patients should not be rewarmed to 37°C and hypothermia should be maintained in the postoperative period, at least for a few hours. Alternatively, a slower rewarming rate (maintaining not more than 2°C difference between nasopharyngeal and CPB perfusate temperature) may be considered, which has been shown to be associated with better cognitive performance.[135] However, with the current trend towards fast-track surgery, there is more emphasis on adequate rewarming of the patient in OT as hypothermia in the ICU is a major hurdle in achieving early

extubation. This needs to be reconsidered.

Temperature also has an effect on gas solubility, so that there is a potential for dissolved gas to form bubbles when cold blood with high oxygen tension passes from the oxygenator to the patient (at a higher temperature) at the beginning of CPB. Therefore, a temperature gradient of not more than 10°C between the oxygenator and patient has been recommended.

Deep hypothermic circulatory arrest

DHCA is used for the repair of complex congenital heart defects and some aortic arch surgery. This can be a potent risk factor for neurological injury. The safe duration of circulatory arrest at 15°C is regarded as 40 to 45 min.[136,137] In clinical practice, circulatory arrest has been applied for periods of 40 to 70 min. This period has been suggested to be safe as far as intellectual and developmental progress is concerned.[138] However, it has been shown that circulatory arrest time of more than 45 min. correlated with a reduction in the IQ.[139]

The gross neurological injury can be detected in the postoperative period, but more subtle injury may not be apparent until much later. Disabilities in speech and language, motor skills, and attention deficit disorder are present by school age in up to 50 percent of children who have undergone complex congenital heart defect repair.[140]

The incidence of neurological complications in children after DHCA ranges from 20 to 80 percent including developmental delays, diminished intelligence, pyramidal deficits, severe hypotonia, focal seizures and choreo-athetosis.[141,142] There are several other factors that can influence the neurological outcome in addition to the duration of DHCA. One of them, the method of acid-base management has already been discussed.

Erythropoietin is known to confer neuroprotective effects in various situations such as hypoxia and cerebral ischaemia. In an experimental animal model, beneficial neuroprotective effects of erythropoietin have been demonstrated after global brain ischaemia induced by one hour of hypothermic circulatory arrest.[143]

Aortic arch surgery remains a surgical challenge, as it is impossible without the temporary interruption of brain perfusion. Therefore it is associated with high incidence of neurological injury. The DHCA in combination with antegrade or retrograde cerebral perfusion is a commonly

used technique for brain protection in this scenario. In a comparison between antegrade versus retrograde cerebral perfusion, it was shown that the incidence of temporary neurological dysfunction was significantly less with antegrade perfusion (16 percent) than retrograde perfusion (43.5 percent). However, there were no differences in permanent neurological dysfunction and mortality.[144] Unilateral antegrade cerebral perfusion via axillary artery with systemic hypothermia at 22°C has also been shown to be safe with satisfactory clinical results.[145]

Antegrade cerebral perfusion along with mild hypothermia (28–30°C) or even normothermia, without circulatory arrest has been used and shown to provide sufficient cerebral protection.[146,147] Further, near infrared spectroscopy guided antegrade cerebral perfusion has also been used.[148] In this method, a decrease in brain oxygenation values in the contralateral hemisphere during unilateral antegrade cerebral perfusion is used as an indication to institute bilateral antegrade cerebral perfusion. There seems to be a paradigm shift from profound hypothermic surgery in patients requiring aortic arch surgery.

Off-pump versus on-pump CABG

CABG with CPB is still the gold standard for surgical myocardial revascularisation.[149] Inspire of advances in techniques and technologies, the current evidence indicates that CPB remains the major source of intraoperative brain injury. Off-pump CABG has gained significant popularity and is being applied to increasing number of patients. Due to avoidance of CPB, it is expected that off-pump CABG will be associated with decreased CNS complication rates. The incidence of stroke, focal neurological deficits as well as neurocognitive dysfunction has been shown to be less with off-pump CABG as compared to the conventional on-pump CABG.[149-152] However, most of these studies are non-randomised, in a large meta-analysis including 37 randomised trials and 3369 patients, it was shown that there was no difference in the stroke at 30 days and at 1–2 years, but a significant reduction in neurocognitive dysfunction was observed at 2 to 6 months only.[153] It seems that the off-pump CABG can especially be useful in a high-risk group of patients, such as elderly patients, those with atherosclerotic disease and with a history of cerebrovascular disease. However, a study performed on elderly high-risk patients has failed to show

any difference in the postoperative cognitive dysfunction with off-pump CABG.[154] A meta-analysis of 11, 398 patients from 8 studies has shown that avoidance of aortic manipulations during off-pump CABG decreases the neurological complications compared to standard technique where ascending aorta is manipulated.[155] Hence, this technique is recommended in high-risk patients.

Central Nervous System Monitoring

Electroencephalogram

CPB and anaesthetic state of the patient can influence the electroencephalographic (EEG) changes. Slowing of the EEG and burst suppression activity can be observed during mild to moderate hypothermia. At deep hypothermia, an isoelectric EEG may be observed.[156] This factor makes the identification of cerebral hypoxia (the sole purpose of EEG) induced EEG changes difficult. In addition, changes in perfusion flow or electrolytes during CPB can modify EEG findings, and roller pump artifacts are also known is occur. The value of EEG monitoring in terms of reducing the neurological morbidity is debatable and routine intraoperative EEG monitoring is not recommended. Postoperative EEG seizures may occur in neonates after cardiac surgery with CPB. EEG seizures are associated with prolonged DHCA and adverse neurodevelopmental outcomes. However, the EEG seizures may be suppressed by the benzodiazepines (that are commonly used during anaesthesia) and are considered a poor surrogate marker for neurological injury.[157]

EEG monitoring may be useful in some clinical situations such as carotid endarterectomy with or without CABG and patients undergoing complex procedures under DHCA. In patients undergoing carotid endarterectomy, the EEG monitoring can be used to determine the need for selective shunting. This is done by a brief test occlusion of the vessel and observing for hypoxic EEG changes. But, there is conflicting opinion on this issue.[158,159] The value of EEG monitoring in patients undergoing DHCA is to ensure that cerebral hypothermia has produced electrical silence and that metabolic demand caused by electrical activity has been reduced to the greatest extent possible.

Jugular venous oximetry

Jugular venous oxygen saturation can be measured by using a fibreoptic catheter placed in the jugular bulb via the IJV. Uncertainty exists over which is the better side for monitoring. Although, the jugular venous saturation appears to be similar on both sides in the normal brain, it may differ in patients with unilateral pathology. Therefore, it may be preferable to choose the side on which the pathology exists. In patients with bilateral brain injury, the jugular vein with the predominant venous drainage may be chosen. This may be identified by computerised tomography (side with the larger jugular foramen) or by ultrasound probe (side with the larger IJV). Jugular venous oxygen saturation is an index of the relationship between global brain oxygen consumption and delivery. Jugular venous desaturation can occur if there is a mismatch between cerebral blood flow (cerebral oxygen supply) and $CMRO_2$. A jugular venous oxygen saturation of < 50 percent is considered to reflect cerebral ischaemia. There is a mild decrease in the jugular venous saturation due to haemodilution at the onset of CPB (normal value: 60 percent), and during hypothermic CPB it usually increases to 70 to 80 percent.[160,161] This increase during hypothermia is probably a result of decreased $CMRO_2$ and alterations in haemoglobin oxygen affinity.[162] With rewarming, there is reversal of these effects and jugular venous saturations return back to normothermic values. However, it has been shown that cerebral venous haemoglobin desaturation occurs during rewarming phase of the CPB.[163]

It has also been suggested that jugular venous haemoglobin desaturation at the completion of rewarming is associated with a greater incidence of postoperative cognitive deficits.[164,165] But, this effect is more likely to occur in patients with preoperative abnormalities in cerebral magnetic resonance imaging.[166] Jugular venous desaturation would thus, imply that brain oxygenation is compromised in some patients. These patients are likely to be those with pre-existing brain injury. Hanel et al[163] have shown that jugular venous desaturation can be prevented by inducing mild hypercarbia ($PaCO_2$ of 50 mm Hg) during CPB rewarming. However, it is not clear, if neuropsychological outcome can be improved by preventing venous desaturation during CPB rewarming. It may be of benefit in a subset of patients who perhaps, need to be identified and studied.[18] In a recent review,

it has been suggested that jugular venous oximetry is feasible, practical and beneficial for patients undergoing CPB. It enables detection of periods of desaturation, which may indicate the need for appropriate intervention.[167]

Off-pump CABG frequently results in significant jugular bulb desaturation. In one study it has been shown that 48 percent of patients undergoing off-pump CABG had jugular oxygen saturation of less than 50 percent.[168] The authors believed that this may be a factor contributing to occurrence of neurocognitive dysfunction comparable to that of on-pump CABG. Changes in jugular bulb oxygen saturation are related to changes in the mixed venous saturation and arterial carbon dioxide tension. It has been shown that mixed venous oxygen saturation of < 70 percent, $PaCO_2 \leq$ 40 mm Hg, and CVP $\geq$ 8 mm Hg had a significant odds ratio for jugular bulb desaturation.[169] Hence, achieving normal values of mixed venous oxygen saturation, $PaCO_2$ and CVP may be important to prevent cerebral desaturation.

Near infrared spectroscopy

Near infrared spectroscopy was first described by Jobsis.[170] It is a technique that can potentially monitor changes in cerebral oxygenation and tissue oxygen utilisation. Theoretically it offers a technique for continuous, noninvasive, bedside monitoring of cerebral metabolism. Like pulse oximetry, these instruments use principles of light transmission and absorption to measure noninvasively the concentration of oxygenated and deoxygenated haemoglobin in the tissue. Due to its noninvasive nature cerebrovascular haemoglobin oxygen saturation (ScO_2) monitoring seems to be a useful tool to monitor cerebral oxygenation. It was suggested that this technology may be clinically useful during open-heart surgery as the changes in ScO_2 during surgery with hypothermic cardiac arrest correlated with the postoperative neurological outcome in a small group of paediatric patients.[171]

ScO_2 values above 80 percent of the baseline or above 50 percent are generally considered target values for adequate cerebral perfusion during CPB. Amongst the several causes of neurological injury, perfusion during cardiac surgery is considered a modifiable factor and ScO_2 is the way to assess the quality of intraoperative cerebral perfusion. However, the evidence regarding utility of ScO_2 is controversial. In one study, ScO_2 was kept above

80 percent of baseline and above 55 percent during anaesthesia including CPB, but the incidence of cognitive dysfunction was similar to that reported in patients without monitoring. [12] The authors of the study suggested that a higher threshold for ScO_2 may be needed to reduce the incidence of cognitive dysfunction. Studies have also shown that ScO_2 cannot be a replacement for jugular bulb oxygen saturation or mixed venous oxygen saturation.[172,173] During off-pump CABG, ScO_2 values decreased during grafting of the circumflex and the right coronary artery, but not during grafting to left anterior descending artery.[174] Cerebral hypoperfusion (20 percent decrease in ScO_2 from the baseline) occurred in 20 percent patients. The clinical utility of the finding is unclear, but normal cerebral perfusion as guided by ScO_2 may be used to guide the acceptable lower limit of MAP or cardiac output (in a given patient) during positioning of the heart for grafting purposes during off-pump CABG. ScO_2 guided bilateral antegrade cerebral perfusion in moderate hypothermic circulatory arrest[148] and adjustments of the aortic cannula[175] for aortic surgery have already been described.

The neurological outcome in paediatric cardiac surgery is also a focus of attention. The long-term neurological outcomes are a major issue as a result of improvements in early outcomes. ScO_2 monitoring has gained popularity, although it is not considered a standard of care. In one study the predictive value of ScO_2 for neurodevelopmental outcomes at 2 years was unclear and patient-related factors largely influenced this outcome.[176] Another study has shown that perioperative periods of diminished cerebral oxygen delivery as indicated by ScO_2 ($\leq$ 45 percent) are associated with 1-year psychomotor development index and brain magnetic resonance imaging abnormalities in infants undergoing heart surgery.[177] In summary, there is no doubt that ScO_2 is a useful noninvasive monitoring tool and deserves a more wider application even in the absence of its validation.

Transcranial Doppler

Transcranial Doppler (TCD) constitutes an easily applied noninvasive method of measuring cerebral blood flow. By applying the Doppler principle, Doppler shift is utilised to calculate the blood flow. Typically, right and left middle cerebral artery blood flow velocity is measured. It can be used during

CPB to detect air or particulate emboli and is the standard monitoring technology to visualise cerebral microemboli.[178] Quantification of cerebral microembolic load is possible with the built-in softwares available in the TCD systems. Surgeons may be guided to alter their techniques in order to decrease the embolic load in a given patient. TCD is being increasingly used during carotid artery surgery. The clinical utility of TCD to detect embolic load is undefined as the causal link between emboli from CPB and postoperative cognitive decline is not determined.[179] Nevertheless, ease of application and the characteristic spectral Doppler produced by emboli make it an attractive monitor during cardiac surgery.

Despite the fact that adverse neurological outcomes are common complications of cardiac surgery, intraoperative brain monitoring has not been given its due attention. A survey performed in the Germany has revealed that in most departments, the central nervous system is not subjected to monitoring during cardiac surgery.[180] It is believed that a multimodal brain monitoring is more useful than a single monitoring technique and can reduce the incidence of neurological complications as well as costs associated with post-cardiac surgery patient care.[181]

Neurobiochemical markers of neurological injury

Protein S-100B and neuron-specific enolase (NSE) have been identified as neurobiochemical markers of brain damage after cardiac surgery with CPB. S-100 B protein is located in astrocytes and Schwann cells. An early increase in S-100 B levels shortly after cardiac surgery is observed. However, it is the sustained release beyond 24 hours that is considered indicative of major brain injury.[47] A correlation between S-100B levels and neurocognitive impairment has not been shown.

NSE is localised to neurons and axonal processes and is also found in erythrocytes and platelets so that its cerebrospinal fluid and blood levels increase after neuronal damage or haemolysis.[140] Persistence of levels over 35 ng/mL at 48 hours after surgery is considered a marker for bad prognosis.[140]

In a multivariate analysis, it has been shown that NSE and S-100B concentrations 6 to 30 hours after skin closure were the only variables that

contributed significantly to a predictive model of the neuropsychological outcome.[182] Therefore, NSE and S-100B levels can provide a valuable tool to monitor and assess the measures to improve cardiac surgery with CPB. In addition, it may provide an insight into the underlying pathophysiology of brain dysfunction.

Adenylate kinase and creatine kinase isoenzyme BB (CK-BB) are some other biochemical markers for neurological injury, [47,140] but have limited value. CK-BB blood levels can increase in up to 98 percent of patients after cardiac surgery with no correlation with neurological damage.[183]

Tan protein, which has been linked to neuro-generative disorders is another biomarker of interest. It is a more specific biomarker as it is only found in the central nervous system. The metalloproteinase and ubiquitin C terminal hydroxylase-L1 (UCH-L1) are the most recently researched markers, but their usefulness is still unclear.[184]

Neuroprotective Measures

It is apparent that emboli are generated during the entire period of CPB. Use of equipment and techniques that are likely to reduce the embolic load should, therefore, be preferred. In this respect, use of the membrane rather than bubble oxygenator and arterial line microfilters are desirable. Some intraoperative manipulations, especially instrumentation of the aorta can be a potent source of emboli. Use of epiaortic ultrasound probes can be useful to detect the aortic atheromas. In a large series, epiaortic ultrasound scanning was employed to detect atherosclerotic disease of the aorta.[15] In 27 patients with severe atherosclerotic disease, the ascending aorta was replaced with no strokes occurring in this group. Some technical modifications can also be employed in patients with less extensive aortic disease to improve the outcome. These include use of femoral or distal aortic arch cannulation sites, no aortic clamping or more proximal placement of aortic clamps, delivery of cardioplegia retrogradely through the coronary sinus or hypothermic fibrillatory arrest, and more proximal placement of proximal anastomoses or use of skip grafts without proximal aortic anastomoses.[32]

The use of a long arterial arch cannula placed beyond the orifice of the left subclavian artery has been recommended for patients with extensive aortic atheromatosis. While this may avoid perfusion related cerebral embolisation,

the risk of plaque fracture and embolisation engendered by the passage of cannula through the potentially diseased aortic arch cannot be overlooked.[185]

Two new devices have been introduced to capture or divert the emboli. The Embol-X intra-aortic filter is a 150 μm net that is inserted through a side port of a modified aortic cannula.[186] It is deployed prior to release of the aortic cross clamp and partial occlusion clamp. In a randomised multicentric trial it was shown that particulate emboli were captured in 96.8 percent of cases in which the intra-aortic filter was deployed, but there was no difference in the mortality, stroke, and transient cerebral ischaemic events between the filter and the standard cannula groups.[187] The Cardion 'cobra' is another device, which is a modified double lumen aortic cannula with an inflatable shield that diverts emboli away from the great vessels of the aortic arch. One lumen is used to perfuse the body while the other perfuses the aortic arch vessels. This enables differential perfusion of the head and body so that differential cooling of the head can be performed while mamtaining normothermic perfusion of the body.[188] The results of these devices are still awaited.

In the absence of epiaortic scanning, manual palpation of the aorta is practised by some surgeons. However, the sensitivity of palpation compared with scanning has been shown to be only 0.46.[189]

Although, the critical level of MAP during CPB is undetermined, hypotension during hypothermic CPB with high flow rates should not be easily accepted and MAP of 50 mm Hg should be maintained. It may be necessary to increase this limit further in select high-risk group of patients. In open cardiac procedures (for valve and congenital heart disease), meticulous de-airing of cardiac chambers before releasing the aortic cross clamp should be carried out. Meticulous rinsing of the LA and LV cavity in patients having intracardiac tumour and thrombi should also be practised. Care must be exercised to maintain acceptable haematocrit, pH, blood-gas and acid-base balance throughout the CPB. In addition, temperature increase over 37°C should be avoided as it can lead to exacerbation of cerebral ischaemia. Slow rewarming (0.2°C per min.) is recommended.

Pharmacological therapy

Neuroprotection can be defined as the treatment initiated before the ischaemic insult with the intention to increase the tolerance of tissue to

ischaemia resulting in improved outcome. It should be noted that unlike most other clinical situations (where ischaemia is unpredictable), the occurrence of ischaemia is known during cardiac surgery. For instance, the initiation of DHCA or even CPB can be considered to cause organ ischaemia. Hence, neuroprotective measures can be planned during cardiac surgery.

New developments are taking place that include the progress into new neuroprotective agents such as glutamate antagonists, free radical scavengers, and anti-inflammatory agents. Although, they look promising, these agents are not available and have yet to be proven effective in the clinical setting.

Barbiturates

Barbiturates reduce $CMRO_2$ and are known to effectively provide cerebral protection in various animal models of cerebral ischaemia. They are supposed to provide neuroprotection by mechanism differing from hypothermia. Nussmeier et al[190] have reported a lesser incidence of stroke after valve surgery in patients who received thiopental, whereas Zaidan et al[191] did not find any evidence of barbiturate neuroprotection in patients undergoing CABG. The surgical procedures and CPB conditions were markedly different between the two trials. Animal experiments have suggested that overall potency of barbiturates as neuroprotective agents is weak.[192] The effect of barbiturates on the incidence of subtle and more common neuropsychiatric deficits, however, is not well studied. Most clinicians agree that barbiturates are not indicated in procedures associated with a low risk of neurological complications. The infants and children undergoing complex repairs under DHCA are at a greater risk of brain injury, and many anaesthesiologists prefer to administer barbiturates during the procedure. This policy is based upon the theoretical possibility that barbiturates may offer additional neuroprotection than that is provided by hypothermia. This practice may be supported by the fact that uniform brain cooling during DHCA may not be achieved.

Thiopental should not be administered before reaching 18°C as effective global cooling is dependent on cerebral blood flow. Barbiturates can reduce cerebral blood flow by causing cerebral vasoconstriction, thus impairing effective brain cooling. Barbiturates should, therefore, be administered just before the arrest, and the onset of circulatory arrest should be delayed for sometime to allow effective circulation to the brain. Some other

anaesthesiologists do not agree with the practice of using high-dose thiopental (30–50 mg/Kg) due to absence of any proven benefit.[193]

Propofol has effects on $CMRO_2$ and cerebral blood flow that are similar to thiopental.[194] It has been shown to have direct neuroprotective action.[195] It has been suggested that propofol induced reduction in cerebral blood flow reduces the delivery of microemboli to the brain.[196] Further, propofol also has free radical scavenging and antiinflammatory properties.[197] However, propofol infused to induce EEG burst suppression was ineffective in improving the neurological outcome in cardiac valve surgery pateints.[198] Etomidate and lidocaine are other agents that suppress the $CMRO_2$, but need further evaluation in terms of their neuroprotective efficacy.

Volatile anaesthetics

Animal experiments have suggested that volatile anaesthetic agents provide improvements in ischaemic outcome. They protect against both focal and global ischaemia, but the improvement in outcome is transient in global ischaemia, whereas it is persistent in focal ischaemia.[199,200] Volatile anaesthetic agents also have pharmacological preconditioning effect that protects the organs from reperfusion injury. Isoflurane and sevoflurane have been studied a great deal. In the absence of human outcome data, it cannot be stated that volatile anaesthetics improve outcome from perioperative ischaemic insults.[201]

Aprotinin

The systemic inflammatory response is considered important in determining the severity of neurological damage. Hence, anti-inflammatory agents such as aprotinin may have a place amongst the neuroprotective measures.

Some early reports have demonstrated a decreased incidence of stroke with the use of aprotonin.[202,203] However, aprotinin has been withdrawn from the market since 2007. The reader is referred to chapter 11 for the details of the subject. The current experimental data has shown beneficial effects on neurological outcome. In a rat model, it was shown that aprotinin decreased the systemic inflammation, and although there was no difference in the cerebral infarct volume, there was a small improvement in the short-term functional neurological outcome in the aprotinin group.[204] In another study performed on piglets, Ishibashi and colleagues demonstrated that aprotinin

reduces cerebral leukocyte activation and accelerates neurological recovery in a dose-dependent fashion.[205] No measurable impact on standard indices of renal function were seen in these young piglets. Therefore, the authors have suggested that the current lack of availability of aprotinin is a serious disadvantage for paediatric patients undergoing CPB.

If one examines the role of blood transfusion, it is seen that neurological complications are associated with total blood product transfusion.[206] In one study, it was shown that return of shed blood increased the risk of cerebrovascular accidents more than 3-fold (3.1 percent versus 0.0 percent) [207] The same study also demonstrated that aprotinin was associated with a significantly lower overall incidence of stroke (1.1 percent), which was independent of retransfusion. Transfusion of uprocessed shed blood constitutes a major source of lipid microparticles. Hence, processing of shed blood with cell saver before transfusion may limit cerebral microembolisation and reduce cognitive decline after surgery. The reports on this issue are controversial, with one demonstrating a clinically significant reduction in postoperative cognitive dysfunction,[208] while another showing no benefit.[209] It seems that limiting the number of transfusions and use of cell saver to process the shed blood constitute important means of neuroprotection following cardiac surgery.

Surgical field carbon dioxide insufflation

Carbon dioxide being several times heavier and more soluble in blood than air, it can be insufflated into the surgical field to displace air, thus decreasing the nitrogen content of gaseous emboli.[210] Such emboli composed of carbon dioxide have a shorter life span and may limit the cerebral injury. However, CO_2 insufflation reduced intracardiac and aortic microemboli (by echocardiography), but no improvement in cognitive outcome could be demonstrated.[211]

Awareness

Patients undergoing surgical procedures under general anaesthesia often express anxiety about being aware of pain and events during surgery. Although, awareness is not strictly a neurological complication, it is being discussed as it is an important consideration in patients undergoing cardiac

surgery. A suitable working definition of awareness can be, “the spontaneous recall of events occurring during general anaesthesia.”[212] Awareness during general anaesthesia can be a horrifying experience and may cause acute psychological trauma.[213] In addition, it may also have medicolegal implications. Despite best efforts, awareness with explicit recall of events with or without pain still occurs. The reported incidence of awareness varies but it is generally believed that it is higher during cardiac surgery (1.1 to 1.5 percent)[214,215] as compared to other surgical procedures (0.2 and 0.16 percent).[216,217] Several factors are considered to be responsible for this increased incidence. These include: 1. CPB alters pharmacokinetics and pharmacodynamics of drugs; 2. oxygenator and tubing may bind large amounts of some drugs; 3. desire to avoid negative inotropic effects of volatile and intravenous anaesthetic agents leading to restriction of their dosage, and 4. the usual clinical markers of anaesthetic depth, such as haemodynamic responses are less dependable as the patients are usually on beta-blockers.

Advances in cardiac surgery, such as off-pump CABG, where the patient is generally expected to awaken at the end of surgery, and minimising the extubation times in patients undergoing conventional on-pump CABG demand a high degree of precision from the anaesthesiologist. He is expected to provide a perfect anaesthetic that causes least haemodynamic disturbance and allows recovery as soon as possible. In doing so, he is also expected to ensure that the patient does not suffer from awareness. The last few years have seen a changing trend from large dose opioid technique to a drastic reduction in the doses of opioids and benzodiazepines or use of shorter acting drugs in infusion forms with or without inhaled anaesthetics. Since the incidence of awareness is associated with smaller doses of anaesthetics,[218,219] such a change towards using smaller doses of anaesthetics may make the patient prone to suffer from awareness. However, in a large series of patients undergoing fast-track anaesthesia, the incidence of awareness has been reported to be as small as 0.3 percent.[220] This may be attributed to the continuous use of either isoflurane or propofol infusions during the entire surgical procedure, as well as to the monitoring of end-tidal anaesthetic gas concentration.

The importance of having a reliable indicator of depth of anaesthesia has long been realised by anaesthesiologists.[221] Initially, the haemodynamic

response to laryngoscopy, tracheal intubation and/or skin incision was used to assess the depth of anaesthesia. Subsequently, EEG and various forms of processed EEG (e.g. spectral edge frequency and total power, among others) were used. However, none of these were found to be very successful.

Bispectral index monitor

In 1997, the Aspect Medical Systems (Natick, MA, USA) introduced a device that displays a single "bispectral index" or a BIS value, which measures the depth of anaesthesia (Fig. 14.1). The bispectral analysis is a higher order statistical analysis that also takes into consideration the phase information from the EEG signal. Unlike earlier methods that relied on tracking and processing a single parameter of EEG, the BIS calculates three different subparameters: 'Burst Suppression Ratio'; Beta Ratio; and 'SynchFastSlow'. The Burst Suppression Ratio is the proportion of suppressed EEG (isoelectric) in an epoch, the Beta Ratio is the log ratio of the power in two empirically derived frequency bands (high and medium frequency range) and the SynchFastSlow is the relative bispectral power in the 40 to 47 Hz frequency band. EEG recordings from thousands of patients undergoing anaesthesia with multiple different anaesthetic techniques were collected by the Aspect Medical Systems. The clinical information related to anaesthetic depth was also collected. After processing these data, a database was created describing the EEG derived subparameter and the corresponding clinical state (level of consciousness). The subpara-meters were then ranked by their ability to predict a particular clinical condition. The exact weighting of each subparameter is a proprietary. The weighted sum of the subparameters is the BIS number. The BIS is a dimensionless number that varies from 0 to 100. In the awake state the BIS is close to 100 and the number decreases with increasing sedation and hypnosis. A BIS value of less than 60 is often regarded as the criterion for adequate anaesthesia, whereas a value of more than 70 is frequently seen during awakening.[222] Its utility as a monitor having high probability of correctly predicting absence of consciousness during general anaesthesia[223-225] and degree of sedation in intensive care patients[226] has been recognised. Therefore, it has been proposed to be a useful monitor for anaesthetic depth during cardiac surgery with CPB,[227] when the usual clinical markers of anaesthetic depth are less dependable. Although, there is no evidence that monitoring depth of

unconsciousness prevents awareness, it is conceivable that by maintaining sufficient depth of unconsciousness, this will be achieved. Indeed, the BIS monitor has mainly established itself as a means of minimizing the incidence of awareness. In addition, BIS has been helpful in providing more rapid awakening of patients undergoing cardiac surgery and also saving cost, by reducing either the level of anaesthesia or length of stay in the recovery room.

