19.1 Preoperative Assessment

Extensive preoperative assessment of the patient will have taken place by the transplant team, a multidisciplinary team dedicated to investigation and optimization of patients preoperatively. This chapter focuses on the preoperative assessment by the anesthetist prior to theatre, and describes important aspects of the history, examination and investigations that influence anesthetic technique and drug choice.

As with all patients undergoing surgery the anesthetist assesses them before the procedure and collates the evidence to plan perioperative care. They may also have been part of the work-up team. Past medical history is noted systematically, including associated complications, and any changes in symptoms or physiological state, for example a reduced exercise tolerance, which will instigate further investigations preoperatively. Airway assessment is important in any preoperative visit, particularly investigating for any indications for a rapid sequence induction (RSI).

Predictable comorbidities, such as diabetes and cardiovascular disease, are well known and these are likely to have been well investigated and treated before the patient reaches the transplant list. Each patient will also have predictable morbidity associated with their underlying pathological process, and for this reason they are cared for by specialist transplant teams. Generally, they are high risk patients undergoing major surgery and careful planning cannot be underestimated. Examination of the patient will likely reveal stigmata of the underlying process and/or their comorbid state.

Allergies are documented, particularly any issues with antibiotics and immunosuppressants that may affect the perioperative care or need to veer from protocol.

19.2 Investigations

Extensive investigation is important in patients presenting for transplantation. As part of the referral process and decision making on the patient’s appropriateness for transplant they will have had laboratory blood work, imaging, and cardiovascular and respiratory function work up. Depending on their medical history the patient will have had further input from the appropriate specialty, for example endocrinology.
Optimization of abnormalities, such as anemia, can be made preoperatively, but many patients will still need more up-to-date laboratory investigations and an updated electrocardiogram (ECG) on the day of admission, particularly since many medications can interfere with the patient’s biochemistry.

Some patients will be critically unwell, such as those for liver transplant, and may require concomitant resuscitation and life-saving surgery, and investigations such as arterial blood gases will provide further information and point of care coagulation testing perioperatively is also required. Optimization in the critical care area preoperatively may focus on fluid balance and inotropic and/or vasopressor support as a bridge to transplant.

19.3 Preparation of the Patient

Immunosuppressant drugs are sometimes started preoperatively. Liaison between teams is vital to ensure protocols are followed. The surgical brief provides an opportunity to discuss the immunosuppression in addition to ensuring theatre team introductions, the discussion of anticipated surgical and anesthetic events, and to address concerns.

Premedication for anxiolysis may be given in certain circumstances, such as heart transplant patients, but are not routine for other organ transplants. Premedication to treat gastroesophageal reflux/prophylaxis of aspiration of gastric contents is given in at risk patients, and a decision communicated with the preoperative staff regarding which of the patient’s usual medications are to be given and fasting time.

Preoperative checks include appropriate consent for the procedure, ensuring adequate blood products are available or have been requested ahead of surgery, and organizing the appropriate postoperative destination, i.e. has a critical care bed been booked for postoperative care.

The anesthetic team should explain the anesthetic risk, postoperative expectation to the patient, including destination and analgesia options, and insertion of invasive lines.

19.4 Intraoperative Considerations

The considerations for each type of transplant surgery are discussed in detail in the relevant section.

General measures include:

- Monitoring; routine monitoring is applied regardless of procedure, invasive monitoring should be considered if indicated, though may be routine in some transplants
- Immunosuppression; already mentioned but is common to all transplants and careful planning is necessary
- Prophylactic antibiotics; local protocols exist for these and with immunosuppression and underlying comorbidities, such as diabetes, these are vital
- Venous-thromboembolism prophylaxis; the stress response to surgery should not be underestimated and the risk of thrombosis in the perioperative period is significant therefore this is part of the perioperative care plan
- Temperature control and pressure area care; hypothermia has significant implications perioperatively and normothermia must be maintained, except for thoracic organ transplantation where hypothermia is targeted. Pressure areas are vulnerable in these patients and long procedures mean careful positioning is paramount

Many centres will have their own protocol for the perioperative care of transplant patients, and a common-sense approach is also required to maintain a balance between adequate anesthesia, analgesia, and cardiovascular stability.

19.5 Postoperative Considerations

Postoperative care is vital to ensure the viability of the newly transplanted graft. Continued optimization of hemodynamic stability and oxygen delivery means the patient must be cared for in the appropriate environment. Most patients will
return to the critical care unit postoperatively, either for level 3 or level 2 care depending on organ support requirement. The exception in our institute is renal transplant recipients, who return to the renal ward postoperatively for ongoing care from the medical and surgical teams, unless there is a clear indication for critical care admission.

The anesthetic management of each organ transplant procedure is described in the following sections.

19.6 Heart Transplantation

The anesthetic management of heart transplant patients before, during and after transplantation presents some specific problems for the anesthetist which may influence early and late results.

19.7 Preoperative Management

As increasing the time taken to implant the donor heart affects 1-year mortality, the procedure is carried out as an emergency [1]. However, the transplant program usually ensures that patients are in the “best possible shape”. Similarly, the potential “full stomach” rarely occurs because the transplant coordinator should make sure that suitable candidates are getting prepared and fasting. The importance of a coordinated approach and excellent communication between “donor team” and “recipient team” to ensure the optimal timing of the various procedures should not be underestimated.