It is unrealistic to expect a monitor that predicts the probability of awareness, to have 100 percent specificity (no false negatives). A case report describes explicit awareness in a patient with BIS of 47.[228] BIS is known to be unaffected by nitrous oxide[229] and by ketamine.[230] It has been shown that BIS is not an accurate measure of depth of anaesthesia when fentanyl with or without propofol[231] or fentanyl and midazolam were used during CABG.[232] The BIS has also not been shown to be robust enough when artefactual signals are present. For example, changes in BIS have been found in patients with pacemakers during cardiac surgery,[233] and with the use of electrical blankets.[234] Large scale multicentre controlled clinical trials designed to determine exactly how effective the BIS monitor is in preventing unintentional intraoperative awareness are necessary. Although, BIS monitoring appears to be generally associated with a low incidence of awareness, a search for the alternative is on.[235]

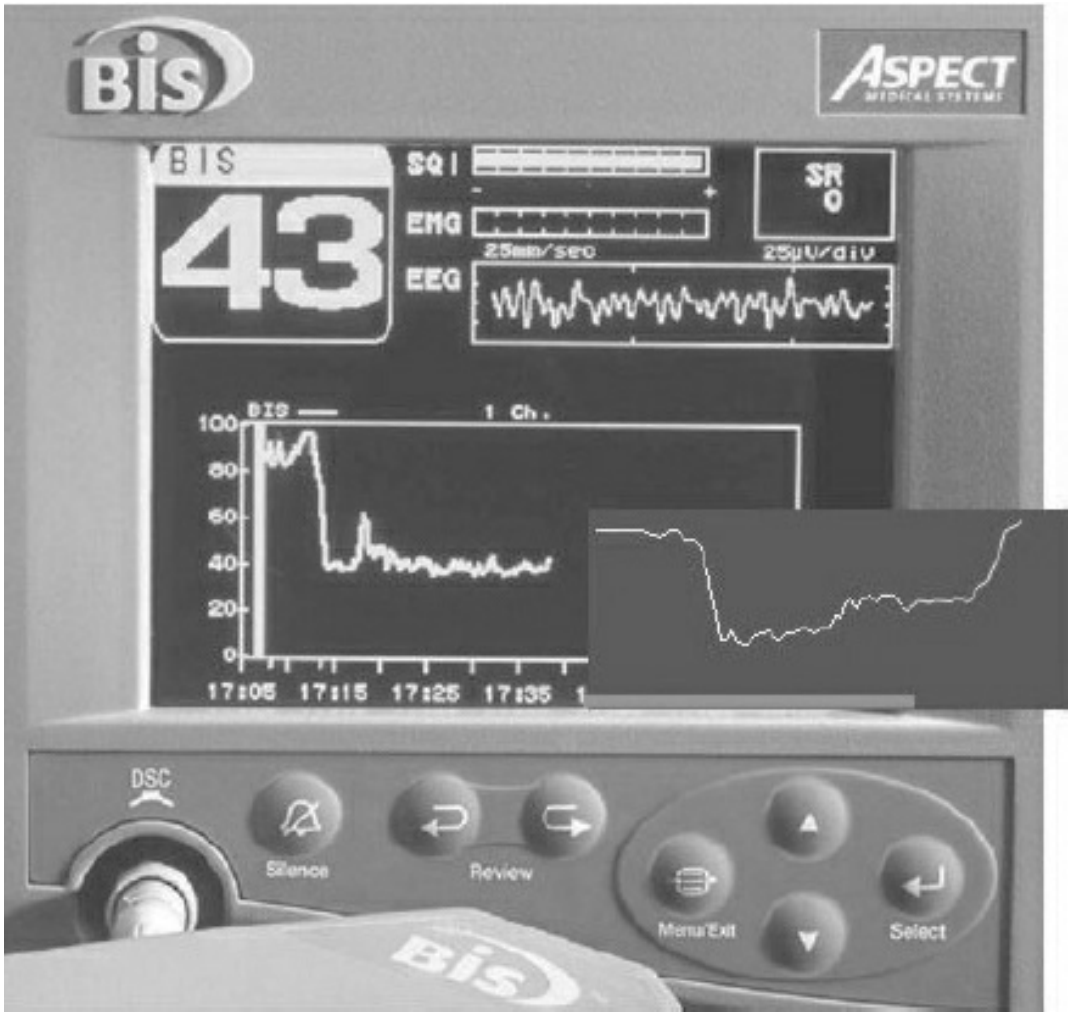

Figure 14.1: The Bispectral index monitor (Aspect Medical Systems, Inc. Natick, USA)

Entropy

Entropy describes the complexity, irregularity, or unpredictability of a signal.[236] For instance, a pure sinusoidal wave is considered to have an entropy of zero because it is regular and predictable, but an irregular wave having large frequency variations will have very high entropy. Spectral entropy has been incorporated in commercially available device by GE Healthcare. The exact algorithm is available to the public.[237,238] Both time domain and frequency domain analysis is utilised in the algorithm. Two entropy indices are available; state entropy computed from the EEG in 0.8 to 32 Hz range (hypnotic elements of the EEG) and response entropy computed from 0.8 to 47 Hz, which includes significant amount of facial EMG.[237] Thus response entropy increases during arousal when the facial EMG increases.

The state entropy ranges from zero (isoelectric EEG) to 91 (fully awake) and response entropy range is 0 to 100. The anaesthetic range is 40 to 60, and state entropy outside this range requires sedation and response entropy more than 10 above the state entropy requires analgesic administration. In a comparison with BIS, it was shown that response entropy and state entropy are comparable with BIS, but the entropy signals were more robust with less interference from EMG.[239]

A carefully planned anaesthetic technique can also help to decrease the incidence of awareness. It has been proven by Ranta et al[215] that the incidence of awareness and recall could be reduced from 4 to 1.5 percent by feedback information to the anaesthesiologist. Due to the feedback, the anaesthetic technique was altered considerably and the authors recommended continuous use of either inhalational or intravenous anaesthetic agents and monitoring of end-tidal concentration of inhalational anaesthetic agents. Using such a technique, Dowd et al[220] in a large series of patients undergoing fast-track cardiac anaesthesia have shown that the incidence of awareness was as low as 0.3 percent.

It is rightly said that anaesthesia is a balancing act and the depth of anaesthesia is a balance between the anaesthetic and surgical stimulus. It seems that continuous administration of anaesthetic agents is most important in prevention of awareness. It should also be remembered that the patient is particularly susceptible to awareness during specific events related to increased surgical stimuli such as intubation, sternotomy, electrocauterisation, DC shock and rewarming phase after termination of CPB, so that, it is beneficial if the anaesthesiologist increases the depth of anaesthesia temporarily in anticipation of a strong stimulus. The BIS monitor can also be effectively utilised towards this goal and can be especially useful in a select group such as sick patients (where excessive anaesthetic may be harmful) or those with previous history of awareness.

Conclusions

Cardiac surgery is a life saving procedure with high success rate. However, it may be accompanied by negative side effects such as stroke. There are multitude of factors and events during cardiac surgery that can cause cerebral injury. Global or focal cerebral hypoperfusion mostly as a consequence of

micro or macroemboli appears to be the reason behind the injuries. The incidence of subtle neurological injuries is quite high and prevention of their occurrence should be the consideration during each cardiac procedure. Despite the high incidence of neurological complications, no definite guidelines for management exist. Non- pharmacological strategies include monitoring of brain oxygenation and perfusion with near infrared spectroscopy and tanscranial Doppler. Epiaortic scanning and TOE examination of aortic pathology enables the surgeon to plan the management so that aortic handling is avoided. In addition, specially designed aortic cannulae and filters can help to minimise the embolic load. Antegrade or retrograde cerebral perfusion during DHCA is also useful. Maintaining adequate MAP, haemotocrit, perioperative temperature and blood glucose level are other useful means of cerebral protection. A multimodal brain monitoring and a protocol-based management of the patients can help to reduce the incidence of neurological complications.[181,240] Further understanding of the subject, improvement in the perfusion technology as well as meticulous anaesthesia, surgery and perfusion should hopefully, reduce the incidence of neurological injury after open-heart surgery.

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Chapter 15: Postoperative Management of Adult Cardiac Patient

Open-heart surgery is now a well established and routine procedure. Although, the underlying cardiac pathology is corrected during a cardiac operation, the patient requires intense haemodynamic monitoring and care during the postoperative period. This is related to the ischaemic insult (due to aortic cross clamping) during cardiopulmonary bypass (CPB). In addition, pre-existing deranged cardiovascular function in some patients may also be a contributory factor. Cardiac surgery has evolved further during recent times. The need to cross clamp the aorta is obviated in beating heart surgery that is performed in patients undergoing coronary artery bypass graft surgery (CABG). However, myocardial ischaemia due to haemodynamic derangements during beating heart surgery (despite the use of intra-coronary shunt) is always a possibility. The number of older and sicker patients undergoing cardiac surgery is also on the rise so that many patients may be receiving pharmacological and/or mechanical haemodynamic support, when they reach the intensive care unit (ICU) after the operation.

The patients also need careful respiratory management. In most centres elective artificial ventilation in the postoperative period is an accepted practice. The duration of ventilation, however, varies widely between different centres. Some centres also extubate patients in the operation theatre immediately after the surgery. Even such patients will require careful respiratory monitoring, as the possibility of re intubation cannot be ignored in them.

The anaesthesiologist is mainly involved in the respiratory management, and the management of sedation and analgesia during the postoperative

period. These two aspects will therefore, be the focus of attention in this chapter.

Respiratory Management

During the early days when open-heart surgery was being pioneered, patients frequently suffered from pulmonary complications. These complications have been attributed to many reasons that essentially consisted of preoperative cardiac and pulmonary dysfunction, intraoperative events and postoperative haemodynamic and residual anaesthetic effects.

The cardiac disease may diminish lung function as a result of passive congestion and hypoperfusion or hyperperfusion giving rise to changes in lung mechanics and disturbances of ventilation and perfusion.[1] The factors related to extracorporeal circulation that have an impact on lung function include mechanical effects, blood and crystalloid prime, complement activation, surfactant reduction, the consequences of using cardioplegia and reaction to protamine.[2,3] In addition, CPB activates adhesion molecules which are associated with systemic inflammation and organ dysfunction. It has been shown that respiratory insufficiency after CPB is associated with increase in intracellular adhesion molecule-1,[4] as well as the proinflammatory cytokines.[5] The occurrence of postoperative pain and the presence of pleural drains and fluid collection also reduces the efficiency of gas exchange. A low cardiac output (CO) state and circulatory support by means of increased intravascular volume may cause passive pulmonary congestion. Following anaesthesia lung function is diminished. This may not only be due to residual effects of anaesthetic agents but to a decrease in functional residual capacity. Airway resistance and respiratory elastance may increase after extubation (up to 2–3 days), especially in obese patients in whom CPB was used.[6]

A compromised lung function due to a multitude of factors is likely to be present in the postoperative period. Therefore, mechanical ventilation in the postoperative period is an accepted norm at many cardiac centres. It was a general practice to ventilate patients for a period of 12 to 24 hours after open-heart surgery in the early 1970s.[7] Many authors, however, demonstrated the safety of early extubation in selected patients, during the subsequent period.[8-12] With the evolution and improvement of extracorporeal techniques with modern oxygenators, haemodilution and arterial filters, a reduced rate of lung

complications was anticipated[13,14] and a few authors even extubated patients immediately after surgery.[15,16] The anaesthetic technique played a relevant part in these reported series.

In the current era of cardiac surgery, with growing pressure on ICU beds, the practice of extubation early after surgery (fast-track) is gaining wider acceptance. This is particularly so in patients undergoing minimally invasive cardiac surgery such as off-pump CABG. However, such a practice has made the management of pain in the postoperative period, a very important issue. Even if such a practice is widely followed, there will be a large group of patients who will need mechanical ventilation in the postoperative period for some duration. This is so because opioids (modest to high doses) are still considered to constitute a popular and conventional method of anaesthetising patients with heart disease. In addition, patients with poor preoperative or postoperative cardiovascular condition may need prolonged periods of ventilatory support, depending upon the time taken for establishing a reasonable cardiovascular stability.

In summary, cardiac patient in the postoperative period may require respiratory support not only due to the residual effect of such anaesthetic drugs as opioids, sedatives and relaxants but also as a result of overall deterioration in the lung function and sometimes deranged cardiovascular condition. Thus the objective of ventilatory support is to ensure optimal oxygenation, carbon dioxide elimination and relief from the work of breathing until anaesthetic effects are minimal and cardiac function is stabilised. Indeed, there is a general agreement with some exceptions that postoperative ventilation should be continued for some time after cardiac surgery.

Methods of mechanical ventilation

Several modes of mechanical ventilation have been described. The physiological considerations of controlled mechanical modes of intermittent mandatory ventilation (IMV), mandatory minute ventilation, pressure support ventilation (PSV), continuous positive airway pressure (CPAP) and high frequency ventilation (HFV) have been summarised.[17] Most of the modern day ventilators incorporate the microprocessor technology and the facility of various modes of ventilation. One such ventilator is shown in figure 15.1. While there have been reports of the use of these more complex applications

of positive pressure ventilation after cardiac surgery,[18-21] there is no conclusive evidence that one mode is more beneficial than another. Nevertheless, for the sake of completeness, some of the modes of ventilation will be described in this chapter.

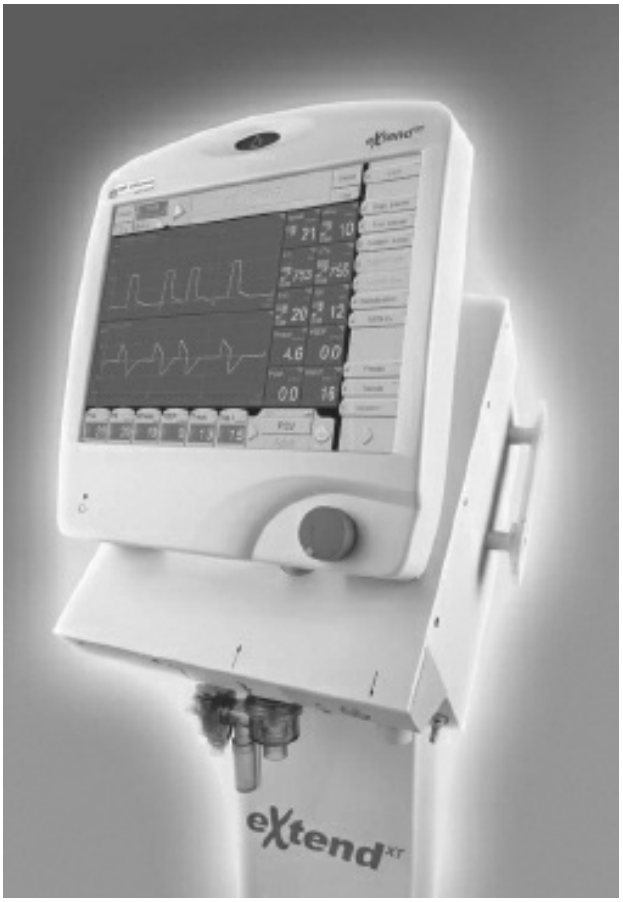

Figure 15.1: The eXtend® ventilator, Taema Horus

Table 15.1: Different modes of ventilation

Volume preset modes
Controlled mechanical ventilation
Assist/control mode
Intermittent mandatory ventilation
Synchronised mandatory ventilation
Pressure preset modes
Pressure support ventilation
Pressure controlled ventilation
Pressure release ventilation
High frequency ventilation

Volume preset modes

Volume preset modes are also known as volume controlled modes. They can be either volume cycled or time cycled. The greatest advantage of these modes is that a predetermined volume is delivered to the patient's lung, even if changes in lung compliance or airway resistance occur.

Controlled mechanical ventilation

In this mode, positive pressure breaths of preset volume are delivered to the patient at predetermined time intervals. If the patient has his own spontaneous respiratory effort, no gas is available to fulfill the spontaneous inspiration between the ventilator cycles. In addition, if the ventilator delivers a spontaneous breath during the patient's expiration, high airway pressures are achieved. If the patient is conscious, then it may create a sensation of breathlessness. This phenomenon is described as "fighting the ventilator". This mode of ventilation is therefore, not used routinely in the ICU, unless the patient is paralysed. The airway pressure tracings of controlled mechanical ventilation (CMV) mode are shown in figure 15.2a.

Assist/Control mode

In this mode, a positive pressure breath is delivered to the patient when the ventilator senses negative pressure in the ventilator circuit. When the patient initiates a spontaneous breath, the pressure in the circuit decreases as there is no fresh gas flow between the cycles. To avoid the danger of no ventilation, in the event of patient becoming apnoeic, a minimal back-up rate is set below which, the ventilator will initiate breaths at a predetermined rate independent of the patient effort. The level of negative pressure at which the ventilator initiates a breath can also be set. The sensation of breathlessness that is sometimes observed in the CMV mode is eliminated and there is a diminished requirement of sedation and muscle relaxation. Therefore, assist/control mode generally leads to improved clinical care as compared with the CMV mode. The patient's spontaneous ventilatory efforts can be suppressed by setting the back-up rate above the patient's spontaneous rate. The airway pressure tracings of the assist/control mode are shown in figure 15.2b.

Intermittent mandatory ventilation

IMV is a control mode of ventilation that allows the patient to breathe spontaneously. A circuitry is provided that supplies adequate fresh gas flow

for spontaneous breaths. The positive pressure cycles are completely independent of the patient's spontaneous ventilation and constitute the mandatory ventilation. The IMV rate is therefore, adjusted in such a way that it can provide adequate ventilation, even if the patient ceases to breathe. The diagrammatic representation of this mode is shown in figure 15.3.

When the ventilator cycle is initiated, the expiratory valve E and valve V are closed and the patient receives the preset tidal volume. A separate fresh gas flow (F) is provided by the ventilator, which is collected in the reservoir bag R. The reservoir bag has a pop-off valve P to avoid excessive pressure in the bag resulting from continuous flow source. When the patient initiates spontaneous breath, the negative pressure in the circuit opens the valve V and allows the patient to breathe from the reservoir bag. The excessive flows that may be available in the breathing circuit during the patient's spontaneous inspiratory effort can escape from the expiratory valve E. In fact, exit of gases from the expiratory valve during the patient's spontaneous inspiration signifies adequacy of gas flows that are sufficient to meet the patient's inspiratory flow demands. The airway pressure tracings of IMV mode are shown in figure 15.4.

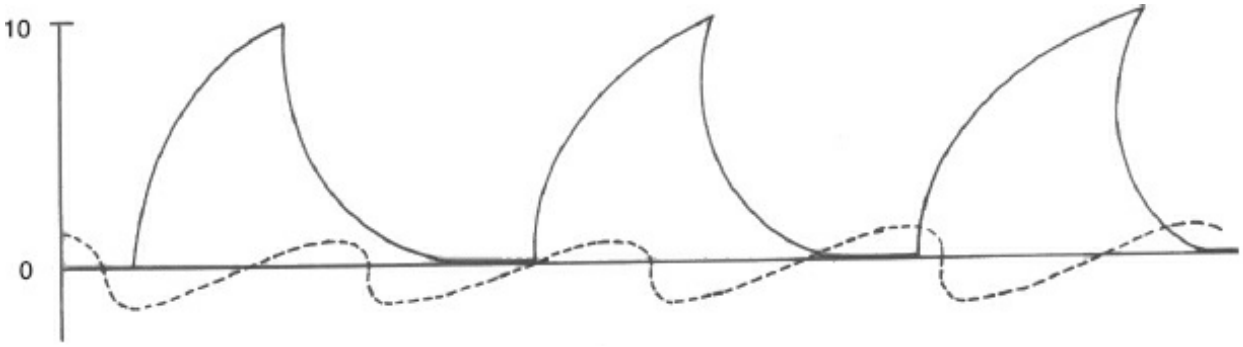

Figure 15.2a: Diagrammatic representation of the airway pressure tracings (em of water) of CMV mode (thick line). The dotted line represents what the patient's spontaneous respiration would have been without the ventilator breaths.

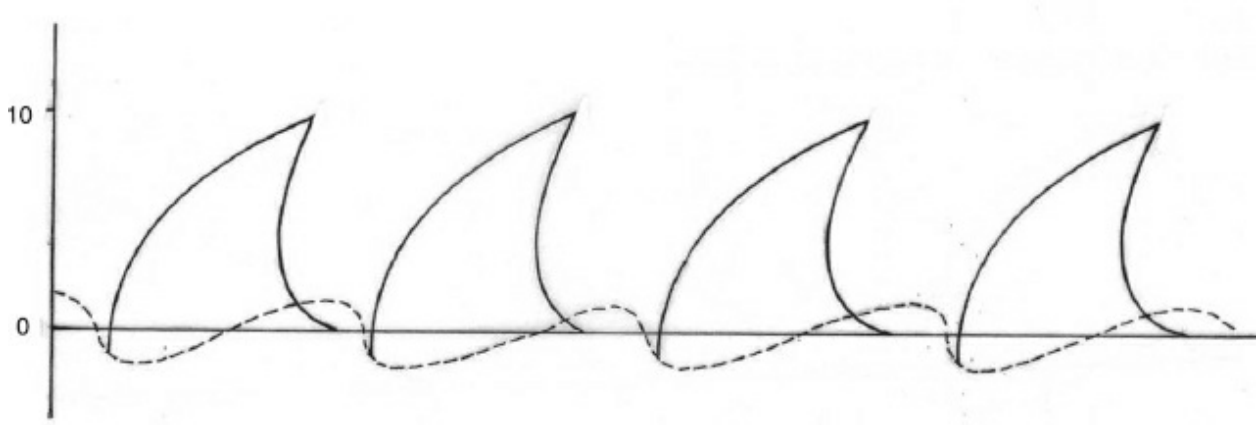

Figure 15.2b: Diagrammatic representation of the airway pressure tracings (cm of water) of assist control mode (thick line). Dotted line represents what the patient's spontaneous respiration would have been without the ventilator breath.

Synchronised intermittent mandatory ventilation

Synchronised intermittent mandatory ventilation (SIMV) allows spontaneous breathing with positive pressure cycles triggered by the patient's inspiratory effort. A demand flow system that provides a fresh gas flow for spontaneous breaths is incorporated. A pressure or flow sensing device located near the patient's airway detects a fall in baseline pressure or flow and activates either the positive pressure cycle or the demand flow device. The positive pressure breaths constitute the mandatory ventilation and can be set depending upon the sufficiency of patient's own respiratory effort (SIMV rate). It is customary to set the SIMV rate to meet the full ventilation of the patient when the spontaneous breathing of the patient is minimal. As the patient's own ventilation improves, the SIMV rate can be gradually decreased. This mode thus, can provide either a full or partial ventilatory support.

The patient acceptability is better than IMV as the ventilator breaths are synchronised to match the patient's spontaneous inspiration. There is a decreased need for sedation and less interference with cardiovascular function with this mode. However, in patients with cardiogenic shock and poor left ventricular (LV) reserve, partial ventilatory support may not be desirable as full ventilatory support maintains better LV function and improves peripheral perfusion.[18] The machine flow during patient's spontaneous inspiration must be sufficient to match the peak inspiratory flow rate of the patient. Patient has to work for his own breath which is not assisted. Therefore, faulty valves and malfunctioning machines can increase the work of breathing further and interfere with the weaning process. The

airway pressure tracings of SIMV mode are shown in figure 15.5.

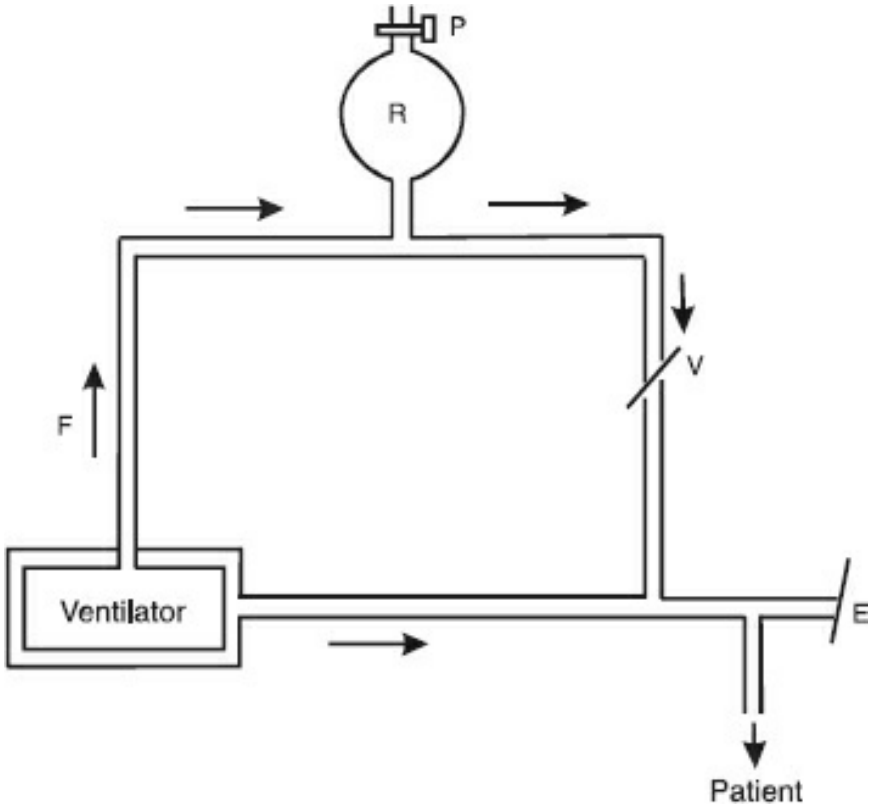

Figure 15.3: Schematic representation of IMV: F, fresh gas flow; R, reservoir bag; P, pop-off valve; V, one way valve; E, expiratory valve (for details refer to the text).

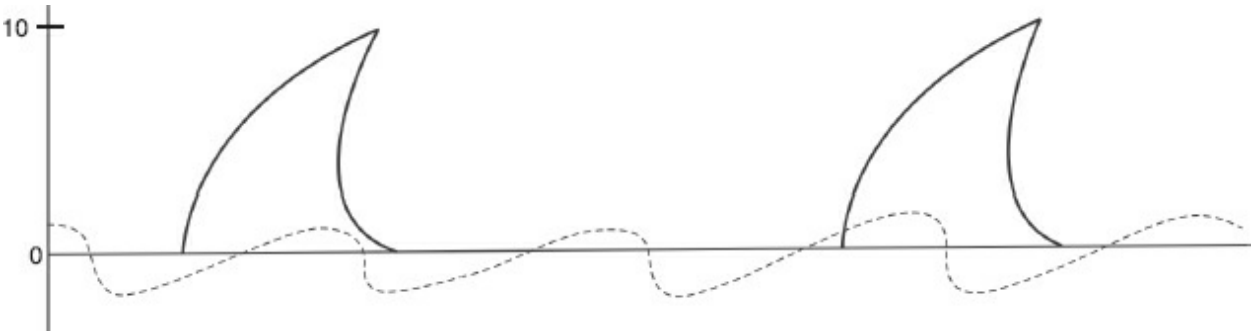

Figure 15.4: Diagrammatic representation of airway pressure tracings (cm of water) of IMV mode (thick line). The dotted line represents patient's spontaneous breaths. Note that cycling of ventilator breath is independent of spontaneous ventilation.

Pressure preset modes

In pressure preset modes, the pressure that is applied to the airway is chosen and the volume delivered to the patient is variable. By choosing the safe airway pressure, the disadvantages of excessive airway pressure (barotrauma)

are eliminated in these modes. However, volume delivery may vary depending upon the lung compliance and airway resistance. Extensive monitoring of the delivered gas volumes and alarm system should, therefore, be incorporated in the ventilator. These modes are either time cycled or flow cycled and either time initiated or pressure initiated.