The patient should be assessed preoperatively by the anesthetist and note made of any previous anesthetic, medical and surgical histories. If the patient is undergoing ‘re-do’ sternotomy, then surgery is more technically challenging, increased time must be allowed for the initial stages of surgery and there is potential for major hemorrhage accessing the mediastinum. Most patients are receiving diuretics and may have low potassium levels whilst other drugs may influence anesthesia; e.g., ACE inhibitors occasionally result in a low systemic vascular resistance during cardiopulmonary bypass. In addition to their cardiac disease many patients have reversible impairment of their respiratory, renal and hepatic function and where time allows these should be addressed.

It is necessary to ensure that information from all relevant investigations is available. These include ECG, urea and electrolytes (U + Es), liver function tests (LFTs), full blood count (FBC), coagulation, chest X-ray and tests of cardiac function. Any abnormality should be corrected preoperatively. The patient should be cross-matched for 4 units of concentrated red cells and there should be fresh frozen plasma (FFP) and platelets available, particularly for those with preexisting abnormalities of coagulation, which will be compounded by cardiopulmonary bypass. Most of these patients would have been assessed regularly by cardiologists and there should be recent angiograms and echocardiograms to estimate the residual cardiac function. Patients are usually on optimum medical therapy and although “sick” there is rarely if ever any reason for cancellation to improve the preoperative status.

Increasing numbers of patients are inpatients in critical care areas and are receiving inotrope infusions pre-operatively to support cardiac function whilst awaiting a donor heart. Internationally, 43% of patients receiving heart transplantation receive Mechanical Circulatory Support (MCS) at the time of transplant. The most commonly used method is Left Ventricular Assist Device (LVAD) support, but other devices that may be in situ are Right sided VADs, Intra-Aortic Balloon Pumps, Extra-Corporeal Membrane Oxygenation (ECMO) and total artificial heart devices [2]. The aim of LVAD support as a bridge to transplant is to improve end organ function, nutritional status and physical fitness to improve survival post-transplant. These patients are usually anti-coagulated, and this should be reversed appropriately prior to surgery. Risks of MCS include clotting factor deficiency, acquired VWD, risk of infections from the device, heparin induced thrombocytopenia, and hemorrhage secondary to anticoagulation [2].
19.8 Intraoperative Management

The principles of anesthesia for other types of cardiac surgery apply and many different anesthetic agents and techniques have been used. The technique of choice varies according to individual transplant centers. There is no evidence that any one technique leads to a better outcome than any other. There is much preparation to be done prior to the arrival of the patient in the anesthetic room (Table 19.1), and transfer to theatre of patients with MCS and inotropic infusions is a challenge requiring careful co-ordination. In order to ensure a timely implantation of the donor heart, effective communication between the organ retrieval and transplant team is vital.

As mentioned earlier, most patients should have been fasted for 6 h and it can be argued that a rapid sequence induction is not appropriate in a patient group with such poor cardiovascular reserve. In addition to standard monitoring, invasive arterial blood pressure monitoring should be inserted prior to induction of anesthesia. Large bore IV access should be achieved. Some anesthetists insist on a central line being inserted prior to induction, in order to facilitate a timely start to surgery after induction of anesthesia, however others feel this is an unnecessary stress on the patient. The patients are preoxygenated. Indeed, most will come down to theater with oxygen. Once all monitoring is established the patient is induced with high dose opiate (in the author’s institution remifentanil target-controlled infusion is used), an IV induction agent ± midazolam. A muscle relaxant is administered, and the trachea is then intubated. Anesthesia is maintained according to local habits with propofol by infusion or with inhalational agents such as sevoflurane. Nitrous oxide is best avoided in view of its cardio-depressant activity and the risk of increasing the size of any air embolus.

The central line and urinary catheter may then be placed if not already in situ. There is variation between centers in the site of placement of the central line, some centers insisting on the left internal jugular vein so that endocardial biopsies may be carried out via the right side. Other centers use the femoral vein for endocardial biopsies. A Swan-Ganz catheter if used would need to be pulled back during the procedure and then re-advanced across a suture line. Therefore, it is not universally used initially. All invasive procedures require strict aseptic techniques in view of the patient’s impending immunocompromise.

Blood gases, U + Es, activated clotting time (ACT) and thromboelastography (TEG) are done as a baseline. The cardiopulmonary bypass pump is primed with 1.5 1 of crystalloid or colloid and this has a significant dilutional effect when the patient is on bypass. Most anesthetists aim for a hematocrit (HCT) of no less than 20% whilst on bypass. If less than this, concentrated red cells are added to the pump. If the preoperative HCT is less than 30%, the requirement for red cells is almost

### Table 19.1  Set up prior to arrival of patient in anesthetic room

| Equipment: | |  |
|---|---|---|
| Infusion pumps—at least 4 | Pressure transducers—at least 3 | CVP line |
| Arterial line | Nasopharyngeal and peripheral temperature probes | Urinary catheter |
| Pulmonary artery catheter (used in some centers) |  |

| Drugs: | |  |
|---|---|---|
| Resuscitation | Atropine | Calcium chloride |
| | | Metaraminol |
| | | Epinephrine (adrenaline) |
| Inotropes | Dobutamine | Norepinephrine (noradrenaline) |
| | Epinephrine (adrenaline) | Milrinone (if increased pulmonary artery pressure and possible right ventricular failure) |
| | | Vasopressin |
| Anesthetic | Remifentanil | Midazolam |
| | Rocuronium | Propofol infusion |
| Others | Methylprednisolone (500 mg at induction, then before removal of Aortic Cross Clamp) | Tranexamic acid |
| | Heparin | Protamine |
| | Antibiotics according to local protocol | Immunosuppressive agents according to local protocol |
Tranexamic acid is infused according to local protocols to stabilize clot formation and reduce bleeding [3]. A transesophageal echocardiography probe is inserted, and a comprehensive examination is performed to assist fluid, inotrope and vasoconstrictor therapy, both in the native heart and the allograft post-implantation.

Once the heart and bypass cannulas insertion sites have been prepared, intravenous heparin is administered, and the patient put on cardiopulmonary bypass. When the pump is at full flow, the ventilation from the anesthetic machine may be terminated, however there is some evidence that continuing positive pressure ventilation at low minute ventilation reduces perioperative inflammatory mediator release and improves oxygenation after weaning CPB [4]. It is customary in UK practice to cool the patient during bypass to around 28–32 °C. A mean blood pressure of 40–80 mmHg is aimed for, although these figures are entirely arbitrary, and the blood pressure may be manipulated by altering the rate of the anesthetic agent, by use of an inotropic or pressor agent or, rarely, a vasodilator. The perfusionist usually repeats blood gases and ACT half-hourly while on bypass. Before the removal of the aortic cross clamp in the donor heart it is necessary to re-administer the dose of methylprednisolone. Some centers administer magnesium slowly during bypass to decrease postoperative atrial arrhythmias.

With the anastomoses complete and the patient rewarmed, cardiopulmonary bypass is terminated by first reventilating the patient and then decreasing the flow from the bypass pump while watching the patient’s response. Due to the ischemic period from explantation to implantation it is usually necessary to administer inotropes at this point. It is customary to start them or increase them prior to the end of bypass, and they are likely to continue for several days post-operatively. The choice of agent is centre dependent, with no evidence of one regime’s superiority [5]; in our institution the first-choice agents are dobutamine and norepinephrine. The new heart is denervated, and as such has an intrinsic rate of 100–120 beats per minute and responds to circulating catecholamines rather than direct autonomic stimulation. It is normally only able to increase its output by increasing its stroke volume. Conduction abnormalities including complete heart block are common and epicardial pacing wires are routinely placed in our institution, with some patients going on to require permanent pace makers later.

Once the surgeon is satisfied with the integrity of the anastomoses and the patient’s cardiovascular stability, systemic anticoagulation is reversed with protamine. Owing to the long period of CPB and inflammatory response to surgery, coagulopathy is common. Coagulation studies, TEG and ACT should be checked, and blood and blood products administered accordingly upon administration of protamine. Once surgery is complete the patient is admitted to the intensive therapy unit (ITU) postoperatively.

### 19.9 Postoperative Management

Care of this patient group is complex. The patient is intubated and ventilated, has multiple invasive monitoring lines and inotropic infusions, and has potential for multiorgan dysfunction. Due to the large doses of immunosuppressant medication administered, the patient is nursed in isolation.

Bloods and blood gases are checked regularly, with any abnormality corrected. Mediastinal and intercostal drain outputs are monitored as the patient has potential for hemorrhage, coagulopathy and cardiac tamponade. If the risk of bleeding is deemed high, then the chest may be left open to prevent tamponade and closed once the patient is more stable [6]. Echocardiography is performed regularly to monitor ventricular function, guide therapy and to identify signs of primary graft failure. Endocardial biopsy is the most sensitive and specific index of graft rejection and is performed every 5–7 days for the first 4–6 weeks.

Primary graft failure is defined as allograft dysfunction that occurs within the first 24 h following transplantation not attributable to other causes. It is the leading cause of early mortality and has a 2–36% incidence in the early post-op period. Treatment is initially with pharmacotherapy, and then can be escalated to MCS if necessary [6].
Disturbances of cardiac rhythm are common in the early postoperative phase. Supraventricular dysrhythmias are the most common postoperative arrhythmia. These abnormalities respond to treatment with standard antidysrhythmic drugs and cardioversion if necessary, however may be a sign of primary graft failure, and thus should be investigated [6].

There is potential for acute kidney injury postoperatively, potentially making fluid management problematic. Initially, in the face of oliguria, loop diuretics may be needed to prevent volume overloading of the right ventricle, but if this is unsuccessful then RRT should be instituted early to control fluid balance [7].

19.10 Right Ventricular Failure

The right ventricle’s (RV’s) thin walled structure makes it particularly at risk of failure from the ischemic time after harvest from the donor. In addition, the anterior position of the right coronary ostia makes passage of air bubbles down the right coronary artery more likely, and the donor heart is naïve to the high pulmonary artery pressures of a chronic heart failure patient. The patient is invasively ventilated causing deleterious effects on pulmonary vascular resistance (PVR). The result is a particular vulnerability of the RV to failure post-transplant, and its management is challenging.

Central venous pressure (CVP) can be used to guide RV filling pressure, and TOE can help to assess RV size and function. Flattened appearances of the interventricular septum, increased chamber size and increased tricuspid regurgitation are signs of a volume or pressure overloaded RV.

Initial management includes correcting hypoxia, hypercarbia and acidosis with the aim of lowering PVR and RV afterload. Volume overload can be treated with diuretics and renal replacement therapy if needed. Alongside other more commonly used inotropes to increase contractility, milrinone can be used for its lowering effect on PVR. Nitric oxide can be added to inhaled gases, acting locally as a pulmonary vasodilator with minimal systemic absorption, it also lowers PVR. If these measures fail, then VAD therapy can be considered [3].