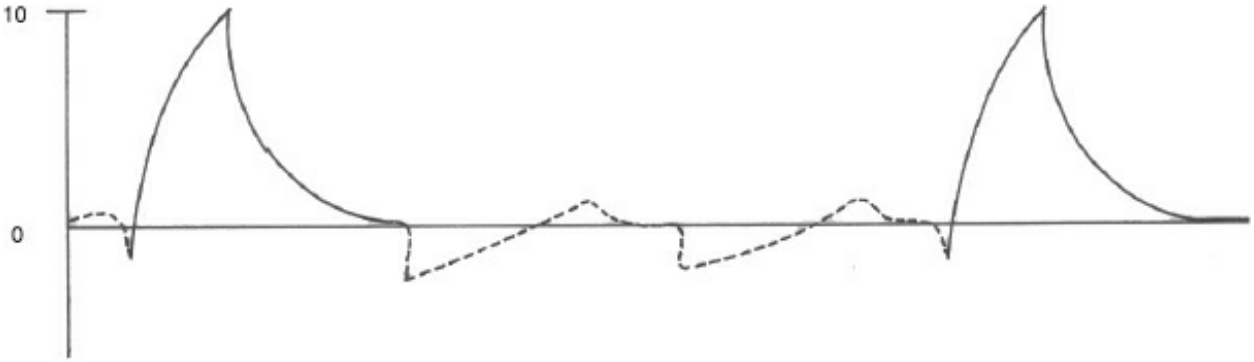

Figure 15.5: Diagrammatic representation of the airway pressure tracings (cm of water) of SIMV mode (thick lines). The dotted line represents patient's spontaneous breaths. Note that the ventilator breaths are synchronised to match patient's spontaneous inspiration.

Pressure support ventilation

In PSV mode, the ventilator provides a rapid flow of gas into the ventilator circuit until a predetermined pressure is achieved. This flow of gas is initiated when a negative pressure is generated near the proximal airway by the patient's spontaneous effort. Therefore, the patient's spontaneous effort must be present during this mode and the patient's breath is augmented with a variable amount of inspiratory positive pressure that can be selected by the operator. Thus, the patient's spontaneous respiratory efforts interact with the ventilator settings to determine the respiratory rate and the tidal volume. The airway pressure and the tidal volume tracings at 2 levels of pressure support (10 and 15 cm) are shown in figure 15.6.

A pressure support of more than 10 cm H_2O is considered an independent mode for positive pressure support. The level of pressure support should be set in such a way that the required tidal volume by the patient is delivered. As the patient's own spontaneous ventilation improves, the pressure support level can be gradually decreased. Subjective comfort by the patient, lower peak airway pressure and higher mean airway pressure during PSV as compared with SIMV have been observed.[22] It has also been shown to be a superior partial ventilatory support mode to IMV or SIMV.[23,24] The work of

breathing is likely to be decreased as every spontaneous breath is assisted as against SIMV/IMV, where the patient is allowed to perform unassisted breathing interspersed with full positive pressure breath. A positive pressure of 5 to 15 cm H_2O is usually superimposed. The facility of back-up ventilation should be available so that, if apnoea sets in, the patient is continued to be ventilated. Since, there is no control on the tidal volume (that can change with the change in patient's condition), constant monitoring and readjustment of pressure support may be necessary.

Pressure controlled ventilation

In pressure controlled mode also, the airway pressure is chosen by the operator but the breaths are initiated by the time and cycled off by the time. The desired inspiration-expiration (I:E) ratio can be obtained by setting the inspiratory and expiratory times. This mode is used with the intention of preventing barotrauma that may occur due to excessive airway pressure with volume controlled modes in patients with poor lung compliance. Conventionally, I:E ratio of 1:2 is used, as longer the expiratory time, lower is the mean airway pressure and less is the circulatory embarrassment. However, in patients with severe decreases in pulmonary compliance, inverse I:E ratios (longer inspiratory times) have shown to reduce the alveolar and airway dead spaces, improve oxygenation, decrease peak airway pressure and not adversely affect the cardiovascular function.[25-27] Spontaneous ventilation by the patient is not possible with this mode and patients must be sedated and neuromuscular blockade is usually required. Likewise, there is no control on the tidal volume and it depends upon the lung compliance and resistance. As the mode is generally used in patients with poor compliance, adequate tidal volume may not be delivered and patients can become hypercarbic. Some degree of hyper-carbia may have to be accepted with this mode (permissive hypercapnoea). The airway pressure tracings with this mode are shown in figure 15.7.

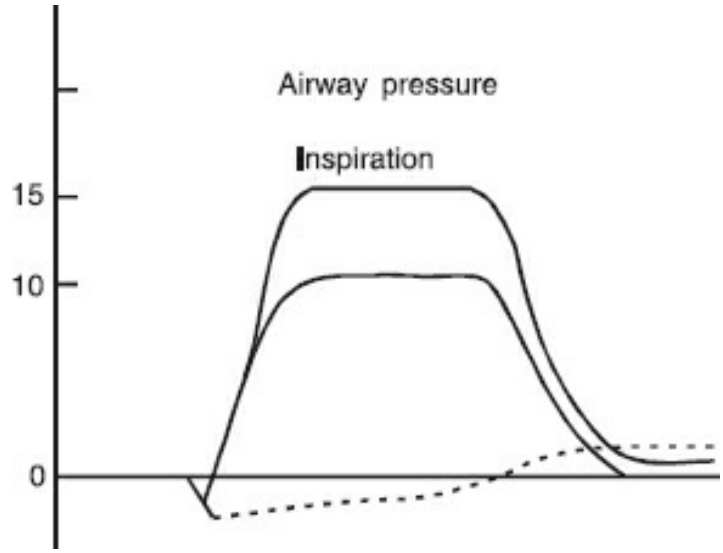

Figure 15.6a: Diagrammatic representation of the airway pressure tracings (thick lines) at 2 levels of pressure support (10 cm and 15 cm of water). Dotted line represents what the patient's spontaneous respiration would have been without the ventilator breath.

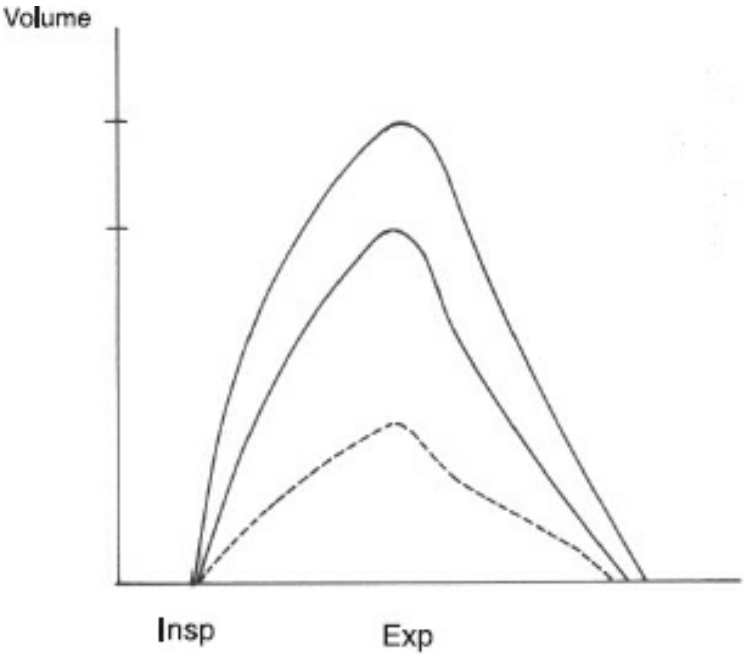

Figure 15.6b: Diagrammatic representation of the tidal volume (thick lines) at two levels of pressure support (10 cm and 15 cm of water), Dotted line represents what the patient's spontaneous respiration would have been without the ventilator breath.

Airway pressure release ventilation

In airway pressure release ventilation (APRV), CPAP is maintained by a continuous flow system and periodically the pressure is released by a release valve. The release valve is driven by a timing device that can be adjusted

appropriately to achieve the desired respiratory rate and I:E ratio. The closure of release valve initiates the inspiratory phase. The airway pressure during the inspiratory phase is determined by another solenoid valve that has a preset pressure which is greater than that during expiration. Opening of the release valve cycles the mechanism from inspiration to expiration by a rapid fall in the airway pressure allowing the gas to exit the lungs (Fig. 15.8). Carbon dioxide removal will depend upon the rate of the pressure release.

The lung volume at the end of inspiration is determined by the preset pressure and the lung compliance. The lung volume at the end of expiration will depend upon the pressure release time, the gradient between inspiratory and expiratory preset pressures, lung compliance and airway resistance. The patient can breathe spontaneously at all times so that both partial and full ventilatory support can be provided with this mode. Primarily, this mode is useful in patients with acute respiratory failure.[28] The airway pressure waveform during APRV is shown in figure 15.9.

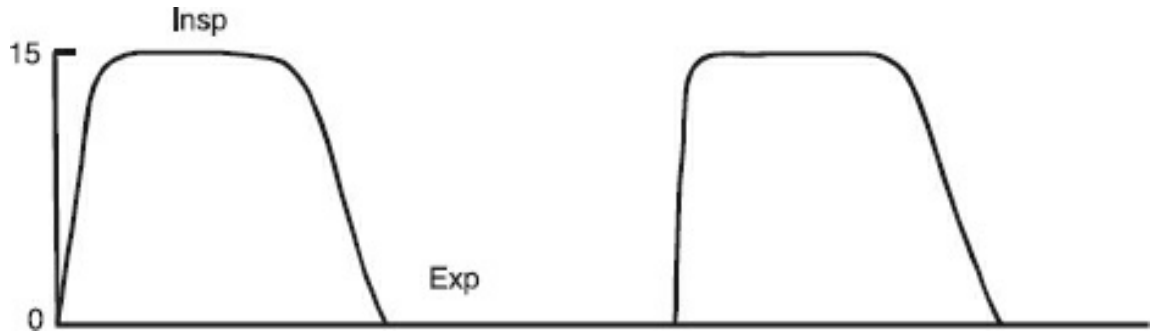

Figure 15.7: Diagrammatic representation of the airway pressure tracings of pressure controlled mode. Note that the inspiratory pressure is maintained at 15 cm of water (chosen by the operator) during inspiratory phase.

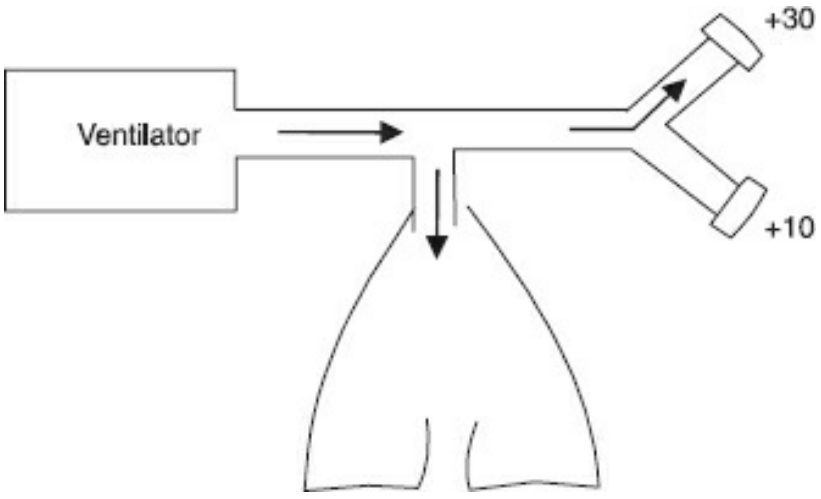

Figure 15.8a: Diagrammatic representation of airway pressure release ventilation. Continuous flow is generated by the ventilator which generates a pressure of 30 cm water as the threshold resistor is set at 30 cm. This determines the inspiratory pressure.

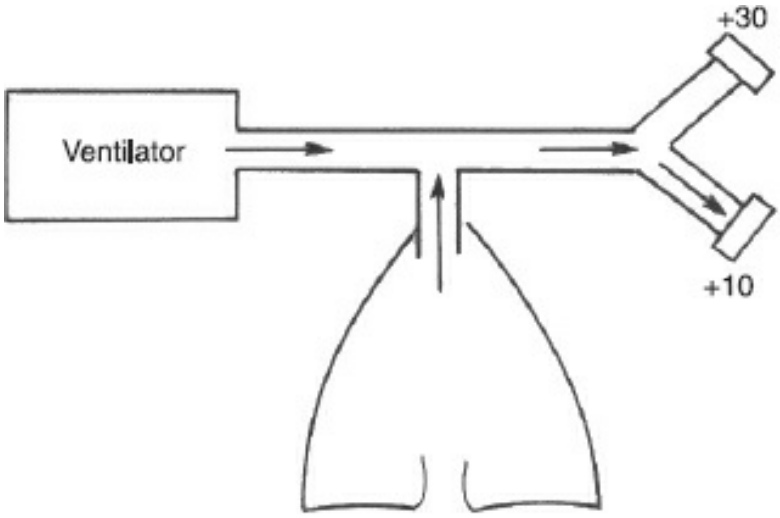

Figure 15.8b: The release valve set at 10 cm water is opened that decreases the pressure in the circuit allowing expiration.

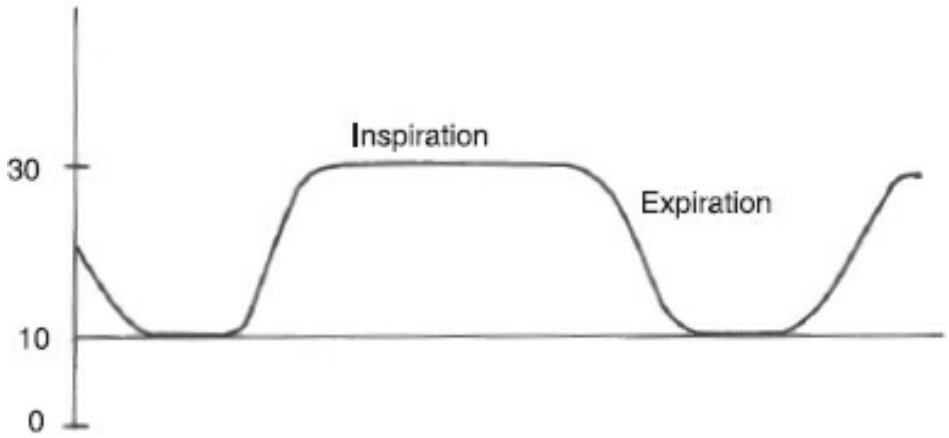

Figure 15.9: Diagrammatic representation of the airway pressure tracing (cm of water) of airway pressure release ventilation mode. Spontaneous breaths are possible during inspiratory as well as expiratory phase.

High frequency ventilation

In HFV, tidal volume less than the anatomical dead space at rates significantly greater than normal are provided. Three common types of HFV, depending upon the respiratory rate and the mode of delivery are available. These systems deliver almost a continuous pulsatile countercurrent flow with minimum respiratory excursions and little change in the mean intrathoracic pressure. This provides better gas distribution with no flow resistance and is

suited for patients with high airway resistance.

High frequency positive pressure ventilation

In this mode small tidal volumes are delivered at a rate of 60 to 110 per minute. An insufflation catheter or endotracheal tube is used for the delivery of gases.

High frequency jet ventilation

In this mode, the gas from a high pressure source (5 to 50 PSI) is delivered through a smallbore cannula that is interrupted by a cycling mechanism allowing high frequencies. Entrain-ment of gas occurs around the jet and augments the tidal volume. The rate varies between 100 to 400/min. The small-bore cannula can be placed within the endotracheal tube. Inadequate humidification is the major problem with this mode of ventilation. It has been used to improve oxygenation in a series of 5 patients with respiratory failure afer cardiac surgery without causing haemodynamic disturbances.[29] No large scale studies are aviailable, but it can be considered as one of the options in patients with respiratory failure.

High frequency oscillation

This mode delivers oscillations at the rate of 400 to 3000 or more. Oscillators have active expiration as an intrinsic part of their design so that hyperinflation of the lungs is less likely to occur as the gases are pulled out actively during the expiratory phase.[30]

There is no evidence supporting any distinct advantage of HFV over more traditional approaches. It is however, indicated in patients with massive air leak from fistulous tract when the conventional techniques have failed.[31] It has also been used during minimally invasive direct coronary artery bypass (MIDCAB) surgery, to prevent the lung from intruding the surgical field during the construction of the vascular anastomosis. In neonates and infants, high frequency oscillation ventilation has been shown to be associated with shorter lengths of mechanical ventilation and ICU stay as compared with conventional mechanical ventilation.[32] The main disadvantage of HFV is barotrauma. This may result due to stacking of breaths, as there is insufficient time and space for the escape of gas.

Positive end-expiratory pressure

Positive end expiratory pressure (PEEP) exists whenever the airway pressure

is greater than the baseline pressure (generally zero cm water) prior to the next inspiratory cycle. The generally accepted terminology refers to such a positive airway pressure as PEEP, if used in conjunction with mechanical ventilation and as continuous positive airway pressure (CPAP), if used in conjunction with spontaneous ventilation. The application of PEEP/CPAP leads to redistribution of extravascular water and increased functional residual capacity. This is the major mechanism by which the lung function is improved leading to an improvement in oxygenation. The commonly used level of PEEP/CPAP is 5 to 10 cm of water.

Newer modes of ventilation

Adaptive support ventilation (ASV) is a mode wherein, the minute volume is controlled by a closed-loop algorithm. The tidal volume and respiratory rate are automatically adjusted to minimise the work of breathing. The ventilator switches automatically from controlled ventilation to assisted ventilation and the ventilatory setting are selected according to the measured lung mechanics. It has been shown to be feasible and safe in non-fast-track CABG patients with weaning times equivalent to that of standard weaning with pressure controlled/pressure-support ventilation.[33]

Pressure regulated volume controlled mode (PRVC), is another mode that controls the minute ventilation at the required pressure. With the automode (PRVCa), it permits effective and safe weaning from the ventilator. In a comparison between ASV and PRVCa, it has been shown that ASV is associated with earlier extubation without an increase in clinician intervention in patients undergoing uncomplicated cardiac surgery.[34]

Noninvasive ventilation applied via a face mask or a nasal mask can be used following transcatheter aortic valve implantation in sick patients. It can also be considered as a treatment of acute respiratory failure following patient weaning from mechanical ventilation and tracheal extubation. In this setting, it has been shown to exert favourable effects on lung function preventing reintubation.[35] In a recent study performed on 799 patients with acute respiratory failure following tracheal extubation, it was shown that most patients tolerated noninvasive ventilation, with outcome similar to those who did not have acute respiratory failure.[36] The study suggests that noninvasive ventilation can be considered as a first-time ventilatory support in acute respiratory failure after cardiac surgery.

Haemodynamic effects of mechanical ventilation

The increased intrathoracic pressure during mechanical ventilation leads to decreased venous return. This is the primary mechanism responsible for reduction in CO during mechanical ventilation. Mechanical ventilation also relieves the work of breathing and reverses hypercapnoea, hypoxia and acidosis. Therefore, initiation of mechanical ventilation can cause hypotension secondary to a decrease in the sympathetic tone leading to relative hypovolaemia and decreased venous return to the right heart.

Intravenous fluid administration to expand the vascular space appropriately, is generally sufficient to restore the CO. However, if hypotension is severe, both the lower extremities of the patient can be elevated 20 to 30 degrees from the horizontal position.

The haemodynamic effects of mechanical ventilation can be more severe in patients who are receiving PEEP. Depending upon the degree of PEEP, the increase in pleural and pericardial pressure decreases the cardiac transmural pressure, which may significantly decrease the end-diastolic volume and stroke volume of both ventricles. In addition, the increased pulmonary vascular resistance due to increased mean airway pressure can lead to right ventricular dysfunction.

In a comparison of pressure controlled and volume controlled ventilation, it has been shown that patients ventilated with pressure controlled ventilation showed significantly higher values for cardiac index, a decreased systemic vascular resistance, as well as significantly lower values for inspiratory pressure when compared with patients ventilated with volume controlled ventilation.[37]

Care of the patient on a ventilator

In every cardiac ICU, an intubation tray must be available. The tray must be checked regularly and must contain an endotracheal tube with proper connection, catheter mount, a working laryngoscope, malleable stilettes, syringe for cuff inflation, Magill forceps and a face mask with angled piece.

When the patient arrives in the ICU, the ventilator is attached to the patient and an appropriate mode of ventilation is selected, (usually CMV or assist/control). Generally 40 percent oxygen mixed with air is administered with the aim of mamtaining the arterial oxygen tension (PaO_2) of 75 to 120

mm Hg. The arterial carbon dioxide tension ($PaCO_2$) should be maintained around 35 to 40 mm Hg. The humidifier must be switched on and the water level should be checked. The chest should be auscultated on both sides to check for air entry. Correct endotracheal tube positioning (1 to 2 cm above the carina) should always be confirmed on X-ray chest.

The chest of the patient must be left uncovered so that the chest movements can be easily observed. The chest should move regularly with the ventilator. It must be ensured that all tubing connections from the ventilator to the patient are firmly attached and there is no strain on the endotracheal tube and the catheter mount. The ventilator readings such as fractional inspired oxygen concentration (FiO_2), inflation pressure, respiratory rate, expired tidal volume, PEEP level, etc. should be noted down every 30 min.

Arterial blood gas measurements and endotracheal suction should be carried out every 4 hours and more frequently, if necessary. Many patients should be sufficiently stable, wide awake with good respiratory and cardiovascular parameters to come off the ventilator in 4 to 6 hours time. Some patients will need overnight ventilation.

Arterial blood gases

It is a general practice to measure the arterial blood gases of the patient in the cardiac ICU, whether he is mechanically ventilated or breathing on his own. This is done with the intention of assessing the adequacy of ventilation and the adequacy of tissue oxygenation. Since CO is an important constituent of tissue oxygenation, the blood gas measurements also provide an indirect estimation of the adequacy of CO.

pH

It describes the acid-base status of the blood (normal 7.35 to 7.45). A pH of less than 7.35 indicates that the patient is acidotic. The important causes of acidosis are: 1. inadequate ventilation that causes retention of carbon dioxide and is described as respiratory acidosis, and 2. inadequate CO that leads to decreased oxygenation of the tissues causing anaerobic metabolism and accumulation of lactate and is described as metabolic acidosis. If the pH is more than 7.45, the patient is alkalotic. The important causes of alkalosis are: 1. hyperventilation that washes out carbon dioxide causing a decrease in carbon dioxide content of blood and is described as respiratory alkalosis; 2. low serum potassium, and 3. administration of excessive bicarbonate to the

patient. These are the causes of abnormal pH that are commonly encountered in a cardiac surgical patient.

Base excess

It is defined as the deviation of the patient's bicarbonate (HCO_3^-) level from the normal (24 mEq/L), after the ventilation is adjusted to maintain the normal pH of 7.4. Since ventilation has been adjusted, base excess describes the abnormalities of acidity of the patient, which is related to other causes (most commonly metabolic). The normal base excess is 0 ± 2 mEq/L. When the base excess is more than –2 (e.g. –10, generally defined as base deficit), the patient is acidotic and in a cardiac patient, inadequate CO is the most common cause. When the base excess is more than +2 (e.g. +10), the patient is alkalotic and low serum potassium and excessive administration of bicarbonate are the common causes.

$PaCO_2$

Arterial carbon dioxide tension reflects the amount of carbon dioxide in the blood (normal 35 to 43 mm Hg). When the ventilation is inadequate, carbon dioxide elimination is hampered leading to an increase in $PaCO_2$ (> 43 mm Hg) and is labelled as hypercapnoea. This leads to respiratory acidosis. When the ventilation is excessive (as may happen with some ventilatory settings), the carbon dioxide is washed out leading to a decrease in $PaCO_2$ (< 35 mm Hg) and is labelled as hypocapnoea. This leads to respiratory alkalosis.

PaO_2

It reflects the amount of oxygen in the blood (normal 85 to 100 mmHg, when breathing air). APaO_2 of less than 85 mm Hg (when breathing air) denotes hypoxia, but such levels (PaO_2 as low as 60 mm Hg) are generally accepted in many cardiac ICUs, if the pH is maintained and the causes such as lung collapse, pneumothorax or pleural effusion are excluded. The hypoxia can also occur due to intracardiac shunts and low CO.

Table 15.2: Normal arterial blood gas results

pH	7.35 to 7.45
Base excess	-2 to +2

$PaCO_2$	35 to 43 mm Hg
PaO_2	85 to 100 mm Hg

Endotracheal suction

It is often considered by many that the endotracheal suction is a simple and safe procedure. However, it can be dangerous, as the patient is not being ventilated and the oxygen is being sucked out of the lungs. It may also introduce infection and damage the airway. In addition, inefficient suction may result in retention of secretions leading to blockage of the airways and the endotracheal tube. It is preferrable to do 'bagging' with oxygen before endotracheal suction. A bag and valve assembly (Mapleson C circuit) with oxygen flow should be attached to the patient and the lungs are inflated with moderately deep breaths using both hands to squeeze the bag gently. As an alternative, Ambu bag may be used. A sterile technique should be followed for endotracheal suction. The assistant should remove the cap from the endotracheal tube connection to help the operator insert the catheter in the tube. The catheter should be inserted beyond the full length of the endotracheal tube without applying suction. The suction is applied when the catheter is fully introduced and is slowly rotated and withdrawn from the endotracheal tube while the suction is applied. The catheter should not be pushed up and down repeatedly as this may cause abrasive injury to the tracheal mucosa. After the catheter is removed, the endotracheal tube connection cap is replaced and the lungs are again inflated with oxygen. The procedure can be repeated, if necessary after venmating the lungs with Mapleson C circuit for 20 to 30 seconds. The ventilator should be properly reconnected after the procedure, to re-establish adequate ventilation. Disconnection from the ventilation should not be longer than 20 seconds.

Weaning

The majority of patients can safely be extubated on the day of operation. A few patients benefit by overnight or extended artificial ventilation after cardiac surgery. The decision to allow the patient to breathe on his own is based on many criteria. In most cardiac centres this decision is based on simple clinical considerations, such as preoperative general and cardiac condition, major problems during anaesthesia/surgery and a satisfactory

postoperative course while being ventilated.

Many ventilatory modes can be used to initiate weaning process and the transition from the ventilator to the patient's own ventilation can be gradual. Although, the ventilatory modes such as IMV, SIMV, PSV, APRV etc. may be used for such a purpose, there is no conclusive evidence that one mode is better than another. In most centres, the patient is connected to a T-piece and allowed to breathe spontaneously for a sufficient time (usually 30 to 45 min.), before extubation is accomplished. The decision to connect the patient to a T-piece is based on the following simple clinical criteria:

- Stable blood pressure (even with modest inotropic support).
- Stable heart rate and rhythm.
- Respiratory function judged to be satisfactory by observing the respiratory excursions after the ventilation is disconnected and arterial blood gases.
- Respiratory rate < 30/min.
- Patient alert and cooperative.
- No recent heavy sedation.
- No gross neurological damage.

After a satisfactory T-piece trial (the above clinical parameters are maintained or improved), the extubation is accomplished. The head of the bed is raised and the patient is attached to the bag and valve assembly with an oxygen flow. Endotracheal suction is carried out, the mouth is sucked and the endotracheal tube is removed after deflating the cuff. The patient is then encouraged to cough out the remaining mucous. Forty percent oxygen via ventimask is administered. Arterial blood gases are checked after 15 min. to confirm the satisfactory ventilation.

The other standard criteria of extubation such as tidal volume exceeding 5 mL/Kg and vital capacity more than 10 mL/Kg are described, but are not commonly used in a cardiac ICU.

Fast-tracking

In this new era of cardiac surgery, the emphasis has been on the reduction of ICU stay (which is a major determinant of cost) after cardiac surgery. Due to the safety and cost effectiveness, "fast-track" protocols have become increasingly popular. With new advances in surgical and anaesthetic techniques, the goal is often to have patients extubated within 4 to 6 hours of

surgery, so that he is transferred to the postoperative ward and then discharged from the hospital, usually by the postoperative day 4. Although, early extubation was not unknown during the early days, in 1993, the attention was once again drawn to the fact that it is possible to extubate majority of patients within a few hours of cardiac surgery.[38] Some patients can be extubated at the end of surgery, but this practice is likely to prolong the operation theatre (OT) time. Therefore, the patient is transferred to the ICU as soon as possible and the postoperative care team manages the extubation.