19.11 Lung Transplantation

Lung transplantation is, in fact, a group of operative procedures comprising single-lung transplant, bilateral sequential lung transplant, lobar transplant and en-block heart-lung transplantation.

COPD, interstitial lung disease, and bronchiectasis (including cystic fibrosis) are the commonest reason for lung transplantation worldwide (36.5%, 29.7% and 18.5% respectively), with pulmonary hypertension and other less common diseases making up a minority of cases. Bilateral sequential lung transplants make up the majority of transplants. The vast majority (85%) of single lung transplants are performed in patients with COPD or ILD, compared to a greater spread across varying pathologies for bilateral sequential transplants [7].

19.12 Preoperative Management

The patient should be seen preoperatively by the anesthetist and particular attention should be paid to past medical, surgical and anesthetic histories. These patients are often oxygen dependent and are unable to tolerate any exertion. It is necessary to assess their cardiovascular and respiratory systems in some detail with regard to function of the right and left ventricles, the presence or indeed absence of pulmonary hypertension, their exercise tolerance, the degree of impairment they currently suffer, and the possible presence of any other system involvement.

The majority of these patients would have undergone a battery of tests. Pulmonary function tests, exercise tolerance tests, full blood count, urea and electrolytes will have been performed prior to listing. Imaging investigations undertaken may include CT of chest which also allows identification of coronary artery calcification, coronary angiography, transthoracic echocar-
diography to assess ventricular function and estimation of pulmonary artery pressures, and lung perfusion scanning to assess suitability and site for single lung transplantation. Microbiology can be useful in identifying colonization with drug resistant bacteria [8]. It should always be remembered that the clinical situation may have deteriorated since those assessments.

Caution is advised with premedication in patients with COPD, as one should aim to avoid respiratory compromise, but it may, in fact, be beneficial in patients with pulmonary hypertension. Some centers would advise the use of agents which decrease airway secretions. Virtually all patients should come down to theater with supplemental oxygen.

19.13 Intraoperative Management

There is much preparation involved prior to the patient’s arrival in theater (Table 19.2).

The patient is identified in the anesthetic room and routine monitoring (ECG, pulse oximetry) established. An arterial line is placed under local anesthesia for sampling purposes and for direct measurement of blood pressure. Opinion varies as to whether the Swan-Ganz catheter should be inserted prior to induction. However, it is certainly recommended in view of the severe cardiovascular instability which may be associated with one lung ventilation. It will normally float to the side with preferential perfusion, but its position should be checked intraoperatively and prior to stapling of the pulmonary artery—if necessary it can be pulled back and reloated. If a Swan-Ganz catheter is not used a CVP line should be inserted to aid decisions on fluid replacement. An epidural catheter is frequently inserted prior to induction.

Particular attention should be paid to the possibility of reactive airways and hemodynamic instability at induction of anesthesia due to the effect of anesthetic agents on coronary perfusion pressure and myocardial contractility. Either a right- or left-sided double lumen tube may be employed but a left-sided tube is preferable since it avoids the risk of non-ventilation of the right upper lobe and is usually easier to place. The position of the tube should be checked by fiberoptic scope at this point and again later once the patient has been positioned on the operating table. In cystic fibrosis patients it may be beneficial to insert a single lumen tube initially to enable flexible bronchoscopy and removal of tenacious secretions to air ventilation intra-operatively and reduce bacterial contamination of the new lungs. This can then be changed to a double lumen tube prior to the start of surgery [9, 10]. Where necessary in bilateral sequential lung transplant, the endobronchial lumen of the tube may be retracted at the time of bronchial transection of the second lung while ventilation is continued to the first transplanted lung. A nasogastric tube is usually placed prior to the start of surgery.

It is not uncommon to encounter hypotension following induction due to several factors, including tamponade secondary to overdistension of the lungs and impaired venous return with positive pressure ventilation, decreased right ventricular output due to increased pulmonary vascular resistance, withdrawal of the preexisting circulating catecholamines associated with anxiety, and the effects of the anesthetic agents. The treatment

| Table 19.2 Preparation for lung transplantation |
|-----------------------------------------------|
| **Equipment** | Double lumen tube          |
|               | Transducers—at least 3     |
|               | Infusion pumps—at least 2  |
|               | CVP line + Swan-Ganz catheter |
|               | 20-gauge arterial line      |
|               | Urinary catheter           |
|               | Core temperature probe     |
|               | Transesophageal echo       |
| **Drugs:**   |                             |
| **Anesthetic** | Propofol                   |
|              | Rocuronium                  |
|              | Fentanyl/alfentanil/remifentanil |
|              | Midazolam                   |
| **Resuscitation** | Ephedrine               |
|                | Metaraminol                |
|                | Epinephrine (adrenaline)   |
| **Inotropes** | Dobutamine                 |
|               | Norepinephrine (noradrenaline) |
|               | Epinephrine (adrenaline)   |
|               | Milrinone                  |
|               | Nitric Oxide               |
| **Miscellaneous** | Antibiotics               |
|                  | Immunosuppressive agents according to local protocol |
of this hypotension should address its cause and usually includes optimization of volume status, inotropes and minimizing intrathoracic pressure.

Intra-operative transesophageal echocardiography is of use for several reasons. It allows assessment of ventricular and valvular function, identification of cardiac defects that require surgery (e.g. atrial septal defect), patency of vascular anastomoses, identification of the presence of air bubbles, and assessment of volume status [11].

Maintenance of anesthesia is with oxygen in air if tolerated and either inhalational anesthesia or a propofol infusion. Theoretically volatile agents affect hypoxic pulmonary vasoconstriction and may affect ventilation perfusion matching, however long-term outcome has not been proved superior with either method and technique varies from centre to centre [11, 12].

### 19.14 Intraoperative Problems

Several problems may be predicted intraoperatively.

Following the start of one lung ventilation (OLV) several problems arise due to the significant effects it has on airway pressure, oxygenation and hemodynamic stability. Patients with restrictive disease may require a smaller tidal volume and increased rate while those with obstructive disease may require an increased expiratory phase to decrease air-trapping. It is not unusual to have to manipulate the ventilator settings to try to maintain the patient’s oxygenation with reasonable airway pressures. On occasion it may be necessary to institute some form of differential lung ventilation (continuous positive airway pressure or oxygen insufflation to the non-ventilated lung) to minimize intrapulmonary shunting.

Some patients develop cardiac or respiratory instability during the procedure. This may be due to inadequate oxygenation, especially during one lung ventilation, or right ventricular failure after clamping of the pulmonary artery. However, it may also be due to hyperinflation of the lungs and air trapping in COPD patients, this in turn leading to decreased venous return, decreased cardiac output and systemic hypotension. In patients with COPD it may be necessary to allow the carbon dioxide levels to rise (permissive hypercapnia) [12]. Respiratory acidosis may then become a problem, however.

Right ventricular failure and associated hypotension may become a major problem after the pulmonary artery has been clamped and those with restrictive diseases may require pulmonary vasodilators to reduce pulmonary vascular resistance, an infusion of prostaglandin E1 has the disadvantage that it also produces systemic vasodilation and arterial hypotension and may worsen oxygenation by increasing intrapulmonary shunting. It may therefore be necessary to use pressor agents to maintain systemic blood pressure. Another option is addition of nitric oxide to inhalational gases. It causes vasodilation of the pulmonary vasculature alone and has no effect on systemic pressure. Despite a lack of evidence on long-term mortality, in some institutions it is considered the drug of choice for the management of pulmonary hypertension. If medical management of cardiovascular instability fails, then mechanical circulatory support (MCS) may be instituted.

Traditionally, heparinization and institution of cardiopulmonary bypass (CPB) has been used for MCS during lung transplantation. Due to high anticoagulation dose and inflammatory response this has been associated with increased blood product administration, increased duration of ventilation and increased duration of ICU stay when compared to no mechanical support. Increasingly, Extra-corporeal Membrane Oxygenation (ECMO) is being used as a method of MCS in these cases. Advantages of its use are a reduction of pulmonary artery pressure aiding right ventricular function, improved gas exchange during one lung ventilation, and the facilitation of gentle reperfusion of the newly implanted lung. There is also evidence of reduced rates of primary graft dysfunction and reduced bleeding post-operatively when compared to CPB [12, 13].

After implantation, the pulmonary artery is slowly unclamped over 10 min, and the lung is recruited and ventilated. There is potential at this stage for cardiovascular instability as cold acidic products of metabolism, and air emboli
are washed into the coronary circulation. TOE is useful at this stage for identification of problems listed previously. A positive end-expiratory pressure of approximately 5–10 cm of water is added to allow adequate oxygenation while keeping the inspired oxygen concentration low. It should also help to minimize alveolar transudate. Occasionally the transplanted lung may exhibit a “pulmonary reimplantation response” which manifests as a low pressure pulmonary edema, poor oxygenation and poor lung compliance. This is now thought to be due to ischemia-reperfusion injury but may also be related to denervation and loss of lymphatic drainage of the transplanted lung. It is occasionally accompanied by pulmonary hypertension and the treatment for this has already been outlined.

19.15 Postoperative Management

Patients are admitted to a single room in the ITU postoperatively. It is customary to change the double lumen endobronchial tube to a single lumen tube at the end of the procedure. Immunosuppressive therapy is continued as per local protocol.

There are several areas of importance in the management of these patients.

19.16 Ventilation

Primary graft dysfunction (PGD) is the commonest cause of post-operative mortality and occurs in 10–57% of patients [10]. Its presentation is analogous to ARDS, and the principles of management are similar.

The aim in all patients is to achieve adequate oxygenation with the lowest inspired oxygen concentration possible and to minimize peak airway pressures, both intra and post-operatively, as this has been shown to reduce rates of PGD. Tidal volumes should be set to 7 ml/kg ideal body weight of the donor if known to avoid over distention and volutrauma, and peak inspiratory pressure should be minimized to less than 30 cmH20 to minimize barotrauma to the newly implanted lungs. MCS is associated with greater incidence of PGD, so bronchoscopic toilet may be beneficial in optimizing ventilation in order to avoid this intervention. The International Society of Heart and Lung Transplant (ISHLT) also recommend cautious use of IV fluids in these patients to optimize gas exchange [8].