The anaesthetic technique plays an important role in these patients. A vapour based technique with modest doses of opioids and benzodiazepines and propofol infusion are used. It is also essential to rewarm the patients adequately in the OT as hypothermia in the postoperative period may lead to shivering (increased oxygen consumption) and delay the extubation. This type of approach has been shown to be effective even in the elderly patients (> 70 years).[39]

Low-dose fentanyl combined with midazolam can be used for induction of anaesthesia, and propofol or inhalational agent can be administered for the maintenance of anaesthesia. Early extubation can be accomplished by using this technique. Using isoflurane based anaesthesia, early extubation was achieved in patients undergoing off-pump CABG.[40] Sufentanil can also be used successfully as a part of early extubation protocol.[41] Remifentanil is another opioid that has been effectively used for fast-tracking. However, postoperative pain management should be planned carefully as the effect of remifentanil is short-lived. Some authors have used spinal analgesia with low-dose morphine and cloni-dine[42] and others have used propofol[43] for this purpose when remifentanil was used. Thoracic epidural anaesthesia is yet another option that can permit significant reduction in the opioid doses and enabling early extubation. It also provides an excellent means of postoperative analgesia.

The ventilator management is guided by noninvasive monitors, end-tidal CO_2 and pulse oximetry. The noninvasive monitoring is combined with clinical observation and the majority of patients do not require arterial blood gas analysis (except the one that is performed on admission to the ICU). Once the patient is awake and making respiratory efforts, extubation can be accomplished after a brief trial of unassisted or partially assisted breathing.

Once extubated, patients who are doing well can be transferred to the ‘step down’ unit with minimal monitoring. A study where pulmonary function tests were performed has revealed that patients can be safely extubated early (within 1 hour) after major cardiac surgery without concerns of further pulmonary derangement.[44] Similar findings have been reported in patients who were extubated immediately after surgery versus those extubated early (within 8 hours) or late (after 8 hours).[45]

Some patients may require readmission to the ICU. Respiratory distress is the most common cause for readmission and this may necessitate reintubation. One study has reported that the incidence of readmission to ICU was 2.2 percent, and age > 65 years, peripheral arterial disease, and drainage > 500 mL were the risk factors in CABG patients, and preoperative congestive heart failure was the risk factor for valve surgery pateints.[46]

The safety and efficacy of the fast-track techniques have been demonstrated following a wide variety of cardiac surgery.[47,48] A recent study has evaluated hospital mortality, acute myocardial infarction, renal failure and stroke in a large number of patients subjected to fast-track protocol. It showed no evidence of increased risk of adverse outcomes in patients undergoing fast-track cardiac anaesthesia.[49] Over the years the fast-track cardiac anaesthesia has gained wider acceptance. It is even being practised in neonatal cardiac surgery.[50]

The anaesthesiologist has to actively participate in this approach and tailor the perioperative management to achieve early awakening and extubation.

Management of Sedation and Analgesia

As is obvious from the above discussion, most patients after open-heart surgery, require mechanical ventilation for some time. There is a trend towards early extubation, but some patients will need extended ventilation (may be overnight). Whichever approach is followed, patients will require pain relief during this period. Analgesics and sedatives that have a respiratory depressant effect can be preferred in patients requiring extended ventilation, but are obviously not the choice in those who are extubated early.

Profound respiratory depression is usually not required as ventilatory

modes such as assist/control, SIMV, and PSV are available in all the ventilators that allow patient's spontaneous breathing to continue. The requirement of sedatives and analgesics will be influenced by the anaesthetic method used. With the high-dose opioid technique, ventilation for many hours is expected and is also considered desirable. There is a less need for sedation and analgesia in these patients.

Patient's needs

The assessment of patient's needs for sedation and analgesia during mechanical ventilation is not simple. Several objective assessment methods such as changes in the haemodynamic parameters in response to stimuli (such as suctioning), plasma catecholamine levels, cerebral function analysis monitors and oesophageal motility studies, ECG R-R variability and bedside scoring system for the level of consciousness can be used. Amongst these, a conscious level scoring system assessed at the bedside is the most practical approach. The Ramsay sedation score[51] (Table 15.3) can easily be used and charted on a regular basis.

Bispectral index (BIS) can also be used to monitor sedation. A target BIS value of 70 can be maintained for adequate sedation. It has been shown that BIS is a better means of predicting oversedation[52], and it is easier to maintain the target BIS value by using a closed loop anaesthesia delivery system rather than manual adjustments of propofol infusion.[53]

Table 15.3: Ramsay sedation score

1. Anxious and agitated
2. Cooperative, tranquil, oriented
3. Responds to commands only
4. Asleep: brisk response to stimulus
5. Asleep: sluggish response to stimulus
6. No response

The patient should be maintained in stage 2 or 3 of this system by giving low dose boluses or modifying the infusion rate of short acting drugs. For long-term ventilation, minimal sedation should be used so that the patient is oriented, comfortable and cooperative, but with additional sedation at night to assist with sleeping.

Drugs

There are many sedatives and analgesics available. The use of muscle relaxants has diminished a great deal, but they still have a place in some clinical situations. Ideally, the drugs should be safe and have a predictable effect with minimal side effects. In particular, the cardiovascular effects should be minimal. It is also desirable that the drugs should not have prolonged respiratory depressant effect, especially if early extubation is planned.

In general, a balanced regime of sedation and analgesia is useful and when overnight ventilation is used, an analgesic infusion, supplemented with bolus doses or an infusion of a sedative provide stability and control (table 15.4).

Table 15.4: Drug infusions

Modest adult dose (60 to 70 Kg)

	mg in 50 mL	***rate per hour***
Morphine	50	1 to 2 mg
Fentanyl	2.5	50 to 100 µg
Midazolam	50	1 to 2 mg
Propofol	500	50 to 100 mg
Vecuronium	50	2 to 4 mg

Additional bolus doses of analgesics may still be necessary for some painful procedures.

Morphine and Papaveretum

These have been traditionally used in intensive care units in patients requiring mechanical ventilation. However, due to their prolonged effect, weaning from the ventilator can be delayed. This of course, does not matter in those patients in whom an extended period of ventilation is planned. The reticuloendothelial system may be depressed with large doses of morphine so that the patient may become more susceptible to infection.[54] In general, when infusions are given for a prolonged period, the rate should be reduced periodically to

ensure that accumulation has not occurred or that the dose required has not become less (as happens when the severity of illness increases). Morphine can be administered as intermittent bolus doses of 3 to 5 mg. When used as an infusion, a rate of 1 to 2 mg/hour is used for an average adult. The nurse administered subcutaneous morphine has been shown to be a satisfactory method of pain relief and has been found to be comparable to patient controlled analgesia (PCA) with morphine.[55] However, PCA significantly decreases pulmonary atelectasis when compared with nurse controlled analgesia.[56] Morphine has been administered as PCA alone or in combination with a background infusion of morphine. However, it has been shown that PCA with morphine effectively controlled postoperative pain after cardiac surgery and the addition of background infusion of morphine did not enhance analgesia and increased morphine consumption.[57]

Morphine administered as intermittent boluses can be used along with propofol infusion. When used intrathecally as a part of anaesthesia protocol, it reduces the postoperative pain scores, increases time to first intravenous morphine dose and reduces the overall postoperative morphine dose requirement.[58]

Fentanyl

Fentanyl is commonly used as an infusion. A typical infusion can be started at the rate of 2 μg/Kg/hour along with intermittent bolus doses of midazolam. It may be administered at a lower infusion rates (0.5 μg/Kg/hour), if combined with propofol infusion. It can also be administered as PCA. It has been found to be useful, especially in infants[59] and babies with postoperative labile pulmonary hypertension.[60]

Remifentanil

Remifentanil is being used increasingly for fast-tracking and is administered during surgery. Postoperative analgesia in these patients is provided by some alternative techniques such as thoracic epidural, propofol or other opioids. Remifentanil can also be used exclusively to provide postoperative analgesia. In one study, it was used as a part of PCA protocol; infusion 0.5 μg/Kg/min, bolus, 0.25 μg/Kg; and lockout time 5 min. Using this protocol, it was shown to provide better pain relief during coughing and on movement as comapred with morphine.[61]

Opioid-induced hyperalgesia has been reported with all opioids, especially in the elderly patients. This may lead to paradoxical increase in the opioid consumption. This aspect has been studied with high-dose remifentanil used during CABG surgery and it was shown that three-hour remifentanil infusion during surgery did not increase postoperative pain or opioid consumption.[62]

Ketamine

Ketamine is not a popular agent for providing sedation and analgesia because, it stimulates the cardiovascular system and can cause hallucinations and confusion.

Nonsteroidal anti-inflammatory agents

These agents have a supplemental role in providing postoperative analgesia. They can also be useful due to their antiplatelet effects in patients undergoing CABG. However, clinical data in support of their use is lacking. They have not been a popular choice due to their adverse effects on blood coagulation.[63,64] Also, they are known to have renal toxicity. One report has described the use of indomethacin (100 mg) suppositories 2 to 3 hours postoperatively and 12 hours later in combination with PCA morphine.[65] The results showed reduced postoperative pain scores and opioid use without an increase in side effects. Likewise, rectal diclofenac suppository has been shown to provide adequate pain relief and decrease the tramadol requirement.[66] Indomethacin along with acetaminophen has been shown to be a well tolerated pain management approach that is cost-effective, simple and feasible to use.[67] Nevertheless, this method is not widely accepted and at best, can be considered an adjunctive therapy to reduce opioid consumption and opioid-induced respiratory depression. A detailed dicussion on the subject can be found in the pro and con section of the Journal of Cardiothoracic and vascular anesthesia.[64,68]

Gabapentin and Pregabalin

Gabapentin in a single oral dose of 600 mg 2 hours before operation[69] and pregabalin, 150 mg before operation and 75 mg twice daily for 5 days postoperatively[70] have been shown to decrease the postoperative opioid consumption with good pain relief. However, the time to extubation is increased.

Volatile anaesthetic agents

These have been proposed as a convenient and flexible means of managing patients on mechanical ventilation. Halothane due to its association with hepatic dysfunction and enflurane for the fear of adverse renal effects, is not considered, but isoflurane in a concentration of 0.1 to 0.5 percent has been described.[71,72] It is however, expensive and a scavenging system is needed. There may also be a concern regarding coronary steal, should there be hypotension in the presence of incomplete revascularisation.

The sedative agents

Benzodiazepines

Diazepam has a longer duration of action and may cause hypotension in the presence of opioids. It can be used in a bolus dose of 2.5 to 5 mg as a supplement to analgesics at night to assist with sleeping, if extended ventilation is planned. Midazolam that has a short elimination half-life has superseded diazepam. However, its effects may be prolonged, like other sedatives and analgesics[73] in the ICU. More commonly, it is used with fentanyl in the form of intermittent boluses (0.025 to 0.05 mg/Kg).

Anaesthetic induction agents

Induction agents such as thiopental, etomidate and althesin have been used. Thiopental in large doses is used in an attempt to diminish the cerebral morbidity associated with open-heart surgery.[74] However, prolonged recovery time does not make it an ideal agent when early extubation is planned. Etomidate causes adrenocortical suppression[75] and althesin has been withdrawn due to sensitivity reaction to its solvent, cremophor EL.[76]

Propofol

Propofol infusion is an excellent method of short term postoperative sedation that provides easy flexibility and rapid recovery. When overnight ventilation is planned, propofol would not seem to be an obvious choice. It can be infused at the rate of 50 mg/hour for an average adult. The rate can be increased by 20 to 50 mg/hour to achieve the desired level of sedation. Like all intravenous anaesthetics, it reduces systemic vascular resistance.[77] The possible adverse effects include bradycardia[78] and heart block.[79] In addition, anaphylactoid reactions can occur,[80,81] and if used with opioids, more

prolonged effects may be observed.[82]

Propofol is widely used to provide sedation in the postoperative period, especially as a part of fast-track protocol. An infusion beginning at a dose of 25 μg/Kg/min. can be initiated. A closed loop anaesthesia delivery system may be used to titrate the doses, but manual adjustment is more commonly employed. Intermittent morphine boluses or a low-dose fentanyl infusion (0.5 μg/Kg/hour) can be combined to provide analgesia. A reduction in the times to extubation can be achieved with propofol as compared with fentanyl infusion in patients with low cardiae risk.[83]

Dexmedetomidine

Dexmedetomidine has been used to provide sedation in the postoperative period. A dose ranging from 0.1 to 0.7 μg/Kg/hour can be used. It has been shown to provide effective analgesia and sedation, less hypotension, less vasopressor requirement, and more bradycardia in comparison to morphine.[84] In a comparison with propofol, dexmedetomidine has been shown to have lower opioid requirement, but no difference in the duration of mechanical ventilation.[85] Further studies are required to define the role of dexmedetomidine in cardiac surgery.

Regional analgesia

Epidural analgesia

Thoracic epidural analgesia with general anaesthesia is another form of anaesthetic technique that can be employed. In the current era of early tracheal extubation, where opioids are used sparingly, providing optimal pain relief after surgery can be challenging. Over the past decade, application of epidural techniques has incresed.[86] The potential benefits include good analgesia, attenuation of stress response, optimal redistribution of coronary blood flow, haemodynamic stability, improved pulmonary function and early extubation. The epidural catheter is placed on the day of surgery in the OT before induction of anaesthesia. It is used for providing analgesia in the intraoperative as well as postoperative period. Both opioids and local anaesthetics can be used for this purpose.

The thoracic epidural anaesthesia has been compared with the conventional morphine PCA. It was found that not only thoracic epidural anaesthesia

allowed earlier weaning from mechanical ventilation but also provided more effective pain relief.[87] The better pain relief provided by thoracic epidural may improve the ability to cough.[88]

There are many other reports that have demonstrated the efficacy of the thoracic epidural anasthesia. However, most of the reports are uncontrolled (not randomised). A recent largest randomised trial (654 patients) was unable to demonstrate clinically relevant benefit of thoracic epidural on the frequency of major complications after elective cardiac surgery compared with fast-track cardiac anaesthesia without epidural anaesthesia.[89] The technique is not without risks. The most dreaded complication of the thoracic epidural analgesia is epidural haematoma. The reader is referred to chapter 6 for the detailed discussion on the subject.

Lumbar epidural route can also be used for pain relief. A study has shown that buprenorphine administered via lumbar epidural route provided similar quality of analgesia as compared to the thoracic epidural route, without increasing the incidence of side effects.[90] Since, lumbar epidural is technically easier, it is a good option for providing postoperative pain relief. Mild sternotomy wound pain may persist two or more months after surgery, but generally does not interfere with daily living. The type of postoperative pain relief (thoracic epidural and intravenous or oral opiates) has not been shown to effect this type of persistent pain.[91]

Intrapleural analgesia

Intrapleural analgesia for patients undergoing thoracotomy has produced controversial results. However, its use has been described in cardiac surgery in patients undergoing MIDCAB surgery.[92] The authors have shown that intrapleural injection of 20 mL of 0.25 percent bupivacaine followed by clamping of chest drainage tubes for 20 min. offered superior analgesia as compared with thoracic epidural analgesia.

In another report, efficacy of bilateral intrapleural block with bupivacaine in patients undergoing CABG has been demonstrated.[93]

Intrathecal Morphine

Intrathecal morphine is used with the objective of providing long-lasting postoperative analgesia. A single bolus dose (5 to 10 µg/Kg) of preservative-free morphine is administered intrathecally before the induction of general

anaesthesia. In one study a dose of 7 μg/Kg of morphine was administered intrathecally and the results showed effective analgesia, earlier tracheal extubation and less ICU length of stay after on-pump CABG.[94] Intrathecal morphine is considered an alternative method of analgesia that leads to reduced morphine requirement in the postoperative period.[58] A close observation of patients is required due to high incidence of respiratory depression.[95]

Other Methods

These include continuous thoracic paravertebral block,[96] and local anaesthetic infiltration of the sternotomy wound and the mediastinal tube sites.[97] The paravertebral block may prove to be a good alternative for thoracic epidural anaesthesia as the risk of epidural haemotoma is obviated. These techniques can help to decrease the requirement of opioids in the postoperative period.

In summary, intraoperative and postoperatively administered opioids are widely practiced and still remain the mainstay of therapy. However, regional techniques can reduce opioid consumption and opioid-induced respiratory depression. Some other analgesics such as nonsteroidal anti-inflammatory drugs and tramadol can also help to reduce opioid requirement.

Cardiovascular Management

The cardiovascular system may be labile in the immediate postoperative period and the maintenance of satisfactory haemodynamic parameters is the obvious goal.

Postoperative hypertension

The provision of good sedation and pain relief after cardiac surgery is an important contributing factor towards control of the postoperative hypertension.

The phenomenon of postoperative hypertension is well documented.[98,99] A large population presenting for cardiac surgery has preexisting hypertension that increases the likelihood of postoperative hypertension in them. The undesirable effects of hypertension include bleeding from the suture lines, aortic dissection, intracranial haemorrhage and an increase in the myocardial

oxygen demand. The level of blood pressure that should be regarded as hypertension in the immediate postoperative period is not well defined. In the early 1970s, pressures of 100 mm Hg diastolic[99] or 160 mm Hg systolic[100] were considered as a cause for treatment. Subsequently, even lower pressures (mean arterial pressure > 90 mm Hg)[101] have been regarded as requiring treatment and this level varies from place to place. In this context, it should be remembered that the radial artery pressure (that is commonly measured) may not represent central aortic pressure soon after CPB.[102]

In patients who have undergone CABG, the blood pressure is lowered with the objective of reducing myocardial oxygen demand, although, the ischaemic episodes may be unrelated to the haemodynamic changes.[102-105] Perhaps, an increase in the coronary perfusion pressure compensates for an increased demand. Attention should also be paid to the myocardial oxygen supply in the postoperative period. The diastolic pressure should not be unduly lowered. The perfusion pressure may also be relevant in mamtaining graft patency and ultimate graft survival. Some centres, therefore, are inclined to accept pressures up to 160/90 mm Hg. Although, the potential morbidity of hypertension is well recognised, there are no established guidelines for its treatment and the practice varies significantly.[106]

Causes

Pain, anxiety and cold are important causes of postoperative hypertension. In addition, the discomfort of chest drains, endotracheal and nasogastric tubes, a full bladder and a urethral catheter may all contribute. The stress response, with raised levels of catecholamines, antidiuretic hormone and renin angiotensin system that occurs after surgery can also be the cause of hypertension.

Methods of treatment

Several methods and management strategies have been described for the treatment of hypertension. Although, the need to treat the hypertension is recognised, it has been reported that careful intraoperative control of haemodynamics did not prevent perioperative myocardial infarction.[107]

Sodium nitroprusside

Sodium nitroprusside is a predominant arteriolar dilator and produces decrease in the blood pressure. Although, it is effective in the dose of 0.5 to 2

μg/Kg/min., it is known to produce rebound hypertension when the infusion rate is reduced or stopped.

It has been a drug of choice for the treatment of hypertension in the postoperative period. However, with the availability of newer alternative vasodilators, it is no longer so. The disadvantages of sodium nitroprusside are its potential to cause cyanide or thiocyanate toxicity, and also coronary steal phenomenon due to coronary arteriolar dilatation. In addition, it produces significant vasodilatation and reflex, tachycardia. At times, it may be difficult to titrate it resulting in unwanted hypotension or hypertension.

Nitroglycerin

Nitroglycerin (NTG) is primarily a venodilator and is not always effective in lowering the blood pressure. However, it has been popular in patients undergoing CABG, as it is useful in the treatment of ischaemia with or without hypertension. It is used as an infusion, generally in the dose of 0.5 to 2 μg/Kg/min. However, there is no evidence that its prophylactic use influences the incidence of perioperative myocardial infarction.[108]

It should be remembered that infusions of NTG and sodium nitroprusside may increase the ventilation perfusion mismatch leading to decrease in arterial oxygenation. It has been shown that substituting labetelol for NTG and sodium nitroprusside improves arterial oxygenation and venous admixture in hypertensive post-cardiac surgical patients who require high FiO_2.[109] Such a change in therapy may allow patients to be weaned from mechanical ventilation sooner.

Calcium antagonists

Calcium antagonists such as diltiazem and nicardipine have proved to be adequate alternatives to sodium nitroprusside and NTG.[110,111] They have been found to be effective in the treatment of hypertension. Diltiazem is useful, particularly in patients in whom arterial conduits have been used for myocardial revascularisation. Intravenous nifedipine has also been shown to be an effective agent for the treatment of postoperative hypertension and is a good alternative.[101]

Clevidipine: is a new dihydropyridine calcium channel blocker, which causes selective arterial vasodilatation without effect on the venous circulation. In addition, it is a potent coronary vasodilator so that reduction in MAP does not impair coronary perfusion. It has an ultrashort duration of

action with a half-life of approximately 1 to 2 min. after intravenous administration. The rapid onset and offset of action make it particularly useful to provide precise and rapid control of blood pressure. It is administered at an infusion rate of 0.4 µg/Kg/min. and can be titrated up to a dose of 3.2 µg/Kg/min. depending upon the patient response. Higher doses (up to 8 µg/Kg/min.) have also been used. Clevidipine has been shown to be more effective in mamtaining the blood pressure within the prespecified range as compared with NTG, sodium nitroprusside, or nicardipine.[112] Thus, clevidipine can be considered a safe and effective treatment for acute hypertension and may be a replacement for sodium nitroprusside.

Beta-blockers

In a situation where tachycardia and hypertension coexist (hyperdynamic state), beta-blockers would seem to be an ideal choice. Labetelol, propranolol, metoprolol and atenolol have all been used effectively. The more recently introduced short acting cardioselective agent esmolol has also been used successfully. A meta-analysis has revealed that esmolol reduces the incidence of myocardial ischaemia, but an increase in bradycardia also occurs.[113] However, the administration of metoprolol and atenolol in incremental doses of 0.5 to 1 mg is widely practised for the treatment of hyperdynamic state.

Postoperative myocardial ischaemia

Improvements in the preoperative care have led to older and sicker patients being subjected to CABG. Postoperative myocardial ischaemia is more likely to occur in these patients. In addition, postoperative conditions such as tachycardia, anaemia, hypothermia, shivering and less than optimal analgesia can be contributory factors. The postoperative myocardial ischaemia confers increased risk and it is believed that patients with documented severe postoperative myocardial ischaemia should be referred to a cardiologist.[114]

Detection of myocardial ischaemia

Patients are most likely to manifest myocardial ischaemia in the immediate postoperative period, usually within 48 hours of surgery. As the ischaemic episodes are usually silent, frequent ECG monitoring may be useful. A 12 lead ECG should be obtained every eight to twelve hours during the night of surgery and then daily for the next 2 to 3 days. Transoesophageal

echocardiography can be useful by detecting regional wall motion abnormalities, but it cannot be performed continuously.

Prophylaxis and treatment

Antianginal drugs

Beta adrenergic blockers due to their ability to suppress tachycardia appear most efficacious in preventing myocardial ischaemia.[105] Diltiazem[115] and NTG[116] infusions have been used to decrease intraoperative ischaemia in patients with coronary artery disease and can be continued in the postoperative period.

High-dose narcotics

Narcotics during surgery contribute to adequate pain relief and stable haemodynamics in the postoperative period. It has been shown that postoperative infusion of sufentanil 1 μg/Kg/hour reduces the myocardial ischaemia following CABG.[117] This approach, however, necessitates prolonged ventilation. Although, other narcotics can be useful for adequate pain relief, their value in maintaining stable haemodynamics and decreased myocardial ischaemia is unknown.

Thoracic epidural analgesia

This has already been discussed and it is expected that it might reduce perioperative myocardial ischaemia. However, evidence of benefits in the cardiac outcome is not available.[118,119]

Other issues

Anaemia can lead to decreased oxygen content and has been shown to increase the incidence of postoperative myocardial ischaemia.[120] The lower acceptable limit of haematocrit is generally taken as 25 percent after surgery, but in the high-risk patients and in those who demonstrate myocardial ischaemia, a higher level of haematocrit (30 percent) is desirable.

Hypothermia has also been shown to be associated with postoperative myocardial ischaemia.[121] Therefore, adequate warming measures and heat conservation methods should be used during postoperative period.

Conclusion

The responsibilities of the anaesthesiologist are not limited to the cardiac operating room. He is actively involved in the postoperative management of these patients. Anaesthesiologists are well suited to provide postoperative care because the respiratory and cardiovascular management are an extension of the operation theatre management. Intensive respiratory management of the patients is his primary concern but is now required to face a peculiar challenge of providing adequate sedation, analgesia and haemodynamic stability, without prolonging recovery time. There are many ways of achieving this goal and the practice varies from place to place. However, only outcome studies of mortality and morbidity together with studies of patient comfort and satisfaction can resolve the issue. Some patients will need extended respiratory support and pose an additional challenge to his capabilities. This has been due to the fact that the patients previously considered “too sick” for surgery are also subjected to surgery. However, future improvements are bound to take place and with better understanding, our management strategies are also likely to improve.

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Chapter 16: Anaesthesia for Cardiac Patient Undergoing Noncardiac Surgery

Patients with cardiac disease presenting for noncardiac surgery pose considerable challenge to the anaesthesiologist They are prone to develop serious perioperative complications such as myocardial infarction (MI), arrhythmias and pulmonary insufficiency which can result in significant morbidity following surgery. It is generally agreed that the number of patients with cardiac disease undergoing noncardiac surgery is on the increase. This may be due to the fact that percentage of older patients presenting for surgery is increasing. With improvement in the cardiac surgical results, a large number of patients who have undergone corrective cardiac surgery are also subjected to noncardiac surgery. These patients, of course, are easier to manage as their cardiac pathophysiology has been restored to normal or at least near normal. However, they might need alterations in their medication such as anticoagulant therapy. The management of patients who have cardiac disease should be based on the following principles.

1. If the surgery is elective or less urgent and the cardiac disease is of such a magnitude that surgical correction is indicated, then it is preferable to perform the cardiac surgery [or some relevant interventional procedure such as percutaneous transluminal coronary angioplasty (PTCA) for coronary artery disease (CAD) or balloon mitral valvotomy (BMV) for mitral stenosis (MS)] before noncardiac surgery is attempted. Nowadays, performing a combined cardiac and noncardiac surgical procedure [e.g. valve replacement and cholecytectomy or coronary artery bypass grafting (CABG) and aorto-femoral bypass] is also a consideration. Alternatively, if the cardiac disease

does not warrant surgical correction, then the medical management should be optimised before subjecting the patient to noncardiac surgery.

2. If the surgery is of emergent nature and does not allow sufficient time for the treatment of cardiac lesion, then surgery should be undertaken with a high or intermediate risk. This stratification should be decided after preoperative evaluation. However, attempt should be made to optimise the cardiac condition by medical management (such as diuretics, inotropes, dilators) or mechanical support [such as intraaortic balloon pump (IABP) counterpulsation], before and during noncardiac surgery.

Whatever maybe the situation, the anaesthesiologist must be familiar with the pathophysiology of the cardiac lesion, the cardiac effects of anaesthetic drugs, the risk indices of cardiac lesions and the management strategies of cardiac lesion. This helps to make an accurate assessment of the patient and offer the optimum anaesthetic management that minimises the perioperative cardiac morbidity. He should also be aware of the possible interactions between the cardiac lesion and the disease for which noncardiac surgery is undertaken (e.g. thyroid surgery in MS).

The pathophysiology of various lesions and the pharmacology of the anaesthetic agents have already been described in their respective chapters. This chapter, therefore, briefly summarises cardiac pathophysiology and preoperative preparation, and sets about achieving the anaesthetic goals.

Coronary Artery Disease

CAD is a very common cardiac disease and many patients are subjected to noncardiac surgery. CAD represents a significant cause of perioperative morbidity and mortality. A careful preoperative evaluation of clinical risks and appropriate application of risk reducing strategies are necessary to improve postoperative outcome. Traditionally during preoperative evaluation, anaes-thesiologists have attempted to have complete understanding of the patient’s cardiovascular status. The information so obtained is expected to modify preoperative medical interventions as well as anaesthetic technique including aggressive treatment of haemodynamic disturbances during surgery. Sometimes, patients may be subjected to coronary revascularisation before the noncardiac surgery is undertaken. One earlier study has suggested that patients who have undergone CABG have a low risk of subsequent

noncardiac surgery.[1] Amore recent meta-analysis has failed to demonstrate any beneficial effect of prophylactic coronary revascularisation in patient with stable CAD before high-risk noncardiac surgery.[2]

However, patients undergoing emergency noncardiac surgery soon after CABG, may still be vulnerable to ischaemic myocardial events.[3] A study has demonstrated that the incidence of myocardial ischaemia is increased when sternectomy for mediastinitis is performed within one week of CABG and this ischaemia is associated with 25 percent incidence of MI.[3] Prior PTCA is also expected to improve the outcome following noncardiac surgery. It was shown that the overall mortality and infarction rate after noncardiac surgery was reduced significantly soon after PTCA (within 11 days).[4] Similar results were not observed after bare metal stent (BMS) placement. A study assessed the clinical course of patients who underwent PTCA with BMS placement six weeks before noncardiac surgery.[5] It was shown that all deaths and Mis occurred in patients subjected to surgery fewer than 14 days from stenting. It was concluded that elective noncardiac surgery should be postponed for two to four weeks after coronary stenting to permit completion of mandatory antiplatelet regimen, thereby reducing the risk of stent thrombosis and bleeding complications. The drug eluting stent (DES) implantation requires delaying the elective surgery further up to 1 year, as the dual antiplatelet therapy (clopidogrel and aspirin) should be continued up to one year to allow completion of the endothelialisation process. This aspect is described later on in the following pages.

Some other factors such as age and physical well being should be considered before subjecting the patient to CABG, e.g. a 75 or 80 year old diabetic patient with significant comorbid disease may not benefit much by undergoing coronary revascularisation (unless he has unstable angina). On the contrary, a 50 year old man with CAD, is likely to derive significant benefit from preoperative cardiovascular investigations and coronary revascularisation. In general pharmacological therapy should be preferred over coronary revascularisation for the reduction of major adverse perioperative cardiac events following noncardiac surgery.

Preoperative Evaluation

Preoperative evaluation is performed not simply to give medical clearance, but should include evaluation of the patient’s current medical status as well

as the recommendations concerning the management and risk of cardiac problems over the entire perioperative period. The anaesthesiologist may recommend changes in medication, suggest preoperative tests or procedures, or propose higher levels of care postoperatively. In order to assist physicians with decision making, clinical guidelines are developed. The clinical guidelines are aimed at improving patient care by providing recommendations about care to be provided in specific circumstances. The American College of Cardiology (ACC) and the American Heart Association (AHA) have formulated guidelines regarding management of cardiac patient undergoing noncardiac surgery. The latest guidelines have been published in 2007 and the following discussion is based on these guidelines.[6] Preoperative tests are recommended only if the information obtained will result in a change in the surgical procedure performed, a change in medical therapy or monitoring during or after surgery, or a postponement of surgery until the cardiac condition can be corrected or stabilised. The current medical status should be assessed on the basis of the presence or absence of the following active cardiac conditions.

- Unstable coronary syndromes

    - Unstable or severe angina
    - Recent MI

- Decompensated congestive heart failure (CHF).
- Significant arrhythmias
- Severe valvular disease.

The intermediate clinical predictors [included in the earlier (2002) recommendations] have been replaced with clinical risk factors with the exclusion of the type of surgery, which is incorporated elsewhere in the approach to the patient. The clinical risk factors include:

- History of heart disease
- History of compensated or prior heart failure
- History of cerebrovascular disease
- Diabetes mellitus Renal insufficiency.

The minor clinical predictors such as hypertension, age more than 70 years, etc. (as per 2002 guidelines) lead to a higher suspicion of CAD, but are

not incorporated into the recommendations for treatment.

The functional status of the patient based on the metabolic equivalent (MET) should also be assessed. One MET represents the oxygen consumption of a resting adult (3.5 mL/Kg). If the patient is unable to meet a 4 MET demand (1 to 4 MET includes activities such as eating, dressing, walking around the house and dish washing), perioperative cardiac and long-term risks are increased. The author believes that although, good functional class denotes mild cardiac disease, there might be exceptions to this (albeit rare). For instance, a patient with severe aortic stenosis or CAD may be asymptomatic with good functional class.

The risk assessment should also include the type of surgery, which has been classified as follows:

- Vascular [cardiac risk (incidence of cardiac death and nonfatal MI) more than 5 percent]

  - Aortic and other major vascular surgery
  - Peripheral vascular surgery

- Intermediate risk (cardiac risk 1 to 5 percent)

  - Intraperitoneal or intrathoracic surgery
  - Carotid endarterectomy
  - Head and neck surgery
  - Orthopaedic and prostate surgery

- Low risk (cardiac risk generally less than 1 percent)

  - Endoscopic procedures
  - Superficial procedures
  - Cataract surgery
  - Breast surgery
  - Ambulatory surgery.

Based on the clinical predictors, functional class and the type of surgery, the ACC/AHA has suggested a 5-step algorithm for the management of the patients undergoing noncardiac surgery[6] In essence, it suggests that: 1. if the patient has a severe cardiac disease, irrespective of the nature of surgery

(except perhaps really minor surgery), the risk is high; 2. If the patient has a mild cardiac disease, the patient can be treated almost like normal, and 3. if the patient has a moderate cardiac disease, risk stratification based on the nature of surgery and functional assessment is necessary. Further, noninvasive testing should be reserved for those patients in whom a substantial change in medical management would be anticipated based on the results of testing. The reader should refer to the original document for details.[6]

In this respect, the 6 min. walk test (6 MWT) has been shown to be a useful clinical tool to screen and risk stratify patients in departments where cardiopulmonary exercise testing (CPET) is unavailable.[7] Patients walking more than 563 meters in the 6 MWT do not routinely require CPET, those walking less than 427 meters should be referred for further evaluation, and in those walking more than 427 meters but less than 563 meters, the number of clinical risk factors and magnitude of surgery should be incorporated into decision-making process.[7]

The patients may have known CAD or may have a high-risk of CAD. In patients having known CAD, the presence of unstable angina has been associated with a high perioperative risk of MI.[8] Such patients should, therefore, be evaluated further by the cardiologist for medical or coronary interventions. In patients with stable angina, the degree of effort that precipitates angina may be a useful guide. The patient who manifests angina after strenuous exercise is a well controlled patient and does not require any change in management. In contrast, a patient who develops dyspnoea with angina on mild exertion, would be at a high-risk for developing perioperative ventricular dysfunction and MI. These patients have high chances of having severe CAD and additional investigations and monitoring may be necessary. Perioperative MI has been shown to be an early event after surgery, occasionally associated with chest pain, usually non-Q wave in nature and carries a high mortality.[9]

Presence of CHF preoperatively is associated with increased incidence of perioperative cardiac morbidity.[10] Increases in B-type natriuretic peptide (BNP) is a good marker of cardiac failure and may predict perioperative complications in cardiac patients undergoing noncardiac surgery.[11] A recent report has shown that a BNP concentration of > 87.5 pg/mL best predicted the long-term mortality after major noncardiac surgery.[12] Stabilisation of

ventricular function and treatment of pulmonary congestion is necessary prior to elective surgery. One recent paper on the basis of regression model has identified seven independent risk factors for major adverse cardiac and cerebrovascular events in noncardiac surgery.[13] These include; history of CAD, history of chronic congestive heart failure, chronic kidney disease, history of cerebrovascular disease, preoperative abnormal ECG, intraoperative hypotension, and blood transfusion.

In patients with a prior MI, the risk is dependent upon the time interval between MI and surgery. In this regard, the current management of acute MI (thrombolysis, angioplasty) has changed the scenario. According to the recommendations of ACC/AHA Task Force, separation of MI into the traditional 3 and 6 months intervals is avoided. It appears reasonable to wait 4 to 6 weeks after MI to perform elective surgery.[6] In patients having acute MI (within 7 days) and recent MI (within 7 days to one month), the management is based on the risk stratification during convalescence as well as the nature of treatment provided for acute MI (e.g. type of stent). It should be noted that in the developing countries, many patients will not have access to tertiary care centres where treatment of acute MI is available. In such patients the practice of separating into the traditional 3 and 6 months intervals should be continued, i.e. delaying elective surgery for 6 months after MI significantly decreases the incidence of perioperative myocardial infarction (PMI).

In patients without any history or symptoms of CAD, several factors that predispose to CAD may be present. These include peripheral arterial disease, diabetes, and hypertension. These factors increase the probability of CAD. Adequate control of diabetes and hypertension is desirable as diabetes is an independent risk factor for perioperative cardiac morbidity[14] and hypertensive patients with left ventricular (LV) hypertrophy are at a higher perioperative risk than nonhypertensive patients.

The surgical procedure should also be taken into consideration. Outpatient procedures do not require any change in perioperative management unless the patient has unstable angina or CHF. In contrast, some surgical procedures may be associated with significant stress and a high incidence of perioperative myocardial ischaemia. Vascular disease is associated with a high-risk of morbidity and myocardial ischaemia. Intra-abdominal, thoracic and orthopaedic procedures constitute intermediate risk.

In summary, past medical history of CAD necessitates in-depth investigation of the current cardiac status of the patient. In some patients it may be necessary to carry out tests to better confirm or define CAD. These include, pharmacological stress testing, stress echocardiography and ambulatory ECG (Holter) monitoring. These may be performed according to the ACC/AHA guidelines.[6] The ultimate aim is to optimise the patient's medical condition so that the perioperative outcome is improved. It is also desirable to inform the patient about the perioperative risks based on the preoperative evaluation.

Anaesthetic goals

Periopertive myocardial ischaemia leading to infarction is the leading cause of cardiac morbidity and mortality following noncardiac surgery. The intracoronary plaque rupture can precipitate the myocardia ischaemia. The stress response during major surgery accompanied by reduced fibrinolytic activity, and platelet activation (prothrombotic state) during major surgery is responsible for plaque rupture.

The anaesthetic management of a patient with CAD undergoing noncardiac surgery is focused towards preventing PMI that carries high morbidity and mortality. Since prophylactic CABG in patients with stable CAD before high-risk noncardiac surgery has failed to provide much benefit, attention has been focused on medical management.

Beta-blockers

It has been shown that intraoperative tachycardia and hypertension are associated with negative postoperative outcomes (hospital stay of more than 10 days with a morbid condition or death during the hospital stay) after major noncardiac surgery of long duration.[15] The authors suggested that intraoperative tachycardia and hypertension may have independent effects on outcome over and above the risk imparted by the underlying medical conditions.

By virture of decreasing myocardial oxygen demand, increasing diastolic perfusion time and reducing the frequency of arrhythmias, beta-blockers are expected to decrease myocardial ischaemia, and hence PMI. Perioperative beta-blockade is being increasingly utilised, particularly in the high-risk group of patients undergoing major noncardiac vascular surgery. The initial

randomized trials by Mangano et al[16], and Poldermans et al[17] are the prominent ones that demonstrated the utility of beta-blockers in providing long-term benefits to the patients. These were followed by a few others,[18] and a comprehensive review by Auerbach and Goldman reported substantial efficacy in patients managed with beta-blockers.[19] They also highlighted several other issues that need to be clarified, such as the choice and the dose of beta-blockers and the target heart rate that should be achieved (65 beats/min.). The debate on who should be treated with perioperative beta-blockers continues, but it is generally agreed that asthmatics and patients with chronic obstructive pulmonary disease tolerate beta-1 selective agents well and constitute relative contraindication. The ACC/AHA guidelines recommend the following.

Class I indication

1. Beta-blockers should be continued in patients undergoing surgery who are receiving beta-blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA class I guideline indications. (Level of evidence: C.)
2. Beta-blockers should be given to patients undergoing vascular surgery who are at high cardiac risk owing to the finding of ischaemia on preoperative testing (level of evidence: B.)

Class IIa indication

1. Beta-blockers are probably recommended for patients undergoing vascular surgery in whom preoperative assessment identifies coronary heart disease. (Level of evidence: B.)
2. Beta-blockers are probably recommended for patients in whom preoperative assessment for vascular surgery identifies high cardiac risk, as defined by the presence of more than 1 clinical risk factor. (Level of evidence: B.)
3. Beta-blockers are probably recommended for patients in whom preoperative assessment identifies coronary heart disease or high cardiac risk, as defined by the presence of more than 1 clinical risk factor, who

are undergoing intermediate-risk or vascular surgery (level of evidence: B.)

The recently published results of the POISE trial (Perioperative ischemia Study Evaluation) have however, further confused the issue.[20] The results of this trial demonstrated that in the beta-blocker group, cardiac morbidity was decreased with a significant reduction in all MI (4.2 versus 5.7 percent), reduced need for coronary revascularization, and reduction in atrial fibrillation. However, there was a significant increase in total mortality (3.1 versus 2.3 percent), stroke (1 versus 0.5 percent) and clinically significant hypotension and bradycardia in patients receiving metoprolol. Some believe that this may be related to the much higher dose of metoprolol (extended release), 200 mg (oral) or 15 mg (intravenous) as well as a cut-off heart rate of 50 beats/min. and systolic blood pressure of 100 mm Hg. However, caution may be exercised with the use of beta-blockers, and it should be prescribed on an individual patient basis.[21]

A focused update on perioperative beta-blockade was published in 2009 by the ACC/AHA.[22] According to this, a class I indication exists for continuation of beta blocker in patients already taking the drug. In addition, class Ila, recommendation exists for patients with inducible ischaemia, CAD, or multiple clinical risk factors who are undergoing high-risk (vascular) surgery and for patients with CAD or multiple clinical risk factors who are undergoing intermediate-risk surgery. Initiation of therapy, particularly in lower-risk groups, requires careful consideration of the risk-benefit ratio for an individual patient.[22] The current European guidelines also endorse that beta-blockers should be continued perioperatively in those who are currently taking them.[23]

In conclusion, although several issues related to beta blockade need to be addressed, the existing evidence does point towards application of perioperative beta-blockade on a selective basis in clinical practice. It appears that it should be continued in patients already on therapy, and started in patients with high cardiac risk undergoing intermediate or high-risk surgery. Future work will need to focus on identifying populations most likely to benefit or to be harmed, including pharmacogenetic analyses and distinctions between individual beta-blockers.[24]

Statins

3-Hydroxy-3-methylglutaryl coenzyme A inhibitors, usually referred to as statins are commonly prescribed for primary and secondary prevention of cardiovascular events. Although this was considered useful in patients with hypercholesterolaemia, more recently, statins have been used in patients with normal cholesterol levels who are at risk for or are known to have CAD. Therefore, the ACC/AHA guidelines recommend statin therapy for management of patients with unstable angina or MI.[25] The heart protection study demonstrated that cardiovascular event reduction was similar in patients treated with statins regardless of baseline low-density lipoprotein cholesterol concentration.[26] It seems, therefore, that there are mechanisms other than reduction in low-density lipoprotein cholesterol that might play a role. Prominent amongst them are the antiinflammatory effect (plaque stability), and reduction in vascular smooth muscle proliferation in response to injury. A metaanalysis has demonstrated potential benefits of continuing perioperative statin therapy in patients undergoing cardiac, vascular, and all other types of surgeries.[27] The benefit was particularly seen with regards to early mortality and was variable with relation to MI, stroke and arrhythmias.

It is important to restart statin early after surgery (oral or via nasogastric tube) as delay (> 4 days) can result in myonecrosis.[28] The ACC/AHA guidelines recommend that statins should be administered to patients already taking statin and scheduled for noncardiac surgery (class I), patients undergoing vascular surgery with or without risk factors (class Ila), and patients with at least one clinical risk factor undergoing intermediate-risk procedure (class lib).[6] In summary, statins are an important class of drugs that decreases cardiovascular morbidity and mortality. However, questions such as type and the dose of statin, and exact time of initiation of therapy need to be answered.

Haemodynamic management

Although, ischaemia is known to occur even in the absence of significant haemodynamic changes, careful monitoring is essential. It is conceivable that patients with active ischaemia prior to the operation will require more aggressive monitoring and treatment than those with chronic stable ischaemic heart disease. The monitoring for cardiac ischaemia should include at least a

multilead ECG. Direct arterial pressure monitoring along with pulmonary artery (PA) catheter can be of further help. In addition, if the facility is available, transoeso-phageal echocardiography (TOE) can be a useful complementary monitoring tool.[29,30]

Haemodynamic control can be achieved by a meticulously planned anaesthetic technique and pharmacological agents such as nitroglycerin (NTG), beta-blockers and calcium channel blockers may be necessary to achieve the desired goal. Inotropes may be required and should be readily available. Because these agents are administered in the form of an infusion, a central venous line should be inserted in these patients. In very sick patients placement of an IABP catheter may be required to support the circulation and has been shown to be beneficial.[31] However, as already emphasised, in non-emergency situations in patients with unstable angina, revascularisation prior to noncardiac surgery must be considered. In this respect, it is important to remember that the indications for revascularisation remain the same and it is not that the revascularization should be performed, just to perform the noncardiac surgery.

Haemodynamic changes associated with laryngoscopy and intubation should be minimised. Opioid-based anaesthetic technique should be preferred. Administration of adequate doses of analgesics (morphine 5 to 10 mg or fentanyl 5 to 10 μg/Kg) should accompany the induction of anaesthesia. The intravenous (TV) induction agent should be properly titrated so that smooth induction and endotracheal intubation are accomplished without coughing, bucking, tachycardia and hypertension. Significant decreases in heart rate (HR) and BP should also not occur. The induction agent or the anaesthetic technique is probably less important than the manner in which it is administered. This is easier said than done and perhaps, the experience of the anaesthesiologist is a crucial factor. Thiopental, midazolam and propofol can be used, but the selection should be based on the individual needs and characteristics of each patient. Hypnotics, inhalational agents and analgesics can be combined along with nitrous oxide for maintenance of anaesthesia. Patients can be extubated at the end of surgery, but depending upon the nature of surgery and the doses of narcotic drugs that have been used, elective ventilation for some duration after the operation can be considered.

Regional versus general anaesthesia

Although general anaesthesia continues to be the most common anaesthetic technique used for cardiac patients undergoing noncardiac surgery,[32,33] there are a few advocates of regional anaesthesia, at least in patients having certain operations. The onset of angina can be indicated by an awake patient, but vast majority of intraoperative ischaemia can be silent so that angina is not a good monitor of cardiac ischaemia. Some authors have shown that the rates of perioperative adverse cardiac events do not differ when general or regional anaesthesia is used.[34-36] Others have shown that the rate of reinfarction is less with spinal anaesthesia as compared with general anaesthesia in patients undergoing transurethral resection of prostate.[37]

Epidural analgesia reduces cardiac preload and afterload, postoperative adrenergic and coagulation responses, and produces coronary vasodilatation (thoracic epidural only). These effects are beneficial to the cardiovascular system and may reduce postoperative myocardial ischaemia. However, evidence showing the benefits of the technique is not currently available.

Non-steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac may be useful in patients with CAD, due to their analgesic and antiplatelet effects. However, substantial data are lacking. Concerns about increased postoperative bleeding make the use of these agents in surgical patients controversial.

Patients with intracoronary stents

There has been a recent change in the management of patients requiring coronary artery stents with more patients getting drug eluting stents implanted. These patients require a long-term dual antiplatelet therapy (clopidogrel and aspirin) in order to reduce stent rethrombosis rates. The management of such patients undergoing noncardiac surgery is a matter of debate and is still evolving. There is a risk of stent thrombosis, if the antiplatelet drugs are withdrawn and excessive bleeding, if they are continued during surgery. It is generally agreed that a local team of multispeciality experts should formulate a plan of management for each patient. The successful use of shorter acting antiplatelet agent tirofiban instead of clopidogrel during the perioperative period has been described to meet these ends.[38]

Recent clinical data show that the risk of coronary thrombosis after antiplatelet drugs withdrawal is much higher than that of surgical bleeding, if they are continued and that the antiplatelet medicines should be continued during the perioperative period except when bleeding might occur in a closed space (e.g. intracranial surgery, ophthalmic (posterior chamber surgery), and spinal surgery).[39] For the same reasons, the risk-benefit ratio of preoperative withdrawal of antiplatelet drugs in order to perform a regional or neuraxial blockade is not justified. Thus, according to the current guidelines, epidural analgesia cannot be administered to these patients, due to risk of epidural haematoma formation. However, one report described the administration of epidural analgesia in 306 patients undergoing vascular surgery.[40] The clopidogrel was withheld only for one day and no patient developed postoperative neurological complications. Such a practice does not appear to be correct in the present scenario.

The ACC/AHA guidelines[6] in relation to the stents recommend that elective procedures for which there is a significant risk of perioperative or postoperative bleeding should be deferred until patients have completed an appropriate course of dual antiplatelet therapy (12 months after DES implantation and 1 month after BMS implantation). In patients with high-risk of bleeding inside a closed space, thienopyridines (clopidogrel) should be discontinued, but aspirin should be continued if at all possible and thienopyridine restarted as soon as possible after the procedure because of concerns about late stent thrombosis. In general, it is agreed that the antiplatelet medicines should not be discontinued (barring surgery in closed space) for 14, 30-46, and 365 days following balloon angioplasty, BMS, and DES implantation respectively. A recent paper has suggested that stent thrombosis is not a real problem, if the antiplatelets are discontinued before noncardiac surgery,[41] however, the delay between the implantation of the DES and the noncardiac surgery in this study was 14 months, which is as per the recommended period of 12 months by the ACC/AHA.[42]

The other aspect of the above discussion is that the cardiologist should defer drug eluting stent implantation, if it is known to him that the patient is awaiting elective noncardiac surgery. In semi-urgent situations, only angioplasty should be performed so that the semi-urgent noncardiac surgery can be performed after 2 weeks. Once the patient recovers from the noncardiac surgery, BMS or DES can be placed.

In conclusion, the merits of a particular anaesthetic technique must be weighed, taking into consideration the cardiovascular status of the patient and the nature of the operation. As has been highlighted, meeting the anaesthetic goals is more important than the particular anaesthetic technique. In general, there is an inclination in favour of general anaesthesia to achieve the anaesthetic goals. As regards the patients with DES, the guidelines are still evolving, and it may be prudent to form a local team of experts comprising of haematologist, anaesthesiologist, and surgeon to decide the therapy for the patient.

Mitral Stenosis

MS of rheumatic origin is the commonest valvular lesion in the developing countries. The patients are usually young. The narrowing of the mitral valve orifice results in an increase in the left atrial (LA) pressure, limited filling of the LV, pulmonary congestion and in severe cases, pulmonary arterial hypertension (PAH) and right ventricular (RV) overload. Due to pulmonary congestion, dyspnoea is the most common presenting symptom and many patients are in atrial fibrillation. The diagnosis is confirmed by echocardiography that demonstrates narrowing of the mitral valve (decrease in mitral valve area), LA enlargement and a gradient across the mitral valve. In addition, fibrosis and calcification of the mitral valve apparatus and presence of LA clot can also be detected. Cardiac catheterisation is usually not necessary.

Preoperative evaluation

The severity of the disease can be judged by the symptoms. Patient having grade IV dyspnoea obviously has a more severe disease as compared to the patient having grade I or II dyspnoea (table 16.1). There may be a history of thromboembolic episode suggesting the presence of LA clot. As tachycardia leads to increase in the transvalvular gradient and pulmonary congestion, some conditions such as pregnancy, fever and thyrotoxicosis present with the symptoms of dyspnoea. History of CHF is usually present. This maybe controlled satisfactorily by medical management. If not, control of CHF should be optimised prior to surgery. Echocardiography is a simple noninvasive investigation that confirms the diagnosis and provides other

information about the severity of the disease. The severity is graded on the basis of valve area: normal area 4.5 cm^2; mild stenosis 1.5 to 2.5 cm^2; moderate stenosis 1 to 1.5 cm^2 and severe stenosis < 1 cm^2. The severity of PAH as determined by the right ventricular systolic pressure (RVSP) should also be noted. It is not uncommon in the developing countries to have patients presenting for surgery with severe PAH (RVSP = systolic blood pressure). Patients having mild stenosis tolerate surgery and anaesthesia well, however, those having moderate to severe stenosis need careful management especially in the presence of PAH.

Table 16.1: Grades of dyspnoea

Grade	*Description*
I	Breathlessness on severe exertion
II	Breathlessness on moderate exertion (brisk walk)
III	Breathlessness on mild exertion (normal day to day activities)
IV	Breathlessness at rest

In summary, preoperative evaluation should include review of exercise tolerance and determination of the presence and severity of previous CHF to assess the functional severity of the lesion. Echocardiography is helpful to assess the magnitude of valvular dysfunction.

In patients with severe MS (valve area < 1 cm^2), PAH and CHF, preoperative BMV (if the facility is available) must be considered or is rather indicated. This is a procedure that can be performed under local anaesthesia and an experienced cardiologist can perform it quickly with high success rate. In all patients with MS requiring elective or less urgent surgery, BMV or closed mitral valvotomy (CMV) should be performed, but patients with mild stenosis can tolerate noncardiac surgery and anaesthesia well. For patients requiring emergency or urgent operation, medical management (digoxin and diuretics) should be optimised to correct CHF and restore normal electrolyte balance.

Anaesthetic Goals

The anaesthetic goals for patients with MS are to control the HR (ventricular rate in AF) and if possible, restore and preserve sinus rhythm. However, it should be ensured that a patient with AF is anticoagulated well before (3 to 4 weeks) restoration of the sinus rhythm (by cardioversion) is considered in order to minimise the risk of embolisation. In addition, adequate intravascular volume should be maintained and systemic arterial vasodilatation should be prevented. In patients with PAH, even mild hypercarbia, which may exacerbate the increased pulmonary vascular resistance (PVR) should be avoided.

For patients with PAH, NTG or sodium nitroprusside (SNP) infusion can be used. Newer agents such as prostacyclin and nitric oxide, which have a selective pulmonary vasodilatory effect can also be useful in difficult circumstances. Monitoring should include electrocardiogram (ECG), direct arterial pressure and central venous pressure (CVP). PA catheter may be used in sick patients with severe PAH. In addition, arterial blood gas measurements and serum electrolytes (particularly potassium) should be measured periodically. The choice of anaesthetic agents should be tailored to the patient's requirements (for details refer to chapter 5). The patient can be extubated after surgery, but elective ventilation for some duration may be considered in view of the deranged lung functions that these patients may have due to chronic lung congestion.

Pregnancy with mitral stenosis

Rheumatic MS is fairly common in young people in the developing countries. Therefore, MS is the most common cardiac lesion seen in women of child bearing age. The cardiovascular system is progressively overloaded during pregnancy. There is an increase in cardiac output (CO) of 22 percent and decrease in systemic vascular resistance (SVR) by 30 percent at 8 weeks of gestation.[43] The changes continue as the pregnancy progresses and by early third trimester, the CO increases to approximately 30 to 40 percent above nonpregnant values. Due to the hyperdynamic circulation, the symptoms of MS are sometimes manifested for the first time during pregnancy. Some patients are followed in antenatal clinics. CMV can be performed safely at any stage of the pregnancy giving significant functional and clinical improvement without adversely affecting the foetus.[44,45] In general, the

indication for CMV is acute heart failure with pulmonary oedema or to prevent the complications of severe MS affecting either the mother or the foetus. With the advent of BMV, it should be the preferred intervention and it has been shown that BMV can be performed successfully anytime before term [46] However, no intervention is necessary in patients with mild MS and the pregnancy may be allowed to continue.