The postoperative ventilatory management is impacted upon by the specific procedure performed and the underlying condition. In patients undergoing single-lung transplant for COPD the more compliant native lung will be ventilated preferentially. Long expiratory time to account for obstructive air flow and a lower respiratory rate would be beneficial in this patient group. In patients who have undergone a single-lung transplant for restrictive lung disease, the majority of ventilation occurs in the more compliant newly implanted lung, risking over inflation and ventilator induced lung injury (VILI), and tidal volumes may need to be reduced. Independent lung ventilation using a double lumen endobronchial tube may be employed in these instances, however this requires larger levels of sedations and ECMO or extra-corporeal CO2 removal strategies may be of benefit [10].

In patients receiving bilateral sequential lung transplantation, the same lung protective ventilation strategies are employed as above. If the allograft is undersized compared to the recipient, then using recipient IBW for TV setting may cause overdistention of the new lungs and so donor size should influence TV choice. If gas exchange is so poor that lung protective ventilation does not meet requirements, then ECMO can be employed to allow satisfactory ventilator settings. Singe cannula VV ECMO techniques allow reduced sedation rates and may be beneficial.

19.17 Hemodynamic Instability

It is essential that preload and afterload are optimized in these patients. There is debate regarding how much crystalloid can safely be given to these patients without effect on the graft and it is not unusual to administer diuretics to
these patients rather than try to give them a fluid load to aid urine output.

Hemorrhage postoperatively is not uncommon, more so in those patients who have required MCS for the procedure. MCS is associated with increased blood transfusion requirements (both concentrated red cells and blood products). Pulmonary hypertension and PGD can influence postoperative recovery and the management of pulmonary hypertension has been discussed. It is prudent to mention that prolonged treatment with nitric oxide may lead to transient methemoglobinemia.

19.18 Analgesia

Thoracotomy pain is said to be one of the most severe types of pain and this in turn can lead to severe respiratory impairment in this group of patients. The provision of postoperative analgesia is complicated by pulmonary denervation, the size of surgical incision and any residual impairment of pulmonary function. Analgesia can be provided by two routes—epidural analgesia and intravenous opiates—either by bolus, infusion or once the patient wakes up, by Patient Controlled Analgesia. Epidural analgesia where possible should be considered the standard form of analgesia for these patients. A thoracic epidural catheter may be sited with the patient awake prior to the start of the procedure assuming there are no contraindications (such as patient refusal, coagulopathy, heparin treatment, sepsis) and may be used both intraoperatively and postoperatively. Each institution usually has its own cocktail of drugs for infusion, but a common regimen is 0.1% L-bupivacaine plus 10 μg of fentanyl per ml infused at between 3 and 8 ml/h. Epidural analgesia decreases the time to extubation and reduces ITU length of stay, resulting in excellent postoperative analgesia when compared to intravenous opioids [14]. In those patients requiring CPB and therefore the use of intraoperative heparin for systemic anticoagulation, epidurals are best avoided in view of the risk of epidural hematoma, although some institutions would dispute this.

19.19 Liver Transplantation

Liver transplantation is the sole definitive treatment for end-stage liver disease [15]. Liver failure may be acute or chronic, with end-stage liver disease (ESLD) related to chronic liver disease the most common indication(s) for liver transplant [16]. The anesthetic considerations in managing such patients is complex and requires meticulous planning, with some nuances in the management between chronic and acute liver failure transplant patients.

Pre-operative assessment in chronic liver disease patients is extensive and involves a multi-disciplinary team approach (for example, hepatologist, transplant surgeon and anesthetist, intensive care physician, transplant coordinator, and other health care professionals, such as psychologist or dietician) before being placed on the transplant list [16]. Acute or fulminant hepatic failure patients require a more truncated, but thorough, work-up prior to potential transplantation.

There are many systemic changes associated with liver disease that make the management of patients with ESLD challenging peri-operatively. Every opportunity should be taken to optimize hematological, biochemical, and physiological parameters where able, and medical co-morbidities such as ischemic heart disease or associated cardiomyopathy. Cardiopulmonary events are the leading cause of non-graft related deaths in liver transplant [16] therefore detailed evaluation of function and physiological reserve of these systems is crucial.

Preoperative assessment includes the investigation and treatment/optimization of:

- Jaundice, hyponatremia, ascites, and pleural effusions
- Diabetes
- Cardiac failure and systemic vasodilation with hypotension
- Renal impairment
- Porto-pulmonary and hepatopulmonary syndromes
- Varices
- Coagulopathy
- Nutritional state and muscle mass
Routine investigations (Table 19.3) will vary depending on the nature of transplant, i.e. waiting list transplants or acute transplants in fulminant hepatic failure, and clinical picture of the patient. Drug handling is altered in liver disease, including drugs of anesthesia and analgesia. The metabolism of drugs used during anesthesia may be altered due to:

- decreased serum albumin and abnormal protein binding
- altered volume of distribution
- decreased hepatic blood flow and extraction ratio
- decreased number of functioning hepatocytes
- altered hepatic biotransformation
- decreased hepatic clearance
- altered pharmacodynamics

The management of general anesthesia is discussed further below.

### 19.20 Preoperative Management

By nature of end stage liver disease (ESLD) the patient may be critically ill preoperatively, and perhaps encephalopathic. Consent should be sought prior to any cognitive impairment, but there may be a necessity to use appropriate consent forms for patients who are incapacitated.