Some patients present for the first time near term with CHF that is refractory to medical management. Elective ventilation is sometimes necessary in these patients. Even in them, BMV can be successfully performed, but the foetus may be at risk due to hypoxia and haemodynamic compromise. As an alternative, beta-adrenergic receptor blockade with the use of either propranolol or atenolol can be utilised. It has been shown that pregnant women with symptomatic MS can be safely managed with beta-blockade giving significant reduction in the incidence of pulmonary oedema with no untoward neonatal side effects.[47] However, this is not the usual practice, as an urgent CMV/BMV is always a possibility in these patients.

Barring obstetric analgesia, the services of the anaesthesiologist in a pregnant patient with MS may be required on two occasions: 1. to anaesthetise the patient for elective or emergency caesarean section and other obstetrical emergencies; 2. to manage the ventilation of the patient with severe MS before BMV, institute the transfer of the ventilated patient to the catheterisation laboratory for BMV, and manage the post BMV ventilation till extubation is executed.

Caesarean section in a patient with mitral stenosis

There are no clear cut guidelines on this topic, although, it appears logical that except for patients with mild MS, BMV or CMV should precede an elective caesarean section. If this is not possible, epidural or general anaesthesia may be considered for patients with mild to moderate stenosis. The question about a patient with severe MS requiring emergency caesarean section is not easy to answer. There are no controlled trials regarding the anaesthetic management of these patients. The aim should be to preserve the maternal as well as the foetal well being. The consequences of decreased venous return or SVR in these patients can be disastrous. Epidural or spinal anaesthesia, may therefore, be hazardous. Opioid-based general anaesthesia can be useful to maintain hemodynamic stability in these patients, but can cause severe respiratory depression in the new bom baby. It is reasonable to

conclude that life of the mother is more important, and compromised haemodynamics of the mother (epidural, spinal or non-opioid general anaesthesia techniques) can also threaten the foetus. Therefore, modest doses of opioids [fentanyl, 10 to 20 μg/Kg (total) or morphine, 0.5 to 1 mg/Kg (total)] should be used accepting the increased risk of neonatal depression. The foetus can be resuscitated for respiratory depression if necessary. Complete "aspiration precautions" should be used during induction of anaesthesia. The usual rapid-sequence induction to provide maximum protection against aspiration pneumonitis is not desirable, as this technique can result in dramatic cardiovascular changes that may not be tolerated by a patient with severe MS. Patients will need elective postoperative ventilation, if modest doses of opioids are used.

Regional anaesthesia: The pain, apprehension and the uncontrollable urge to bear down, causes considerable strain on the heart by increasing the HR and CO and may precipitate acute heart failure even in patients with mild to moderate MS. Continuous lumbar epidural analgesia may be useful, but hypotension must be anticipated and prevented or treated immediately. A careful extension of the epidural block may be performed in patients with mild to moderate stenosis requiring caesarean section. Increments of small doses of local anaesthetics (plain solution) should be administered to obtain an adequate level of analgesia. BP should be continuously monitored and intravascular volume should be maintained by administration of IV fluids. In patients with severe MS, general anaesthesia (as described earlier) should be preferred. However, prospective randomised trials may be necessary to provide a definite answer to the question. Since, this particular problem is no longer faced by the developed countries, such trials will have to come from the developing countries.

Whatever technique is used, careful hemodynamic monitoring is of paramount importance. An intra-arterial line for continuous pressure monitoring and a CVP line for right sided pressure monitoring and infusion of inotropic and dilator drugs are recommended. A PA catheter may be used to help monitor the degree of PAH. If PAH and RV dysfunction occur, inotropic support (dopamine or dobutamine, 5 to 10 μg/Kg/min.) and pulmonary vasodilatation (NTG or SNP 0.5 to 1 μg/Kg/min.) should be instituted. Hypovolaemia is notwell tolerated, but autotransfusion after delivery should be a consideration in guiding the volume therapy.

Administration of ergometrine for control of bleeding after the delivery of

foetus should be avoided as it can cause transient increase in BP. It also causes uterine retraction leading to autotransfusion effect. Therefore, if control of haemorrhage is desirable, oxytocin infusion should be preferred.

What, if the facility of BMV is not available? Pregnancy may be allowed to continue in patients with mitral valve area of >1.5 cm^2. In the rest, CMV can be performed, by explaining that there are risks to the foetus with general anaesthesia even though lack of untoward foetal effects have been demonstrated.[48]

In conclusion, anaesthesia for the pregnant patient with MS, requires an understanding of the pathophysiological changes produced by the lesion and the normal cardiovascular adaptations to pregnancy. There is no one anaesthetic technique that is exclusively indicated or contraindicated.[49] The key to the success is careful monitoring and maintenance of haemodynamics. The emergence of BMV as a safe and effective procedure has definitely influenced the management strategies of the patient. General anaesthesia appears to be preferable in severe valvular stenosis undergoing caesarean section.

Mitral Regurgitation

Rheumatic fever is the commonest cause of mitral regurgitation (MR) in developing countries. MR produces volume overloading of the LV. This is a chronic condition and leads to compensatory changes such as LV hypertrophy and dilatation as well as LA dilatation. If the condition is left untreated, chronic pulmonary congestion leads to pulmonary vascular changes with recurrent attacks of CHF. Fatigue and dyspnoea on exertion with or without palpitation is the commonest presenting symptom.

The diagnosis is confirmed by echocardiography. The severity of regurgitation is graded on the basis of regurgitant jet area (mild < 4 cm^2, moderate 4 to 8 cm^2 and severe > 8 cm^2) or the area of the LA cavity occupied by the regurgitant jet (¼: jet reaches up to ¼th LA cavity, ¾: jet reaches ½ LA cavity, ¾: jet reaches ¾th LA cavity and ¾: the jet occupies the whole LA cavity). In addition, the RVSP indicates the severity of PAH. The LV dimension can also provide a clue to the severity of the lesion. LV internal end-systolic dimension of greater than 4.5 cm is considered as severe disease with poor outcome.[50]

The estimates of ejection fraction may be misleading, because there are two outlets for the blood from LV. The regurgitant mitral valve provides a low pressure, low resistance route in addition to the usual aortic route. The blood entering the aorta constitutes the forward output which matters for systemic perfusion. The blood entering the LA may be more than that entering the aorta. This constitutes the regurgitant fraction that can increase in the presence of systemic vasoconstriction or bradycardia.

Preoperative assessment should include the severity of symptoms and the disease based on echocardiography. The CHF should be treated adequately by digoxin and diuretics.

Anaesthetic goals

In general, patients suffering from MR (except those with severe MR and severe PAH), tolerate anaesthesia well. HR should be maintained at normal or elevated levels to maintain CO. Bradycardia leads to increased regurgitant fraction and reduced systemic CO. Vasodilatation is preferred as increases in SVR increase the regurgitant flow. Vasodilators, thus should be used to improve “forward” output, provided excessive hypotension is avoided.[51] Likewise, hypovolaemia should be avoided. Inotropes may be necessary as myocardial contractility is impaired. Monitoring should include ECG, direct arterial pressure, CVP and PA catheter, if severe PAH is present.

In one study, it was shown that the intraoperative period may be complicated by hypotension and bradycardia that is easily treatable. However, the postoperative course was complicated by a high incidence of morbidity (27.4 percent, mostly pulmonary oedema and prolonged tracheal intubation) and mortality (11.9 pecent).[52] The increased morbidity and mortality was especially in those with atrial fibrillation, high-risk surgery and lower LV ejection fraction.[52]

Aortic Regurgitation

Chronic aortic regurgitation (AR) of rheumatic origin is common in the developing countries. It results in volume overloading of the LV that causes eccentric hypertrophy (increase in the chamber size but no increase in wall thickness). A competent mitral valve protects the pulmonary circulation until late in the disease process, when the LV contractility is impaired and forward

CO falls. At this stage pulmonary congestion develops due to raised left ventricular end-diastolic pressure (LVEDP). The progress of the disease is gradual and the patient may remain asymptomatic for a long time. However, there is a rapid deterioration, once LV failure occurs. The diagnosis is confirmed by echocardiography and the severity of AR is graded as mild, moderate, and severe. In addition, the LV dimensions should also be noted. There is increased risk with CHF, impaired contractility and a LV internal end-systolic dimension of more than 5.5 cm.[53]

Anaesthetic goals

In general, unless CHF or LV dysfunction is present, the patients tolerate surgery and anaesthesia well. In one study, it was shown that patients with chronic severe AR had higher perioperative cardiopulmonary morbidities and in-hospital deaths as compared with case-matched controls.[54] Some anaesthetic principles are useful. A slightly higher than normal HR (90 to 100 beats/min.) is beneficial, as reduced diastolic time allows less time for regurgitant flow and thereby avoids LV distention. Bradycardia is dangerous and must be prevented as the LV distention can cause increase in LVEDP and compromise subendocardial blood flow. Vasodilators are also beneficial, as decreased SVR reduces the regurgitant flow. However, hypotension should be avoided. The patients have a wide pulse pressure with high systolic pressure and low diastolic pressure, so that the mean arterial pressure (MAP) is near normal or marginally elevated. Therefore, it is useful to monitor MAP and avoid diastolic hypotension. Inotropes may be required if ventricular contractility is impaired.

Aortic stenosis

Once again, rheumatic fever is the commonest cause of aortic stenosis (AS) in the developing countries. However, degeneration and calcification of a congenitally abnormal valve are also known to occur. In contrast to rheumatic AS, the calcified AS tends to occur in older population and therefore, may be associated with CAD. This group of patients, therefore, should also be examined and investigated (if necessary) for the evidence of CAD. AS is the most serious valvular lesion because of its potential for sudden death and inability to resuscitate the patient by external cardiac

massage during cardiac arrest.

The normal aortic valve area is 2.5 to 3.5 cm^2. As the valve orifice narrows, resistance to flow develops so that pressure gradient between LV and aorta increases. The pressure gradient leads to pressure overload on the LV, which causes compensatory concentric hypertrophy (increase in wall thickness without increase in chamber size). The increased wall thickness leads to reduced diastolic relaxation and compliance, increased oxygen demand and reduced oxygen delivery due to reduced coronary perfusion (consequence of increased LVEDP). Symptoms of angina, CHF, syncope and sudden death usually begin to occur when the valve area decreases below 1 cm^2. Echocardiography confirms the diagnosis and provides valuable data such as, gradient across the aortic valve, LV wall thickness, interventricular septal thickness, and LV contractility. A gradient of more than 50 mm Hg across the aortic valve indicates the need for surgical correction. However, a decrease in gradient from a previously higher value indicates LV failure (presuming that flow is same). Cardiac catheterisation is generally not required but may be indicated in older population to perform coronary angiography and confirm or rule out CAD.

Anaesthetic goals

The main anaesthetic goals are to maintain sinus rhythm, adequate intravascular volume and SVR. Sinus rhythm is beneficial because ‘atrial kick’ may account for up to 40 percent of ventricular filling due to decreased LV compliance. Adequacy of intravascular volume may be monitored by the PA pressure monitoring, as slight changes in the intravascular volume are reflected in the PA pressure in presence of poor LV compliance. However, PA catheter can induce arrhythmias, therefore, some anesthesiologists prefer to monitor CVP. Patients with AS may experience angina even without CAD and have little or no coronary flow reserve. They are at risk from peripheral vasodilatation which can produce sudden hypotension that can impair coronary as well as cerebral perfusion. The anaesthetic agents that produce mild myocardial depression and therefore, myocardial work and oxygen demand, also produce hypotension and decreased coronary perfusion pressure. Therefore, judicious use of anaesthetic agents in appropriate dosage is necessary. It is a good policy to use increments of small bolus doses (e.g. morphine, fentanyl, midazolam, thiopentone, etc.) while keeping a watch on

the haemodynamics.

In addition to the usual pharmacological agents, two additional interventions may be helpful in very sick patients. 1. The preoperative placement of an IABP catheter to improve coronary perfusion and 2. balloon aortic valvuloplasty (if feasible) to reduce the stenosis prior to noncardiac surgery. Palliative balloon aortic valvuloplasty prior to surgery can be beneficial and allows even major neurosurgical procedure such as craniotomy to be performed safely.[55] Therefore, it should be considered if the facility is available. Epidural anaesthesia has also been successfully used in a 74 year old patient with symptomatic severe aortic stenosis undergoing ileocecectomy.[56] Adequate fluid loading and intermittent phenylephrine administration was used by the authors to maintain haemodynamic stability throughout the operation. Selected patients with severe AS, who are otherwise not candidates for aortic valve replacement, can undergo noncardiac surgery with acceptable risk when appropriate intraoperative and postoperative management is used.[57] In one study on elderly patients with severe asymptomatic AS, it was shown that intermediate-to-low-risk noncardiac surgery can be performed relatively safely.[58] However, intraoperative hypotension requiring vasopressor use was more commonly required in them as compared with controls. Therefore, intra-arterial pressure monitoring should be performed in patients with AS so that hypotension can be diagnosed and treated promptly.

In summary, patients suffering from valvular heart disease are young in the developing countries, and often multiple valvular lesions are present in the same patient. While dealing with these patients, the pathophysiology of the lesion must be understood. Most valvular lesions cannot be completely treated by medical management. Therefore, the aim is to stabilise the haemodynamics and not restore ‘normal’ haemodynamics (which may not be possible).

In patients with multiple valvular lesion, the priority should be given to the anaesthetic goals for the more severe lesion. In this respect, AS should always be given the highest priority followed by MS. Amongst the regurgitant lesions, MR should be given a higher priority than AR as the lungs are affected early in MR, and AR is well tolerated for a long time. The severity of the lesion should of course be taken into account before such priority is awarded. For instance, if a patient has mild MR with severe AR,

perhaps AR should be given the priority, and in a patient with severe MS with severe MR, the priority must be given to MS and faster HR (which may be beneficial to patients with MR) should be avoided as it is detrimental to MS and may precipitate CHF The choice of anaesthetic agents should be based on these considerations and as has been highlighted, there is no one particular agent or technique that is superior to others. A balanced approach that is tailored to the patient's needs depending upon the severity and pathophysiology of the lesion should be the aim of the anaesthetic management.

Patients with Prosthetic Valves

Patients who have undergone prosthetic valve replacement may also present for noncardiac surgery. These patients do not pose any haemodynamic problem, but preoperative echocardiogram to confirm normal functioning of the prosthetic valve should be performed before elective surgery. The other important consideration in these patients is that they are receiving anticoagulant therapy (warfarin). This might lead to excessive intraoperative bleeding. Therefore, anticoagulant therapy should be stopped 3 to 8 days before elective surgery and replaced by heparin, which should be stopped 6 hours before surgery. The anticoagulant should be restarted as soon as possible following surgery but is usually done on the 1st postoperative day. In female patients of child bearing age, tissue valves are implanted which do not require anticoagulant therapy. So this consideration is not necessary in these patients. However, if tissue valve is not implanted, the same considerations apply.

Congenital Heart Disease

Anaesthesiologists may have to deal with patients having a wide spectrum of congenital heart diseases (CHD). Most data on the subject are in the form of case series or isolated case reports. Advances in modern medicine have led to survival of the children to adulthood. Consequently, the number of adult patients with CHD is rapidly increasing and these patients will be presenting with greater frequency for noncardiac surgery.[59] A single management scheme for all patients is not possible. What is important is to understand the

pathophysiology of each congenital heart defect and tailor the anaesthetic plan to the specific needs of the individual patient. Discussion on all CHDs is beyond the scope of this chapter and only a few important lesions will be considered. Two important points should be examined in all patients.

1. Patients with CHD are susceptible to develop upper respiratory tract infection so that it should be treated adequately before subjecting the patient to elective surgery.
2. Antibiotic prophylaxis for subacute bacterial endocarditis is indicated in operations that can cause transient bacteraemia such as dental and intraoral procedures, tonsillectomy, bronchoscopy, etc.

Tetralogy of Fallot

Tetralogy of Fallot (TOF) is a fairly common congenital heart defect. There could be a wide range of anatomical and physiological variations in this condition. The infundibular and/or valvular pulmonic stenosis is responsible for a variable degree of right-to-left shunt across the VSD. One of the greatest risks in dealing with patients with TOF, is the intraoperative development of hypercyanotic spell. A decrease in SVR can cause increased right-to-left shunting and can lead to further arterial desaturation. Other mechanism of hypercyanotic spell is sympathetic stimulation leading to tachycardia and infundibular spasm causing further reduction in the pulmonary blood flow. After induction of anaesthesia, the saturation generally improves despite peripheral vasodilatation, as the state of anaesthesia per se decreases the catecholamine release and prevents the infundibular spasm and the hypercyanotic spell. Propranolol has been the most commonly used beta-blocker[60,61] for the treatment of hypercyanotic spell but other agents such as metoprolol, atenolol and esmolol can also be used. Choice of anaesthetic agents should be such that SVR is maintained, PVR is decreased, heart rate is slowed and myocardium is mildly depressed.

Pulmonary outflow obstruction due to infundibular spasm is less likely to produce a cyanotic spell in patients who have previously undergone a palliative shunting procedure such as Blalock-Taussig shunt, Waterson shunt, or Pott’s shunt. Nevertheless, preservation of SVR is important in these patients to maintain shunt flow.

Congenital heart defects with left-to-right shunting

Congenital heart defects with left-to-right shunting [atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), etc.] have a relative overperfusion of the pulmonary circuit. This is expected to achieve higher peak anaesthetic concentration in the blood, of inhalational agents. This may theoretically allow a more rapid inhalational anaesthetic induction. However, in clinical practice, no significant increase in the speed of induction is observed.[62] Likewise, intravenous anaesthetic induction agents might be expected to have a slower onset of action due to a delay in reaching the brain because of recirculation through the pulmonary circuit. Clinically, however, this effect is found to be unimportant.

Most patients, unless PAH is present, tolerate surgery and anaesthesia well. However, careful selection of anaesthetic agents with proper haemodynamic monitoring is essential. Measures to lower PAH such as prevention of hypoxia and hypercarbia and use of pulmonary vasodilators such as NTG and SNP may be necessary. Choice of anaesthetic agents should be such that they preserve ventricular function and vascular resistances in such a way that pulmonary blood flow and forward CO is maintained. No single approach or technique can be considered for all patients, but each patient's haemodynamic needs should be evaluated for appropriate anaesthetic plan for an individual patient.

A patient with long standing VSD, who has developed irreversible PAH and reversal of blood flow (right-to-left) across the VSD (Eisenmenger's syndrome) poses a challenge to the anaesthesiologist. Fortunately such a situation is rarely encountered. In these children, a sudden increase in PVR or decrease in SVR can cause further increase in right to left shunt and rapid clinical deterioration.[63] Avoidance of over-sedation and loss of airway during anaesthetic induction is very important in these patients. Use of anaesthetic agents or techniques that increase SVR also tend to increase PVR, hence a balanced approach is more desirable. Even epidural anaesthesia (despite its potential to decrease SVR) has been used to produce stable haemodynamics.[64] Many anaesthetic agents and techniques have been used with success, in patients with Eisenmenger's syndrome.[65] Adult patients with Eisenmenger's syndrome are at an increased risk with noncardiac surgery,

but with current techniques, the risk of death is less than previously thought.[66] It should be remembered that significant complications including death can occur even with relatively minor surgery and these patients should be referred to centres with expertise in the care of such patients.

Patients who have previously undergone surgical correction of the defect, essentially pose no peculiar problem. However, atrial rhythm disturbances following repair of ASD and heart block or residual VSD following VSD closure may be present.

Patients with Fontan Circulation

In Fontan surgery, a serial circulation is created in which the ventricle pumps blood to the systemic circuit, and pulmonary blood flow occurs via a cavo-pulmonary connection. These patients can have associated comorbidities such as ventricular dysfunction and arrhythmias. Adequate oxygenation and ventilation is crucial in these patients and increases in PVR should be prevented. Milrinone is a good choice for inotropic therapy as it reduces PVR and SVR. Apatient with Fontan circulation undergoing laparoscopic cholecystectomy was managed successfully by limiting the intra-abdorninal pressure to 8 cm of water and use of milrinone.[67]

Some Other Conditions

Dilated cardiomyopathy

The management of a patient with dilated cardiomyopathy (DCM) undergoing noncardiac surgery is always a challenge to the anaesthesiologist as the perioperative course may be complicated by cardiac arrhythmias or heart failure. In DCM, impairment of ventricular systolic function occurs and as the contractile function diminishes, stroke volume is initially maintained by augmentation of the end-diastolic volume and despite a severely decreased ejection fraction, stroke volume may be almost normal. Anaesthetic management is based on afterload reduction, optimal preload and minimal myocardial depression as these patients are extremely sensitive to cardiac depressant anaesthetic drugs. Use of vasoactive drugs, intensive haemodynamic monitoring (including PA catheter) as well as mechanical support device, such as IABP, may be necessary in these patients.[68]

Successful use of abdominal field block along with conscious sedation has also been described in these patients.[69]

Hypertension

Hypertension has been classified as a minor clinical predictor according to the ACC/AHA guidelines.[6] Stage 3 hypertension (systolic BP more than 180 mm Hg and diastolic BP more than 110 mm Hg) should be controlled before surgery. Effective antihypertensive regimen should be established before undertaking elective surgery. If surgery is urgent, rapid acting agents can be administered that allow effective control in a matter of minutes or hours. Beta-blockers are particularly useful in this respect. The preoperative antihypertensive treatment should be continued through the perioperative period. At times, in a patient in whom the hypertension is well controlled, preoperative hypertension (diastolic BP between 110 and 130 mm Hg), immediately before surgery may be detected. In such a situation, it has been suggested that surgery should not be postponed, but treated with intranasal nifedipine (10 mg).[70] By using such a practice, it was shown that there was no difference in the postoperative complications, and unnecessary surgery postponement and attendant costs were avoided.[70] Such a practice should be limited to those patients who have no previous MI, unstable or severe angina pectoris, renal failure, pregnancy induced hypertension, LV hypertrophy, previous coronary revascularisation, AS, preoperative arrhythmias, conduction defects, or stroke.

Patients with Cardiac Implantable Electronic Devices: Pacemakers and Implantable Cardioverter Defibrillator

Cardiac pacing is one of the most reliable documented treatment for various cardiac arrhythmias, especially bradyarrhythmias. The initial pacemakers consisted of a single-lead asynchronous system, which paced the heart at a fixed rate. Over the years, the technological advances have revolutionized the pacemakers, and currently, more sophisticated multiprogrammable devices are available. In addition, automated implantable cardioverter defibrillators

(ICD) have been designed to treat fatal tachyarrhythmias. With the availability of pacing devices to suit many conditions, potential indications for pacing are rapidly expanding. The ACC/AHA/Heart rhythm society (HRS) have established indications for permanent pacemaker or anti-tachycardia devices.[71] A large population lives with a permanent cardiac pacemaker or an ICD. Consequently, more and more patients with complex pacing systems are likely to present for noncardiac surgery. The safe anaesthetic management of such patients requires an understanding of the various modes of pacing, their indications and contraindication and the treatment strategies in the event of perioperative pacemaker failure. A practice advisory for the periopertive management of patients with cardiac implantable electronic devices has been published.[72] A detailed discussion on the various modes of pacing is beyond the scope of this chapter. The reader is advised to refer to standard cardiology books for such details. This description will be limited to a brief outline of various pacemaker functions and the anaesthetic considerations of such a patient undergoing noncardiac surgery.

Pacemaker identification code

A new five letter code system to describe the operation of implantable pulse generators and defibrillators has been adopted by the North American Society of Pacing and Electrophysiology. The additional letter, ‘R’ in the fourth position (programmability) describes newer rate responsive generators and position five (anti-tachycardia function) describes ICDs (table 16.2). The first letter describes the chambers paced, the second letter describes the chambers sensed and the third letter describes the mode of response.

Common pacing mode functions

Asynchronous pacing (AOO, VOO, DOO)

These generators are the most simple and only have an output circuit and no sensing circuit. Pacing stimuli are delivered at a fixed rate and may compete with patient’s intrinsic rhythm which can cause sustained tachycardia or fibrillation.

Single chamber demand pacing (AAI, AAT, VVI,

VVT)

These generators may be either atrial or ventricular and contain a sensing and pacing circuit. The pacing occurs only when it is needed and avoids tachycardia and fibrillation within the paced cardiac chamber (atrium or ventricle).

Dual chamber pacing (VAT, VDD, DVI, DDD, DDI)

Dual chamber pacemakers are designed to more closely approximate normal, atrioventricular synchronised cardiac function.

Programmable Pacemaker

These pacemakers have the capacity to change the paced rate in proportion to the metabolic demand so as to normalize the haemodynamic status. Various types of sensors have been designed which respond to the parameters such as body movements (vibration), minute ventilation, changes in ventricular repolarization, central venous temperature, central venous oxygen saturation, and RV contractility.

Anaesthetic considerations in a patient with pacemaker

Preoperative evaluation

The preoperative evaluation should include establishing whether a patient has a device, defining the type of device, determining whether a patient is device-dependent for pace-making function, and determining the device function.[72] In addition, underlying disease that necessitated the implantation of pacemaker must be considered. These patients have high incidence of associated diseases including diabetes, hypertension, CAD and complex congenital heart disease. As in any other cardiac patient, the drug therapy for the primary cardiac disease such as beta-blockers and calcium channel blockers, antihypertensives, antianginals, etc. should be continued. Return of symptoms for which the pacemaker was implanted should indicate that a further cardiology consultation is necessary. The general physical examination should be performed to rule out the presence of any bruits, and signs of congestive heart failure. The location of the pulse generator should

be noted. Generally, generator for the epicardial electrodes is kept in the abdomen, and over one of the pectoralis muscles for the endocardial electrodes. A12-lead electrocadiogram, X-ray chest (for visualization of the continuity of leads), and measurement of serum electrolytes (especially potassium) should be performed.

Table 16.2: Pacemaker identification code

Letter position	1	2	3	4	5
Category	Chambers paced	Chambers sensed	Response to sensing	Programmability, rate modulation	Anti-tachyarrhythmia function
Letters	O = none	O = none	O = none	O = none	O = none
	A = atrium	A = atrium	T = triggered	P = simple programmable	P = pacing (anti-tachyarrhythmia)
	V = ventricle	V = ventricle	I = inhibited	M = multi-programmable	S = shock
	D = dual (A+V)	D = dual (A+V)	D = dual (T + I)	C = communicating	D = dual (P+S)
				R = rate modulation	

The anaesthetic and monitoring requirements of the underlying cardiovascular disease are applicable while managing these patients. It is also important to evaluate the function of pacemaker in the preoperative period. Assistance from the cardiologist and the manufacturer's representative may be obtained for this purpose. Reprogramming the pacemaker is generally indicated to disable the rate-responsiveness. The ICD also needs to be disabled before anaesthesia.

The anaesthetic technique should be used according to the need of the patient. Both narcotic and inhalational techniques can be used successfully. These anaesthetic agents do not alter current and voltage thresholds of the pacemaker.[73] Depolarizing relaxants are a potential problem since fasciculations may cause myopotential inhibition of demand units. Pacemaker function should be verified before and after initiating mechanical ventilation, as there may be dislodgement of pacemaker leads by positive pressure ventilation.[74] There are no contraindications to regional anaesthesia (if the underlying disease permits). However, if seizures occur due to local anaesthetic toxicity, pacing inhibition can occur.

Intraoperative loss of pacing

It is a serious matter in a pacemaker dependent patient who does not have an

adequate escape rhythm (sufficient to maintain haemodynamics). Therefore, facility to institute emergency pacing (transcutaneous or transoesophageal pacing) should be available.

Electromagnetic interference is caused by strong ionizing beams of radiation, nuclear magnetic resonance imaging and surgical electrocautery. The indirect sources of electromagnetic interference are orthopaedic saw, tele-metric devices, mechanical ventilators, litho-triptors, cellular phones and whole body vibrations. These are potential sources of mechanical interferences that could affect the pacemaker. Diagnostic radiology and computed tomographic (CT) scans do not affect the function of pacemaker. Amongst these, electromagnetic interference caused by the use of electrocautery is the most common cause for intraoperative pacemaker inhibition and loss of pacing. In order to reduce the cautery interference, the electrocautery return pad should be placed as far away from the generator as possible (usually on the thigh). Electrocautery should be used at the lowest effective current and in short bursts with long pauses. Using bipolar rather than unipolar electrocautery should be considered. In addition, use of a magnet to eliminate sensing function (asynchronous mode) of the pacemaker may be used. However, individual manufacturers may have to be consulted for the specifications of the magnet (not just any magnet will work). Another alternative is to pre-operatively reprogramme the device to asynchronous mode. However, competition between paced and spontaneous beats could result in tachycardia or fibrillation. The ECG is distorted by electrocautery, so mechanical evidence of the heart function should be monitored by manual palpation of the pulse, pulse oximetry, precordial stethoscope or an arterial line.

When in doubt, the simplest approach is to leave the unit in demand mode and utilise manoeuvres to reduce electrocautery effects such as using bipolar electrocautery and application of magnet only during periods of dangerous pacemaker malfunction.[75] After any procedure where electrocautery is used, programmable pacemakers should undergo a parameter check to be sure that random reprogramming has not occurred.[75]

Acute hypokalemia and respiratory alkalosis can increase resting membrane potential and cause pacing miscapture and loss of pacing. Acute hyperkalemia and acidosis on the contrary can decrease resting membrane potential and can cause ventricular tachycardia (VT) and fibrillation (VF). Normal electrolyte and acid-base balance should be maintained during the

entire perioperative period.

Defibrillator paddles should not be placed over the generator but perpendicular to the line drawn between the generator and the electrode. If pacing is lost and there is no escape rhythm, cardiopulmonary resuscitation should be initiated and temporary pacing (transthoracic or transoesophageal) should be attempted. If this is not available, pacemaker pocket should be opened and the existing leads should be attached to an external generator. As a last resort, chest should be opened and epicardial leads applied.

Anaesthetic considerations in a patient with ICD

The ICD performs the function of continuously monitoring the patient's cardiac rhythm and treat VT and VF by either delivering counter-shocks or combinations of countershocks and antitachycardia pacing stimuli to the heart. Obviously the patient who needs ICD implantation is likely to have a high incidence of spontaneous arrhythmias (VT or VF), CAD and LV dysfunction. The ICD device has been available commercially since 1986 but over the years, several more complex and sophisticated versions have been available. The pacing functions have also been incorporated with pacer cardioverter defibrillator (PCD). The device is being implanted more commonly nowadays, and such patients may present for noncardiac surgery[76,77]

Preoperative evaluation should take into account the underlying disease for which the ICD was implanted. The selection of anaesthetic drugs and techniques should be based upon the severity of the patient's underlying medical disease. Intraoperative monitoring should include continuous two lead ECG monitoring. A central venous line should be avoided with recently placed (< 1 month) transvenous PCD leads to avoid dislodgement of the endocardial wires.[78] The invasive arterial pressure monitoring is generally necessary and allows monitoring of the pulsatile blood flow.

The ICD/PCD device must be disabled before the start of surgery, as use of electrocautery is not recommended by most manufacturers in the presence of an active ICD/PCD. This is because the use of electrocautery (within 15 cm) or direct defibrillation may result in permanent damage to the unit. Positioning a strong magnet (in consultation with the manufacturers) over the pulse generator will also temporarily suspend the automatic detection and

therapy capabilities of the ICD/PCD device. The facility for emergency transvenous pacing must be available in the operation theatre (OT). The electrocautery grounding pad should be at least 15 cm away from the PCD and the electrocautery should be used in short bursts with low energy. In the worst situation, the surgeon should be persuaded not to use the cautery at all (use ligatures instead). The placement of external defibrillator paddles in the standard position may damage the device permanently. Therefore, the paddles must be placed at a right angle to a line joining the implanted patch electrodes.[79] The ICD/PCD needs to be interrogated post-countershocks to determine functional integrity of circuits and programmed parameters before enabling the device. As ICD/PCD is disabled during surgery, all necessary antiarrhythmic drugs such as lidocaine hydrochloride, beta blockers, amiodarone, etc. must be readily available in the OT.

The current guidelines recommend that all implanted pacemakers and defibrillators should be interrogated before and after every invasive procedure. However, in one study, the ability of newer devices to withstand system malfunction or failure due to electromagnetic interference was tested. It was shown that all devices withstood periprocedural electromagnetic interference without malfunction.[80] The authors concluded that routine post-surgical interrogation of pacemaker and ICDs may not be necessary. However, this needs to be confirmed by larger studies.

An increasing number of paediatric patients with permanent pacemakers and ICDs require noncardiac surgery. Children with these devices are more vulnerable to lead failure and inappropriate shocks as compared with adult population.[81] More care should be exercised in children.

ICD/PCD patients should not be exposed to magnetic resonance imaging scanners or lithotripsy units as they form a source of electromagnetic interference. The OT personnel should wear nonconductive latex gloves for protection against the countershock delivered by the device.

In view of the problems outlined above, it appears preferable to manage these patients at centres equipped to deal with such problems.

Patient with Ventricuiar Assist Device

Ventricular assist devices (VAD) are used to assist or replace a failing ventricle. The device can be used for single or both ventricles, and can be divided into two types; the pulsatile and nonpulsatile. The pulsatile device

fills by gravity or vacuum assistance via the inflow cannula (placed in the LV apex or left atirum) into a clear plastic chamber. Once this chamber fills with blood, it is ejected pneumatically or via an electromechanical pump into the aorta via the outflow cannula. Some degree of anticoagulation is generally required for pulsatile devices. The examples are, Thoratec (Thoratec laboratories, Pleasanton, CA), Abiomed AB 5000 (Abiomed, Danvers, MA), Heartmate XVE (Thoratec Corporation), and the Novacor LVAS (World-Heart Corporation, Oakland CA).

The nonpulsatile VADs use a centrifugal pump or impeller to propel blood forward. The advantages of these devices are that there is much less shear stress on the cells, leading to less haemolysis, and there is less chance for embolic complications as there is no stasis of blood. Some of the nonpulsatile VADs are designed for longer-term use.

Patients with VADs may present for noncardiac surgery, even during immediate post-implantation period.[82] In patients with LVAD, the right ventricle is vulnerable in the immediate post- implantation period, as it has to adapt to changes in geometry from the septal shift that occurs with LV decompression.[83] Tricuspid regurgitation may also be present due to displaced papillary muscles. RV failure may ensue if PVR is increased, therefore, the patient may be on inotropes and/or pulmonary vasodilators to improve the right sided CO. Any hypoxia or hypercarbia can place additional strain on the right heart.

Patients with VADs are generally considered a “full stomach”, as the device or cannulae are positioned in the preperitoneal space. Therefore, rapid sequence induction with cricoid pressure should be performed.[82] Appropriate maintenance of fluid status and use of inotropes should be individualised. Positive pressure ventilation, and positive end-expiratory pressure may significantly decrease the venous return, and hence, should be set to the lowest possible level.

Monitoring is crucial in these patients. In nonpulsatile devices, the pulse oximeter may not work, necessitating frequent arterial blood gas measurements. Ultrasound can assist in arterial cannulation. Likewise, CVP catheter is also desirable to assess the volume status and infusion of inotropes. TOE is of exceptional value in evaluating the function of VAD itself and in case of univentricular VAD, for monitoring the function of nonsupported ventricle.[84]

Regional anaesthesia may be desirable in some situations, but is generally contraindicated as the patients are on anticoagulants. Laboratory tests should be used to guide transfusion of plasma and platelets. Cardiovascular collapse may occur and should be managed as per advanced cardiac life support protocol. However, chest compressions should be avoided as it may dislodge the VAD cannula, which can be lethal.[85]

Appropriate antibiotic prophylaxis and aseptic precautions are essential in order to prevent device getting infected. With proper understanding, and adequate preoperative preparation and intraoperative care, patients with VAD can be managed successfully.

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Chapter 17: Anaesthesiologist and the Cardiac Catheterisation Laboratory

During the past two decades, considerable advances in invasive cardiology have taken place. Owing to ageing population with significant co-morbidity, newer transcatheter interventions are being pioneered and complex interventional procedures involving prolonged catheterisation time in potentially critically ill patients are being performed. Some such procedures include device closure of cardiac defects, transcatheter aortic valve implantation (TAVI), transcatheter mitral valve repair and percutaneous left ventricular assist devices. Adult patients with congenital heart abnormalities are also being subjected to percutaneous interventions. Consequently, the demand for anaesthetic support for interventional cardiology procedures is increasing. The anaesthesiologist plays an important role and should have detailed knowledge of the intervention, and its potential complications. Further, an increased interplay between the interventional cardiologist and the anaesthesiologist is necessary. Sometimes, a multidisciplinary approach needing cardiac surgical involvement is also necessary. Over the years, the multidisciplinary management of these cases has been appreciated. It is perhaps due to this as well as the common goal of best patient outcome that the hybrid operation theatres have been designed.

Cardiac Catheterisation Procedures

The presence of an anaesthesiologist may be necessary during conduct of several paediatric cardiac catheterisation procedures. The anaesthetic principles applicable for individual cardiac lesion are also applicable in this

setting and usual guidelines should be followed. The anaesthesiologist should be aware of certain concerns in the cardiac catheterisation laboratory. Access to the patient, especially the airway, may not be ideal due to the presence of imaging equipment all around the patient and a movable table. An easy access to the patienf s airway must be assured to the anesthesiologist whenever he needs it.

In general, children are subjected to either diagnostic or therapeutic interventions. Over the years, increasing numbers of patients with congenital heart defects (CHD) are being subjected to transcatheter interventions for the treatment of CHD.

A large number of patients in the catheterisation laboratory do not require a general anaesthetic and are adequately sedated by the cardiologist. Some patients, however, require general anaesthesia. These include, uncooperative children and those who need to remain absolutely still during the procedure. In addition, a standby service may sometimes be requested in high-risk patients such as hypo-xaemic infants, patients in congestive heart failure (CHF) and obstructive valvular lesions (e.g. tight mitral stenosis). Occasionally, the anaesthesiologist may be required for carrying out resuscitation, if complications arise during the procedure.

Interventional cardiology has progressed rapidly over the years and newer transcatheter interventions are being pioneered. Table 17.1 lists the lesions that are treated with interventional cardiac catheterisation. It is not uncommon to receive patients in a grossly moribund state of cardiovascular health. Some of the examples are, patients presenting for ventricular tachycardia ablation, percutaneous valve replacements, placement of ventricular assist device, and percutaneous device closure of paravalvular leaks. These patients may be on significant inotropic and vasopressor support or intraaortic balloon pump (IABP). A multimodality imaging is advocated for transseptal puncture or catheter navigation for accurate placement of these devices. The cardiac anaesthesiologst should be proficient in transoesophageal echocardiography (TOE) inluding 3-Dimaging for this purpose. The cardiac intervention may be associated with the risk of migration of wires, catheter and other devices, or misguided punctures of cardiac structures that can lead to rapidly progressive haemodynamic collapse.[1] Such complications may entail emergent conversion from an endovascular approach to an open sternotomy with possible cardiopulmonary bypass (CPB). The anaesthesiologist should, therefore, be profident in

transferring an acutely unstable patient to a cardiac operating room (if the procedure was not being performed in the hybrid theatre).

Table 17.1: Procedures performed in the cardiac catheterisation laboratory.

Diagnostic procedures

Coronary angiography

- Patients with coronary artery disease.
- Elderly patients with valvular lesion (e.g. aortic stenosis) to detect associated coronary artery disease.
- Young patients with cyanotic heart disease to rule out abnormal coronary arteries.

Diagnostic catheterisation in congenital heart disease.

Interventional procedures

Coil embolisation

- Aortopulmonary collaterals
- Blalock-Taussig shunt
- Anomalous coronary arteries

Transcatheter device closure

- Patent ductus arteriosus
- Atrial septal defect
- Ventricular septal defect
- Left atrial appendage occlusion
- Paravalvular leaks

Balloon dilatation

- Pulmonary stenosis
- Mitral stenosis
- Aortic stenosis
- Tricuspid stenosis
- Atrial septostomy

Valve replacements and assist devices

- Transcatheter aortic valve implantation
- Transcatheter pulmonary, tricuspid and mitral valve replacements
- Percutaneous left ventricular assist devices

Intravascular stent placement

- Coronary artery stenosis
- Renal artery stenosis
- Aortic aneurysms

Electrophysiological procedures and therapeutic radiofrequency ablation

Pacemaker and implantable cardioverter-defibrillator implantation

Elective cardioversion

Interventional Procedures

Intracardiac shunt closures

Endovascular devices for the closure of intracardiac shunts such as patent foramen ovale (PFO), atrial septal defect (ASD), and ventricular septal defect (VSD) are available. For dosure of PFO and ASD, a catheter deployed dosure device is advanced from the femoral vein into the right atrium and across the septal defect. Fluoroscopy and TOE or intracardiac echocardiography (ICE) are used to guide the appropriate deployment of the device as well as to confirm the adequacy of closure. The ASD closure may take as long as 2.5 hours.[2] ICE allows these procedures to be performed without general anaesthesia in a much quicker time.[3] However, the probe cost is the limiting factor and ICE should be used in patients at high-risk for general anaesthesia or those with contraindications to TOE. With TOE guidance, ASD, with defident inferior vena-cava rim has also been closed with a device.[4] In patients requiring TOE, general anaesthesia with endotracheal intubation should be practised. Due to potential for right-to-left embolisation, all fluid lines must be carefully de-aired. Other potential rare complications include acute or delayed device embolization.

Device closure of VSD is mostly performed in children. Adults may develop acute defects after myocardial infarction, and may be haemodynamically unstable. Therefore, invasive monitoring and inotropic support may be necessary. All other considerations described for ASD and PFO closure should also be applied. One recent paper has reported successful closure of VSD in 28 patients with the procedure time ranging between 46 and 300 minutes.[5]

Patent ductus arteriosus closure

Most of the patent ductus arteriosus (PDAs) are diagnosed and treated in early childhood, but a small group of patients may present later in adult life with congestive cardiac failure or pulmonary hypertension. The devices used to close the PDAs vary from coils to self expanding occluders. PDAs as large as > 10 mm in diameter have been successfully closed in adults,[6] and large series have reported high success rate.[7] A fine guidewire is placed

retrogradely into the PDA from the femoral or upper limb artery under fluoroscopic guidance. Sedation or general anaesthesia is required because the procedure may take long duration and patient should be immobile to allow accurate deployment of the catheter across the PDA. General anaesthesia is preferred in patients with pulmonary hypertension. Hypoxia, hypercarbia, and high airway pressure can increase the pulmonary vascular resistance (PVR), and should be avoided.

Left atrial appendage occlusion

Left atrial appendage (LAA) is the usual site for thrombus formation and constitutes the major source of atrial thrombi in patients with atrial fibrillation. Atrial appendage occlusion devices are placed in the orifice of the LAA in patients with non-valvular atrial fibrillation. This is done with the intention of preventing stroke. Due to a higher incidence of bleeding complications, it is suggested that invasive monitoring should be performed and preparations for managing pericardial tamponade and major bleeding should be kept ready.[8]

Transcatheter aortic valve implantation

TAVI is performed as an alternative to open aortic valve replacement (AVR) for high-risk patients. It involves the catheter deployment of a bioprosthetic valve. The valve can be deployed by a retrograde approach via the femoral artery or an antegrade transapical approach that requires minithoracotomy. The valves currently in use are, the Edwards SAPIEN balloon expandable transcatheter heart valve (Edwards Life-sciences, Irvine, CA) and the Corevalve Percutaneous Aortic Valve Implantation System (Medtronic, Inc, Minneapolis, MN). Since, there is a possibility of the procedure getting converted to an open AVR, it should ideally be performed in a hybrid operating room. Invasive arterial and central venous pressure should be monitored with a large bore venous access for rapid blood transfusion. General anaesthesia should be preferred even in transfemoral approach due to the risks of vascular injury and haemodynamic instability. In addition, TOE can be easily performed. TOE is extremely useful to guide the placement of the valve, as well as diagnose the procedural complications such as paravalvular leak and pericardial tamponade.

The procedure involves placement of the right ventricular pacing lead (as

rapid ventricular pacing is induced during valve deployment) followed by balloon aortic valvuloplasty, which is a prerequisite for TAVI. External defibrillators and preparation for immediate resuscitation should be available for all patients. Once the aortic valvuloplasty is accomplished, the TAVI is positioned across the aortic valve, rapid ventricular pacing is instituted, and the valve is deployed by balloon inflation. Rapid pacing is not required with Corevalve device because it is self-expanding. Haemorrhage from vascular injury, coronary artery occlusion leading to myocardial ischaemia, device embolisation and atrioventricular conduction defects are the major complications that can occur during the procedure. Although the procedure has been performed under sedation, general anaesthesia is preferred. [9,10] However with the advent of ICE, TAVI can be considered under local anaesthesia and sedation.[11]

Transcatheter pulmonary, tricuspid and mitral valve replacements

Devices for transcatheter pulmonary and tricuspid valve replacements and a catheter mounted clip device (Mitra Clip) for mitral valve repair are available. The MitraClip device is used to correct mitral regurgitation. It is a potential alternative to surgical mitral valve repair. It is performed under general anaesthesia with fluoroscopic and TOE guidance. Recent results with the use of Evalve MitraClip have shown that it leads to increase in cardiac index and decrease in pulmonary artery pressure.[12] The procedure has also been performed under deep sedation using remifentanil and local anaesthesia in a patient who had serious contraindications to general anaesthesia.[13]

The transcatheter cardiac valve procedures are likely to be performed more frequently as the technology improves and the indications become more clearly defined. Ideally, these procedures should be performed in a hybrid operating room by a multidisciplinary team.

Balloon mitral valvotomy

Balloon mitral valvotomy (BMV) is a commonly performed procedure in the developing countries due to prevalence of rheumatic heart disease.

In almost all the patients, the procedure is performed under local anaesthesia and mild sedation and the anaesthesiologist is not required.

Sometimes BMV is performed in young children, who may be uncooperative and necessitate administration of general anaesthesia or monitored intravenous sedation. In addition, the anaesthesiologist is required as a standby for some patients who are very sick and in CHF. These may be patients with tight mitral stenosis. Rarely, some patients may be on a ventilator and they too will require the care of an anaesthesiologist. His presence is requested by the cardiologist due to his resuscitative skills and often quick intubation and restoration of ventilation will be expected and required. One should be aware that due to crowding of imaging equipment, he may have to execute his skills in less than ideal circumstances. He should, therefore, meticulously check all his resuscitation equipment, before the procedure is started. An extra length of ventilator tubing may be necessary. It may also be a good practice to assess the airway of the patient and be prepared for a difficult intubation.

Aortic and pulmonary artery stenting

Endovascular stent placement in coarctation of aorta or right ventricle to pulmonary artery conduit are performed. General anaesthesia with invasive pressure monitoring is generally required. Massive bleeding may occur during the procedure due to vessel rupture, hence, rapid transfusion facilities and surgical backup should be readily available.

Percutaneous coronary intervention and assist devices

Intracoronary interventions such as angioplasty, stenting, rotational atherectomy, etc. are commonly performed in the catheterisation laboratory. Anaesthesia support may be required in high-risk procedures such as those with major comorbidities and poor cardiac functional reserve. In very sick patients with haemodynamic instability, haemodynamics can be supported by intra-aortic balloon pump or venoarterial extracorporeal membrane oxygenation during the intracoronary intervention. Also, left ventricular assist devices such as the Impella device (Abiomed Inc, Danvers, MA) or the Tandem Heart (Cardiac Assist, Inc. Pittsburgh, PA) can be used. These are catheter mounted devices that are deployed for haemodynamic support. Invasive monitoring is mandatory and general anaesthesia with endotracheal intubation is necessary.

Implantable cardioverter defibrillator/Pacemaker cardioverter defibrillator implantation

These devices are implanted in patients who are at risk of sudden cardiac death because of ischaemic or non-ischaemic dilated cardiomyopathy, inherited arrhythmia syndromes, hypertrophic cardiomyopathy, long QT syndrome, and syncope with inducible sustained ventricular tachycadia.[14] Most of these patients suffer from ischaemic or dilated cardiomyopathy with poor ejection fraction. Over the years, the device has evolved considerably with incorporation of pacing functions [pacemaker cardioverter defibrillator (PCD)], better sensing leads, and reduction in size so that it can now be implanted via transvenous route.

As repeated induction of ventricular tachycardia (VT)/ventricular fibrillation (VF) followed by defibrillation is necessary during the procedure (that is very unpleasant to the patient), intravenous sedation or general anaesthesia is required.[15]

Anaesthetic considerations

The underlying cardiovascular status of the patient must be considered. During the procedure, repeated induction of VT or VF and defibrillation to test implantable cardioverter defibrillator (ICD)/PCD, leads to further deterioration in myocardial function.[16] Repeated induction of VF also leads to circulatory compromise that may lead to cerebral injury, although there is no such evidence.[17]

Anaesthetic agents with minimal effects on cardiac conduction and defibrillation threshold would be ideal. In this respect, isoflurane due to its minimal effect on conduction system should be preferred and lignocaine should be avoided or if at all required, should be used in minimum doses. In addition, minimal myocardial depression is desirable. It is also preferable to use anaesthetic agents of shorter duration of action so that neurological status of the patient can be assessed immediately after the procedure.

The choice of anaesthetic agents may be based on the pathophysiological needs of the individual patient, but a technique combining morphine, propofol and isoflurane has been successfully used for the management of

such patients.[15]

Inhalational anaesthesia supplemented with small doses of fentanyl or midazolam can also be used. With the advent of smaller transvenous ICDs, as well as the experience gained over the years, it is now feasible to implant them safely in the abdominal or pectoral area without surgical assistance. Therefore, the need for the usual practice of adnunistering general anaesthesia is less felt. Local anaesthesia with deep sedation only for defibrillation threshold testing has been described.[18] Different intravenous anaesthetic agents like propofol, etomidate, midazolam, ketamine, thiopentone and fentanyl have been used safely to deepen the sedation during defibrillation threshold testing. It has been shown that propofol led to delay in recovery of arterial pressure after defibrillation threshold testing and thiopentone led to delay in arousal and discharge of patients.[19]

Haemodynamic monitoring must include direct pressure monitoring due to induction of VF and defibrillation during ICD testing. Central venous catheter is necessary for access to emergency cardiac pacing and administration of inotropes. Pulmonary artery catheter is not recommended as it may cause displacement of transvenous lead of the ICD. Near infrared spectroscopy and TOE have also been used.[20] External defibrillation paddles must be kept ready during AICD testing as the device may fail to defibrillate.

Device and Lead removal

Lead removal may be necessary due to infection or dysfunction (e.g. lead fracture), and device upgrade may necessitiate device removal. Lead removal can be technically difficult, and may cause haemothorax, pneumothorax, thromboembolism, cardiac tamponade, vascular avulsion and valvular damage. Leads may get impacted to the myocardium or other locations such as the right atrium or superior vena cava. Large bore venous access should be established and blood should be readily available. In addition, cardiac surgeon and perfusionist should be present.[21]

Electrophysiological procedures

Diagnostic electrophysiological procedures combined with therapeutic radiofrequency ablations (if abberant conduction pathways are identified) are commonly performed for the treatment of atrial fibrillation, and tachyrhythrrtias. Pulmonary vein isolation that involves creation of an

electrically isolated band between the junction of the pulmonary veins and the right atrium is performed using radiofrequency or cryothermy. Prolonged periods of induced or persisting tachyarrhythmias may occur leading to haemodynamic instability. Therefore, external pads should be placed for defibrillation. In addition, reactive pericardial collections can occur. These procedures may take long time and hypothermia may occur. Therefore warming blankets should be used.

These procedures may also be associated with haemodynamic instability in the form of bradycardia, tachycardia, and hypotension. Anaesthetic agents that do not influence the cardiac conduction system should be used. There are little data regarding the effects of anaesthetic agents on cardiac conduction pathways. Most volatile agents have some effect on the conduction system, the clinical significance of which is unknown. Nevertheless, it may be prudent to avoid volatile anaesthetic agents in patients with prolonged QT intervals.[8] Ramifentanil and propofol can be used in this situation.

Interventional procedures in adults with congenital heart disease

Adults who have undergone corrective procedures for congenital heart diseases during childhood are increasing. They may be subjected to cardiac interventions in the catheterisation laboratory. Managing these patients may be challenging and careful preoperative assessment is essential. In patients with right-to-left shunt, increases in the PVR and decreases in the systemic vascular resistance (SVR) can be detrimental. SVR should be maintained with vasopressors, if necessary and volatile anaesthetics should be titrated carefully. In patients with left-to-right shunt increase in SVR should be avoided. In patients with cavopulmonary circulation (Fontan/Glenn shunt), the driving pressure for the pulmonary blood flow is the central venous pressure. Therefore, if positive pressure ventilation is required, lowest airway pressure should be used to maintain normocarbia.[22] Spontaneous ventilation with inspiratory support is another good option. In patients with arterial shunts, (e.g. Blalock-Taussig), arterial pressure should be monitored on the contralateral side for accuracy.

Elective cardioversion

Cardioversion is used to convert supraventricular and ventricular arrhythmias to sinus rhythm. Emergency cardioversion is required for arrhythmias causing haemodynamic instability. Sedation is required as the procedure is uncomfortable. When everything is in readiness for cardioversion, patient is pre-oxygenated and then administered a sedative agent (midazolam or diazepam 2.5 to 5 mg). The oxygen mask is removed just before administration of the shock. Following shock, the patient is ventilated with oxygen until consciousness is regained and he is able to maintain the airway.

Anaesthetic Considerations

The anaesthesiologist can manage many patients with monitored intravenous sedation techniques, while some require general endotracheal anaesthesia. The indications for using the two techniques are not well defined, but should be determined based upon the patient's condition and the procedure being undertaken. General anaesthesia should be preferred in procedures that take long duration, where patient movement is not desirable, TOE guidance is required, or in presence of patient comorbidities. Sedation can be provided by a variety of agents that can be administered intravenously. Combination of pethidine, promethazine, and chlorpromazine has been used effectively to sedate children in catheterisation laboratory. Although, this technique is still followed at a few centres, it has some disadvantages. Significant respiratory depression and hypotension may occur. The technique does not always ensure that the patient will remain motionless and requires close monitoring for any supplemental medication. Nowadays safer drugs are available and are commonly employed (Table 17.2).

Ketamine

Ketamine has been a popular agent for sedating children in the catheterisation laboratory and has been the most frequently used technique in one of the reports.[23] Another report has described it as a simple, safe and effective method for anaesthetising children in the cardiac catheterisation laboratory for interventional procedures.[24] The authors administered a bolus of ketamine (1 mg/Kg) intravenously, followed by an infusion of 50 to 75 μg/Kg/min. for the duration of the procedure. It has also been used in the dose of 2 mg/Kg intravenously or 4 to 6 mg/Kg intramuscularly in combination with heavy

premedication of diazepam without much problem.[25] Oral administration of ketamine with satisfactory results has also been reported.[26] However, this drug may be associated with emergence delirium,[27] which can be minimised with midazolam. In a recent study S(+)–ketamine has been shown to be superior to racemic ketamine in terms of better analgesic and sedative effects.[28]

Benzodiazepines

Diazepam (0.1 to 0.2 mg/Kg) or midazolam (0.1 to 0.2 mg/Kg) can be used, but midazolam is more attractive due to its shorter duration of action. It has also been used effectively in combination with an opioid or ketamine. Midazolam can also be used alone to provide sedation especially in adult patients.