The case anesthetist will assess the patient preoperatively paying attention to comorbidities and up to date investigations. A full anesthetic history is also taken. If there are abnormalities further intervention is guided by these findings, for example uncorrected coagulopathy. In the event of fulminant hepatic failure, intracranial pressure monitoring may be used peri-operatively; this is routine in our local liver unit for such patients, occasionally jugular bulb oxygen saturation monitoring is used. Critically ill patients may require renal replacement therapy preoperatively and decisions should be made regarding its potential continuation intraoperatively.

Premedication for anxiolysis is not routine but may be considered, for example temazepam orally 1–2 h preoperatively. Gastric acid reduction/prophylaxis of gastric acid aspiration is given: our local unit uses ranitidine orally, if the patient isn’t already on a proton pump inhibitor, the night before and morning of surgery.

### 19.20.1 Blood Products

Blood loss is very variable and cell salvage is used intraoperatively, with the severity of pre-
transplant liver disease, as calculated using the model for end-stage liver disease (MELD), strongly predictive of the need for peri-operative transfusion support [16]. The number of cross-matched packed red blood cell (PRBC) units requested pre-operatively has decreased with newer surgical techniques, the use of cell salvage, and maintenance of a low central venous pressure intraoperatively. Complex cases or re-transplants are likely to require more consideration regarding cross-match requirements. Preoperative PRBC cross-match is likely to be between 5–10 units with the use of other blood products guided by preoperative coagulation tests, including point of care (POC) coagulation testing, which is repeated perioperatively.

Treatment of coagulopathy is likely to include transfusions of fresh frozen plasma (FFP), platelets, and perhaps cryoprecipitate. There is no consensus on the optimum regime or threshold for treatment, and practice is variable across the continent(s), for example coagulation factor concentrates are used widely in mainland Europe but the United Kingdom generally uses FFP. Our local transplant unit advocates considering pre-thawing of 4 units of FFP to treat intraoperative coagulopathy.

19.21 Intraoperative Management

19.21.1 Pre-induction Preparation

In addition to pre-operative patient assessment and blood product preparation, further planning of the intra-operative management is required before induction of anesthesia.

19.21.1.1 Monitoring and Equipment

Waiting list patients may be hemodynamically stable, and therefore the use of routine monitoring requirements should be used before induction of anesthesia. Additional monitors include peripheral nerve monitoring when neuromuscular blocking drugs are used, and temperature in procedures longer than 30 min.

Invasive arterial blood pressure monitoring may be used pre-induction in unstable or critically unwell patients, the arterial line sited after local anesthetic infiltration. All other access lines will be inserted post induction.

The appropriate number of infusion pumps, a rapid infuser for intravenous fluids and blood products, and cell salvage equipment should be available for all cases. Transesophageal echocardiography (TEE) is used in some centres [15] but may be complicated in those with known esophageal varices.

19.21.1.2 Lines

All large blood vessel access lines are performed aseptically with full surgical scrub by the anesthetist and using real-time ultrasound guided insertion. Below are the lines used in our local transplant unit:

- Right internal jugular vein: quad lumen central venous catheter (CVC); 7.5Fr pulmonary artery catheter (PAC); large bore venous access such as the Arrow MAC 2 lumen CVC.
- Left radial artery: 3Fr arterial line for blood sampling
- Right femoral artery: 4Fr arterial line for uninterrupted invasive blood pressure monitoring.
- Percutaneous access to the left internal jugular vein in the (rare) instances where veno-venous bypass is required, for venous return from the pump. The surgical ‘piggy-back’ technique +/- portal vein-inferior vena cava (IVC) shunt creation means this is usually not required.

19.21.1.3 Drugs

Infusions of vasopressor and inotropic drugs may be made in advance, but the aim of low central venous pressure to minimize surgical blood loss means this may not be routine in every centre. Emergency drugs, such as epinephrine 1:10,000 and 1:100,000 concentrations, are drawn up pre-operatively in 10 ml syringes. Other usual emergency drugs include atropine, glycopyrrolate, and metaraminol.

Drugs for anesthesia are discussed below.
19.21.2 Induction of Anesthesia

Induction of anesthesia is via large bore peripheral venous cannula (PVC). In time-critical transplants the patient may not be adequately fasted, necessitating a rapid sequence induction (RSI) of anesthesia. This means the patient is preoxygenated to denitrogenate the lungs and create an oxygen reserve for consumption during apneic phase between induction and tracheal intubation, and cricoid pressure is used in the UK. Those who are fasted but with risk factors for regurgitation and aspiration of gastric contents, for example those with ascites and increased intra-abdominal pressure, will also need a RSI.

Propofol is widely used. It undergoes extrahepatic metabolism and can be used in those with ESLD. Due to the altered cardiovascular response to stress in those with liver cirrhosis [18] the hypotensive response may be exaggerated.

Muscle relaxant options include suxamethonium and rocuronium, in RSI, and atracurium. Atracurium does not depend on liver metabolism and is used as a continuous infusion intraoperatively in our local unit. There are some reports that suggest using rocuronium during liver transplant appears to be a predictor of primary allograft function; in all patients whose neuromuscular recovery time was >150 min experiencing primary graft dysfunction [19].

The action of many opioids is prolonged in severe liver disease; however, fentanyl metabolism is largely unaffected [15]. Remifentanil undergoes ester hydrolysis in tissue and plasma and its duration of action is unaffected by liver disease. Alfentanil has less cardiovascular side effects than fentanyl or remifentanil, but the dose should be reduced [20, 21].

The endotracheal tube should have a large volume low pressure cuff to avoid mucosal damage during the lengthy procedure.