Propofol

Propofol is a very attractive choice for catheterisation laboratory procedures due to its short duration of action. It is being considered as an alternative to ketamine and is used in the dose of 1 to 2 mg/Kg bolus followed by an infusion at the rate of 50 to 200 µg/Kg/min. Since propofol does not provide adequate analgesia, supplementation with opioids is often practised. Propofol, however, causes cardiovascular depression and it has been shown that the decrease in SVR caused by propofol can result in clinically important changes in cardiac shunt direction and flow.[29,30] In children with cardiac shunt, it leads to a decrease in the ratio of pulmonary to systemic blood flow, and it can lead to arterial desaturation in patients with cyanotic heart disease.[29,30] Therefore, caution should be exercised in patients in whom systemic after-load reduction may be harmful, such as patients with severe aortic stenosis, cyanotic heart disease with cyanotic spells, and patients with compromised myocardial function. Overall, it is a preferred agent in children with good ventricular function in whom rapid recovery from anaesthesia is desirable. It can also be used to supplement other anaesthetic agents, such as ketamine, midazolam or opioids. Kogan et al[31] have described a novel mixture of ketamine and propofol for diagnostic and interventional catheterisation in 45 children spontaneously breathing room air. Propofol (4 mg/mL) and ketamine (2 mg/mL) were infused in the same syringe in a constant ratio (with additional small boluses as needed). The authors

demonstrated that lower doses of both drugs were needed (mean ketamine dose of 26 µg/Kg/min. and propofol dose of 68 µg/Kg/min.) for successful sedation. Haemodynamic and respiratory changes from baseline were minimal. The combination of agents appears to preserve the advantages and avoid most of the disadvantages of both agents by allowing lower doses of each agent and counterbalancing the undesirable haemodynamic effects of both.

Table 17.2: Intravenous doses of commonly used agents.

Drug	*Adult*	*Paediatric*	*Infusion rate*
Opioids			
Fentanyl	20 to 50 µg bolus (up to 2 to 3 µg/Kg)	2 to 5 µg/Kg	—
Morphine	5 to 7.5 mg bolus	0.1 to 0.2 mg/Kg	—
Sedatives			
Diazepam	5 to 10 mg	0.1 to 0.2 mg/Kg	
Midazolam	5 to 10 mg	0.1 to 0.2 mg/Kg	1 to 2 µg/Kg/min.
Propofol	50 to 100 mg	1 to 2 mg/Kg	25 to 75 µg/Kg/min.
Sedative-analgesic			
Ketamine	20 to 40 mg	1 to 2 mg/Kg	30 to 90 µg/Kg/min.

Opioids

Opioids, such as fentanyl and morphine are also used, but are generally combined with midazolam or propofol. Morphine can be used in the increments of 0.1 to 0.2 mg/Kg and fentanyl in 2 to 5 µg/Kg. The advantages of opioids are that they provide good analgesia and haemodynamic stability. Remifentanil has been used as a continuous infusion in the dose of 0.2 or 0.3 µg/Kg/min. with sevoflurane and has been shown to provide stable hemodynamic conditions and allowed for rapid and adequate recovery.[32]

Dexmedetomidine

Dexmedetomidine is an attractive alternative that can be used alone or in combination with opioid.[33] It can be administered as a loading dose (0.5 µg/Kg) followed by an infusion. Hypotension and bradycardia are the most frequent side effects of dexmedetomidine. It has not been well studied in the setting of a cardiac catheterization laboratory.

Inhalational agents

Inhalational agents can be used for the maintenance of anaesthesia. However, halothane and sevoflurane can be used for induction of anaesthesia. Sevoflurane produces rapid loss of consciousness and recovery with minimal cardiovascular effects so that it can be used as the sole anaesthetic agent.

Whatever technique is used, the anaesthesiologist must have a ready venous access as well as capability to quickly accomplish endotracheal intubation and establish ventilation. Sometimes, sedation can be further supplemented with administration of oxygen, nitrous oxide and halothane/isoflurane via mask. Occasionally, ventilation may have to be assisted with a bag and mask. The haemodynamic monitoring is provided by the cardiologist.

General anaesthesia with endotracheal intubation is required for children undergoing complicated interventions (Clamshell device closure), extremely uncooperative children, and very small babies where general anaesthesia with spontaneous respiration may be risky. In such instances, anaesthetic principles applicable to the particular cardiac lesion should be followed. However, short acting agents should be used so that patients can be extubated at the end of the procedure.

It should be remembered that with any of the above anaesthetic techniques where the patient is allowed to breathe spontaneously, a clinically significant increase in arterial carbon dioxide tension and decrease in oxygen saturation can occur.[34] This might lead to acute increase in pulmonary artery pressure and PVR in pulmonary hypertensive patients. In addition, the hypoxia may lead to or compound the cerebral injury occurring as a result of embolic phenomenon.[35] Therefore, continuous monitoring of end-tidal carbon dioxide and oxygen saturation is desirable in these patients.

Arrhythmia and large amount of blood losses are other common complications. Surgical help may be needed in situations such as, haemopericardium producing cardiac tamponade, embolisation of closure devices and acute mitral regurgitation produced during BMV. The last two complications require emergency CPB so that the patient will have to be transferred to the operation theatre (as soon as it is available).

Disruption of the pulmonary artery and its branches during balloon dilatation procedures can occur.[36] Haemoptysis is indicative of such a complication. Immediate endotracheal intubation should be performed for airway control and ventilation in the presence of severe haemoptysis.

In conclusion, interventional cardiology has progressed rapidly over the years. It seems that a dedicated anaesthesia team is required to cope with the complexities of the patient population and the interventions. In addition, the challenges posed by the off-site nature of the cardiac catheterisation laboratory should be accounted for. Despite the recent endorsement of the use of ketamine and midazolam for interventional paediatric cardiac catheterisation by the cardiologist without the presence of an anaesthesiologist,[37] it is believed that the presence of an anesthesiologists who is a skilled practitioner in sedation, airway management, and resuscitation is mandatory.[38] Such a practice will allow the cardiologists to fully concentrate on their demanding technical tasks in this growing population of children having complex lesions undergoing complex procedures. A variety of agents such as propofol, ketamine, midazolam, fentanyl, and remifentanil have been used, for sedation but general anaesthesia with endotracheal intubation is also practised.

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Chapter 18: Anaesthesia Protocol for Adult Cardiac Surgery

Welcome to the Cardiac Operation Theatre

By going through the preceding chapters, the reader must have appreciated that cardiac anaesthesia and cardiac surgery have become a rapidly advancing and changing field. Newer techniques, newer medicines as well as monitoring devices are being continuously introduced. It is, therefore, easy to appreciate that there could be several effective and safe methods of conducting anaesthesia for a patient undergoing cardiac surgery. Indeed, the practice varies from centre to centre, although the anaesthetic principles remain the same.

The aim of this chapter is to outline the anaesthetic protocol that is being followed for adult cardiac surgery at G. B. Pant hospital. The author appreciates that this is but one method of anaesthetising the patients that has worked successfully in this hospital.

Anaesthetic Check List for Cardiopulmonary Bypass

Anaesthesia machine

- Switch on and check the machine
- Mapleson C circuit—test for leaks

- Oxygen (O_2), nitrous oxide (N_2O) and air sources plugged in correctly
- Vaporiser off and filled
- Ventilator: secure circuit and test for leaks

Intubation and Bag-mask ventilation

- Facemask (adequate sizes)
- Airway (size 2 and 3)
- Magill's forceps
- Heat and moisture exchanger filter with $EtCO_2$ port.
- Endotracheal tube: 7.5 or 8 mm for females, 9 mm for males
- Cut the endotracheal tube; generally 23 cm for adult male and 21 cm for adult female.
- Scissors
- Long catheter mount
- Laryngoscope
- Stilette (malleable)
- Gum elastic bougie
- Cuff inflating syringe
- K–Y jelly
- Thread, dynaplast and bandage for fixation of the tube

Monitoring trolley

- ECG, arterial and central venous pressure (CVP), $EtCO_2$, temperature, SpO_2, and activated clotting time.
- ECG cable and pressure transducers ready for use.
- Thermodilution Swan Ganz catheter and cardiac output (CO) monitor in selected poor risk patients.
- Transoesophageal echocardiogram (TOE)
- Defibrillator available with external paddles.
- Suction apparatus available.
- Check blood availability.

Syringe pumps

2 to 3 mounted on the right hand pole

Lay up

- Morphine 10 mL syringe 15 mg in 10 mL×3
  or
  fentanyl 10 ml syringe 500 µg in 10 mL×3
- Diazepam 2 ml syringe 10 mg in 2 mL
  or
  midazolam 5 mL syringe 5 mg in 5 mL (with the availability of fentanyl and midazolam, they are preferred over morphine and diazepam).
- Pancuronium 5 mL syringe 8 mg in 4 mL
  or
  vecuronium 5 mL syringe 8 mg in 4 mL
- Thiopentone 10 mL syringe 250 mg in 10 mL
- Calcium 10 mL
  gluconate
- Atropine 0.6 mg in 1 mL 2 mL syringe
- Scalp vein needle/Y-cannula 21/23 G
- Cannula 0elco/Optiva/Accucath) 22 G × 2
- Cannula Qelco/Optiva/Accucath) 14 G × 1
- Internal jugular lines:

  - Triple lumen
  - 2 mL syringe + blue needle.

- Pulmonary artery catheter if indicated.
- Temperature probe.
- Heparinised saline: 500 units in 500 mL.

  - 10 mL syringe of heparinised saline + T connector (for aspirating and flushing the arterial cannula).
  - 10 mL syringe of heparinised saline + 3 way tap (3 syringes for aspirating and flushing the lumen of triple lumen catheter).
  - 10 mL syringe of heparinised saline + 3 way tap + 200 cm pressure monitoring line for connecting the arterial cannula to the transducer.

- 500 mL Ringer’s lactate + wide bore blood transfusion set + 3 way tap +

wide bore drip extension set.

Anaesthesia trolley

Top

- Tray for anaesthetic drugs
- Syringe trays: 20,10,5, 2,1 mL
- Needle trays: 16,18,20, 22,24, 26 G
- Kidney tray or sharps disposal box for the used ampoules
- Three way taps

The various drugs and other material should be readily available and arranged in the drawers of the anaesthetic trolley.

Drawer 1

Milrinone
Noradrenaline
Amiodarone
Megnesium
Chlorpromazine
Phenoxybenzamine
EACA/TA

Dopamine
Isoprenaline
Adrenaline
Dobutamine
Verapamil
Diltiazem
Atropine
Diazepam
Midazolam
Heparin
Protamine
Nitroglycerin
Nitroprusside
Morphine
Fentanyl
Thiopentone

Propranolol
Metoprolol
Atenolol
Calcium—gluconate
Dexamethazone
Hydrocortisone
Efcorlin
Aminophylline
Sodium-bicarbonate
Xylocard
(2 percent vial)
KC1
Lasix
Pancuronium
Vecuronium

Drawer 2

- Adhesive plaster
- Scissors
- Towel clips
- Dressings (transparent and others)
- Labels

Drawer 3

- Glucose saline 500 mL × 2
- Ringer's Lactate 500 mL × 2
- Haemaccel/starch 500 mL 7 × 2
- Blood transfusion sets
- Dial-a-flow
- Microdrip sets with chamber

Preoperation

- Read all the case notes and investigations and check preanaesthetic check-up and consent.
- Confirm patient's identity/fasting status

Premedication

- All the oral drugs such as propranolol, nifedepine, etc.
- Morphine 0.2 mg/Kg and phenergan 25 mg, intramuscularly, 1 to 2 hours before operation.

Transfer to operation theatre

- Water blanket on table.
- Underneath towel to tuck over the arms later.
- ECG on.
- ECG electrodes for IABP, if necessary in sick patients
- ECG electrodes for TOE
- Preoxygenate if necessary (but usually not required).

- Y cannula or scalp vein needle in right hand and give morphine (3 to 5 mg)/fentanyl (50 µg) or diazepam/midazolam (1 mg), but not both.
- Left radial artery: percutaneous 22 G cannula, attach T-connector, then 200 cm extension line to the transducer. Strap securely and note blood pressure (BP) (use right radial artery for cannulation, if the left one is to be used as arterial conduit in patients undergoing CABG).

Induction

- Morphine: 10 to 30 mg (0.5 mg/Kg)
  or
- Fentanyl: 1 to 2 mg (10 to 20 µg/Kg) (decrease the dose appropriately, if early extubation is planned)
- Diazepam/midazolam: 2.5 to 5 mg (be careful as benzodiazepines in combination with opioids may lead to severe hypotension)
- Pancuronium: 6 to 8 mg
  or
- Vecuronium: 6 to 8 mg
- Thiopentone: 50 to 100 mg slowly

Note: The choice of doses should also be determined by the preoperative cardiovascular status of the patient. For instance, in a frail patient, restrict the dose of morphine/fentanyl and avoid diazepam/midazolam as it can lead to precipitous hypotension if used with opioids. Diazepam/midazolam can also be administered after intubation. Also, consider administration of incremental doses of induction agents.

- Intermittent positive pressure ventilation (IPPV) with 6 litres N_2O and 3 litres O_2, but increase the oxygen in sick patients.

Intubation

- Intubate with appropriate size endotra-cheal cuffed tube.
- Manual ventilation first and then switch over to mechanical ventilation [FiO_2 of 0.33 to 0.5 (N_2O/O_2)].

Peripheral venous cannula for infusion

- 14 G cannula: right hand/wrist, attach Ringer's lactate drip with extension looped to the head end.

Right internal jugular vein cannulation

- Triple lumen catheter.
  or
- 30 cm long 16 G central venous catheter (cavafix): 2 lines usually required either both in internal jugular vein (IJV) or one each in internal and external jugular vein.
  Introduce about 15 to 20 cm.
  Careful with aortic aneurysms, coarctation of aorta and aortic regurgitation (i.e. avoid carotid artery).
- 7 F Swan Ganz catheter in poor risk patients. (IJV catheter will not be required if Swan Ganz catheter is used).
  Connect the line to the transducer and note central venous pressure (CVP) or pulmonary artery (PA) pressure.

Note: In poor risk patients, the 14 G peripheral line and triple lumen or Swan Ganz catheter should be inserted under local anaesthesia before induction.

- Additional 5 F check flow in femoral artery for pressure monitoring or easy access for intra-aortic balloon pump (IABP) catheter later on in poor risk patients.
- Temperature probe.
- Nasogastric/orogastric tube.
- Tuck towel over arms and under trunk.
- Anaesthetic screen.
- Diathermy pad.
- Urinary catheter.

Patient is now ready for the surgical procedure.
Check the ventilation of the patient at this stage:

- Rate 12 to 16/min.
- Minute volume to give $PaCO_2$ of about 35 to 40 mm Hg.
- Bacterial/viral filter with heat and moisture exchanger.

Check CVP and BP.
Arm drip functioning well.
Additional doses of morphine/fentanyl may be considered at this stage if BP is high.
Fill in the anaesthetic chart.

Towel up:	One wing clipped to the right drip pole and the other clipped to the left hand pole. Both firmly clipped at the corners of anaesthetic screen. One manometer line from surgeon to transducer for on-table pressure measurements in selected patients.
Check:	Defibrillator-paddle leads passed from the table - switch on. Pacemaker availability.

Bleed the patient if Hb is >10 gm percent for autotransfusion.
Collect the blood in citrate phosphate dextrose (CPD) bag via central venous catheter, approximately 7 percent of estimated blood volume if Hb is 10 to 12 gm percent and 10 percent of the estimated blood volume if Hb is more than 12 gm percent.

Estimated blood volume (mL).

Males: 75 × weight in Kg.

Females: 65 × weight in Kg.

Simultaneously, perform TOE at this stage (standard views) and confirm the diagnosis. Also, note the myocardial contractility and volume status in the transgastric midpapillary view.

Blood pressure control

- Hypertension commonly occurs during surgery.
- Ensure that the patient has received sufficient analgesia (morphine/fentanyl).
- Halothane/isoflurane 0.5 to 2 percent.
- Give chlorpromazine 2.5 to 5 mg increments, if halothane/isoflurane is

not enough.

- Start nitroglycerin infusion (0.5 to 1 μg/Kg/min.) for patients undergoing coronary artery bypass grafting (CABG).
- Nitroprusside/nitroglycerin infusion (0.5 to 1 μg/Kg/min.) in patients undergoing mitral valve surgery with high PA pressure and aortic valve surgery for finer control of BP.
- Metoprolol/atenolol: 1 mg increments if heart rate is more than 100/min. and BP is not controlled with above measures.

Note: BP will often rise with the sternal split and fall 20 to 30 mm Hg when the heart is lifted by the sternal retractor.

Pancuronium/vecuronium: 2 mg increments, only if patient moves before CPB or rarely after one hour of induction, if bypass is not established by then.

Take samples for activated clotting time [(ACT), no heparin]: 5 mL syringe, and arterial blood gases (heparin), 2 mL syringe.

Disconnect ventilator during sternal split to avoid injury to pleura

Have ready

- Calcium gluconate: 10 mL syringe (not in aortic stenosis).
- Adrenaline 4 mg in 500 mL glucose saline.
- Dopamine 400 mg in 500 mL glucose saline (in addition to or with anticipated renal problem).
- Dobutamine 500 mg in 500 mL glucose saline (in poor risk patients).

Blood is rarely required before bypass.

Add pancuronium 4 to 6 mg, morphine (10 to 15 mg)/fentanyl (250 to 400 pg) and diazepam (5 to 10 mg)/midazolam (5 to 10 mg) to the pump prime.

Draw up heparin 3 mg/Kg.

Give heparin at the request of the surgeon, as he inserts aortic purse string. Usually given via central venous line, after aspirating blood to make sure, it is certain to reach the circulation.

Start timer as the heparin is given and record the time and dose on anaesthetic chart.

Check ACT 5 min. after the heparin dose. If less than 400 seconds give additional heparin in the dose of 1 mg/Kg (note, it is not safe to institute CPB, if ACT is less than 300 seconds).

On bypass

Partial bypass

When bypass commences

- Give 100 percent O_2
- Chart the time
- Turn off halothane/isoflurane
- Look at venous pressure: it should fall
- Look at arterial pressure: usually small pump pulsations only
- There should be no diaphragmatic movement

Record : Urine volume on the chart.
Temperature on the chart.

Total bypass

When ascending aorta is clamped, ventricular fibrillation (VF) or venae cavae snared.

- Ventilation to manual circuit
- Spill valve open: nil fresh gas flow
- Chart the time
- Start the timer for myocardial ischaemic time

Administration of cardioplegia

Delivered by the perfusionist by using one of the pump heads.
Record the amount delivered and time on the anaesthesia chart.

Chart major events only

- Commencement of CPB.
- Aortic cross clamp time
- Volume of pump prime
- Release of aortic cross clamp

Drugs on bypass

- Heparin repeated as half dose at one hour.
- 1/4th dose at 2 hours and every hour thereafter, if CPB continues.

- Pancuronium 2 mg after each hour of bypass.
- Morphine (5 to 10 mg)/fentanyl (100 µg) after each hour of bypass.
- Pancuronium 4 mg, if diaphragm moves.
- Chlorpromazine 5 to 10 mg sometimes indicated, if mean arterial pressure (MAP) is more than 100 mm Hg.
- Norepmephrine (5 to 10 mg), if MAP is less than 40 mm Hg.
- Thiopentone 25 mg increments at 5 to 10 min. interval while rewarming to prevent awareness. (Note: In patients undergoing normo-thermic bypass, begin thiopentone infusion at the onset of CPB (3 to 5 mg/min.) Alternatively, infusion of propofol (5 to 10 mg/hour) may also be considered.
- Check arterial blood gases every 1/2 hour on bypass (sample to be drawn from the pump).
- Monitor ACT every 1/2 hour during CPB. If less than 400 seconds at any stage, administer additional heparin in the dose of 1 mg/Kg. This dose will be in addition to the hourly dose of heparin that has already been described.

  Chart temperature and MAP at regular intervals and urine output at the termination of CPB and before transferring the patient to ICU.

Aortic clamp off

When the heart has been closed or distal coronary grafts have been completed.

- Assist de-airing (in open cardiac procedures), by giving a head down tilt to the table and gently ventilating the lungs.
- Coronary perfusion is restored after aortic clamp is released, but heart may be in VF.
- Charge defibrillator to 20 to 30 Joules.
- Shoot when requested by the surgeon.
- Observe both heart and ECG.
- Give 50 mg xylocard into the CVP line if more than one defibrillation is required.

End of bypass

- Recommence ventilation.
- Only 100 percent oxygen (no nitrous oxide).

- For safety reasons (not forgetting to initiate ventilation), start ventilation when final proximal vein graft is being sutured in CABGs and as soon as acceptable cardiac rhythm is established in other surgeries.
- In addition, gently breathe the patient using oxygen when the final cavity [e.g. aorta, left atrium (LA) or right atrium (RA)] is being tied.
- Recommence ventilation **WITHOUT FAIL.**
- LA pressure line will be inserted by the surgeon in some patients if necessary.

Coming off bypass

RA pressure, pulmonary capillary wedge pressure (PCWP) or LA pressure and appearance of the heart will guide you regarding optimum filling for an adequate systemic pressure.

Inotropes

Timely start inotropes if necessary e.g. patient with poor LV function, showing poor myocardial contractility, low BP with rising RA, PCWP or LA pressure. Take help of TOE, if available.

Off bypass

- Make sure ventilator is ventilating (oxygen only).
- No nitrous oxide. It can depress the myocardium and increase the size of air bubbles in circulation.
- Check:

  - inflation pressure.
  - tidal volume/minute volume.
  - lung movement.

Note: Time the end of bypass on chart.

Record BP, CVP, LA pressure and urine volume during bypass on chart.

Maintain optimum CVP/LA pressure by giving bagged pump blood, if Hb is more than 8 gm percent.

Transfuse autologous blood first, if collected (after protamine).

Consider transfusing fresh warm blood and cold blood thereafter.

Protamine

1.3 × initial dose of heparin given slowly when requested by surgeon (after venous decannulation).

Additional 50 mg, if bagged (heparinised) pump blood is given.

Blood sample

5 to 10 min. after protamine is completed (ACT and arterial blood gases).

If bleeding:

Think ahead and order blood well in advance.

Enough protamine? give 50 mg.

Consider transfusing FFP, platelets and warm blood.

End of operation

- Continue IPPV.
- If systolic BP more than 120 mm Hg, give halothane/isoflurane to ensure that patient remains settled during transfer to ICU and does not become hypertensive. Alternatively, give morphine (5 to 10 mg)/fentanyl (50 to 100 µg) or diazepam (2.5 to 5 mg)/midazolam (1 to 2 mg).
- Secure IJV line firmly.

Inotropes

Usually not necessary to run while transferring, but in fragile patients may be necessary. Run adrenaline infusion with syringe pump during transfer.

Transfer after clamping chest drains, removing all drips, and urine bag, unplugging ECG cable and finally disconnecting pressure line with three way tap attached. Leave arterial pressure display until last.

Transfer the patient with portable ventilator and ECG monitor.

Protocol for off-pump CABG

Patients undergoing off-pump CABG can be extubated early (within 4 hours of surgery). Therefore, the dosage of opioids should be appropriately reduced. For instance, induction dose of morphine can be decreased to 0.3 to 0.5 mg/Kg and that of fentanyl to 5 to 10 µg/Kg. In essence, the protocol is

similar to the one outlined above except for the following changes.

Heparin

- 1.5 mg/Kg before the coronary artery stabiliser (Octopus or Guidant) is placed on the myocardium.
- Repeat 0.75 mg/Kg heparin each hour to maintain ACT of ≥ 300 sec.

Placement of the coronary artery stabiliser leads to considerable haemodynamic instability, especially when it is placed on the lateral walls of the myocardium to stabilise the circumflex coronary artery (and its branches) or the right coronary artery. In order to maintain the haemodynamics, following manoeuvres can be performed:

- Infusion of volume: 100 to 200 mL of Ringer's lactate or colloid (tetrestarch).
- Trendelenburg position (10 to 20°).
- Dopamine (5 to 10 µg/Kg/min) or epinephrine (0.025 to 0.05 µg/Kg/min) can be infused.
- MAP of 70 mm Hg or more is desirable, but lower values (up to 60 mm Hg) may be accepted in exceptional situations.
- If it is difficult to maintain MAP of ≥ 70 mm Hg, the coronary stabiliser should be removed and the heart allowed to recover, before it is placed again.
- Monitor ECG, MAP, CVP and PCWP carefully during the anastomosis and try to maintain MAP of ≥ 70 mm Hg at all times with the help of intravenous fluids and inotropes.
- Sometimes, there can be substantial blood loss during the distal anastomosis. The following methods can be utilised for blood conservation.

  i. Acute normovolaemic haemodilution.
  ii. Use of cardiotomy reservoir to collect the blood lost from the operative field.
  iii. Use of cell saver to collect the blood lost from the operative field.
  iv. Combination of (i) and (ii) or (i) and (iii).

- Off-pump CABG can be converted into the conventional CABG with

cardiopulmonary bypass at any point of time. The usual criteria for such a decision are:

- Technical difficulty faced by the surgeon.
- MAP decreasing to very low values ($\leq$ 50 mm Hg) with PCWP rising to $\geq$ 20 mm Hg.
- Intractable arrhythmias and significant ST segment changes ($\geq$ 4 mm).
- Mixed venous oxygen saturation (SvO_2) < 60 percent.

Cardiac intensive care

- Attach to ventilator, giving 40 percent oxygen and aim to ventilate to a PaO_2 of 90 to 120 mm Hg and $PaCO_2$ of 35 to 40 mm Hg. Auscultate both sides of the chest for air entry.
- Attach radial artery pressure line to appropriate transducer and ensure that pressure is satisfactory.
- Attach CVP, PA, and LA pressure line (if present) to transducer, exclude air before flushing. Check the transducers for zero.
- Plug in ECG.
- Chest drains undamped.
- Tell the surgical resident, arterial and venous pressures, inotrope rate to be set on infusion pump and last potassium measurement.
- Immediate X-ray chest, ECG and routine arterial blood gases and electrolytes to be arranged by resident incharge.
- Sedate with morphine 3 to 5 mg.
- Many patients should be sufficiently stable, wide awake with good respiratory and cardiovascular parameters to come off the ventilator in 4 to 6 hours time. Some patients particularly those who have undergone valve surgery (with high PA pressure) and poor LV function should be ventilated overnight. For care of the patient on a ventilator, weaning methods, extubation etc. refer to chapter 15.

About the Book

Cardiac anaesthesia is an ever expanding field. The third edition of the **Clinical Practice of Cardiac Anaesthesia** has been updated throughout and many chapters have been made more comprehensive. In particular, the off-pump cardiac surgery, transoesophageal echocardiography, blood management techniques, and thoracic epidural techniques have been expanded to understand the current thinking on these subjects. A new chapter on cardiovascular physiology has been added. The focus has been to provide the latest and clinically relevant information without it being too extensive.

It has been written in a lucid style and simple language to help the practitioner with the clinical practice. It is very well illustrated making it easy for the reader to comprehend the subject. The colour pictures of transoesophageal echocardiography demonstrating the various cardiac conditions help the reader to understand this relatively new monitoring modality. It will be useful for the students pursuing the postdoctoral DM or DNB fellowship course in cardiac anaesthesia. In addition, it will be useful for all postgraduate students of anaesthesia, senior residents, and junior consultants working in the field of cardiac anaesthesia. Some chapters, such as those on haemodynamic monitoring, cardiac patient undergoing noncardiac surgery, postoperative management, and closed heart procedures will be useful for the anaesthesiologists practicing general anaesthesia.

About the Author

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A recipient of Commonwealth Medical Fellowship in the year 1989, Dr. Tempe enjoys excellent reputation as a teacher, researcher and cardiac anaesthesiologist not only in India but internationally. He was awarded the Dr. B.C. Roy National award (the highest honour in the field of Medicine in India) as an Eminent Medical Teacher in 2006. He was elected as the Fellow of the Royal College of Anaesthetists (FRCA, London) in 2009, and National Academy of Medical Sciences (FAMS) in 2010. He has contributed a chapter in the “Miller’s Anesthesia”, seventh edition, which is the leading textbook in anesthesia throughout the world. He has been the Chief Editor of the “Annals of Cardiac Anaesthesia” and is on the Editorial Board of the “Journal of Cardiothoracic and Vascular Anesthesia” and the “British Journal of Anaesthesia.” He has widely traveled around the world as an invited faculty for the various conferences including the World Congress of Anaesthesiologists.