19.21.3 Maintenance of Anesthesia

Volatile agents are predominantly used in the maintenance of anesthesia; isoflurane is the vapor of choice, with oxygen-air mix carrier gas, up to a minimum alveolar concentration (MAC) of 1.0, because it maintains splanchnic blood flow better than other volatiles [15] and may improve blood supply to the transplanted graft. Lower MAC may be used in encephalopathic patients and guided by intracranial pressure monitoring.

Our local unit also uses a continuous infusion of alfentanil, with or without midazolam, after induction. Other centres may have different protocols.

Ventilation parameters aim to optimize oxygenation and control end tidal carbon dioxide concentrations to a partial pressure of 4–4.5 kPa for neuroprotection.

The patient is carefully positioned, and assessment of pressure areas is essential to maintain skin integrity, which is at significant risk in the critically unwell.

A nasogastric tube is inserted in theatre.

19.21.4 Intra-operative Monitoring, Care, and Management of Complications

The table below summarizes the phases of liver transplant surgery (Table 19.4), and the anesthetic implications:

19.21.4.1 Cardiovascular System and Fluids

Continuous 5 lead ECG monitoring, including ST segment analysis [17], is used throughout as well as routine monitoring. Additionally, continuous display of invasive blood pressure, pulmonary artery pressure and mixed venous oxygen saturation is adopted by our local unit. Less invasive cardiac output monitors may have replaced PACs in some centres, except where there is a significant concern of pulmonary hypertension, however patients with severe porto-pulmonary hypertension at preoperative assessment are unlikely to be transplant candidates [16].

As mentioned above, TEE is increasingly used. This allows ventricular size, function, and filling to be assessed, or detect any thrombus or air embolus in the event of hemodynamic instability.
Hemodynamic instability may be caused by:

- Hemorrhage
- Cross clamping
- Reperfusion
- Co-existing cardiovascular disease

There is a significant decrease in venous return during cross clamping with sequestration of fluid to the lower limbs and gut, effectively reducing adequate circulating volume, however overzealous administration of resuscitation fluid may cause volume overload and compromise graft function if engorged on reperfusion.

Hypotension in early reperfusion is common, and biochemical abnormalities should be sought and treated. Beyond this the management is small increments of vasoconstrictor or inotrope, such as epinephrine, with an infusion if required.

Due diligence in patients with concomitant cardiovascular disease is required and should be included in the differential diagnosis of hypotension.

The primed rapid transfusion device may be required.

### Table 19.4 Phases of liver transplant surgery

| Phase           | Surgical component                                                                 | Anesthetic implications                                                                 |
|-----------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| Pre-anhepatic   | Inverse T or extended subcostal incision. Dissection and mobilization of liver and surrounding structures. Identification of the porta hepatis. Division of hepatic artery and bile duct. | Hemorrhage: dissection, varices, adhesions, pre-existing coagulopathy. CVS instability: ascitic drainage and hypovolemia, low SVR, maldistribution of blood to splanchnic circulation. Over treatment with fluids and/or blood products may cause splanchnic congestion and exacerbate bleeding. |
| Anhepatic       | Cross clamp of supra- and infrahepatic vena cava. Portal and hepatic veins divided. Explantation of native liver. New liver transplanted, and caval and portal anastomosis. Potential need for veno-venous shunt (VVS). | No production of clotting factors, worsening coagulopathy, fibrinogen deficiency/fibrinolysis. Absent citrate/lactate metabolism, with increasing levels of both. Progressive hypocalcemia. Metabolic acidosis. Reduced cardiac output; potential VVS to maintain venous return and maintain renal perfusion, reduce splanchnic congestion, and delay metabolic acidosis. Reduced gluconeogenesis. Hemorrhage: surgical cause. |
| Neo-hepatic     | Graft reperfusion and vessel reconstruction. Assessment of graft function: bile production, decreasing lactate, normalizing calcium, improved cardiovascular stability. | Abrupt increase in potassium and hydrogen ion concentration; monitor of dysrhythmias and treat with calcium infusion +/- sodium bicarbonate. Increased preload and cardiac output. Progressive hypotension and decrease in SVR. Post reperfusion syndrome. |

### 19.21.4.2 Respiratory System

Continuous monitoring of airway pressure and inspired and expired gases is mandatory, with end tidal carbon dioxide targets as previously discussed.

Positive end expiratory pressure may be required if oxygenation is problematic, for example ascites causing diaphragmatic splinting. Positive pressure ventilation may contribute to hypotension secondary to increased intrathoracic pressure and reduced venous return.

Ventilation augmentation to increase minute volume during reperfusion will improve the removal of the increased carbon dioxide production secondary to liver metabolism and wash out of products of ischemia.

### 19.21.4.3 Renal/Biochemistry/ Metabolic/Hematology

There is no proven strategy for avoiding renal failure, other than optimizing fluid balance, maintaining adequate perfusion pressure, normothermia, and avoiding nephrotoxins [17, 22]. Preoperative jaundice also contributes to the risk of renal failure.
Veno-venous bypass may be used to optimize renal perfusion and reduce venous congestion depending on surgical technique. Patients on RRT preoperatively may need this continued intra-operatively.

Biochemical and hematological derangements are common, particularly acid-base balance, potassium, calcium, hemoglobin, clotting, and platelets, which are monitored regularly.

Our local unit measures arterial blood gases, Na+, K+, ionized Ca++, lactate, and glucose:

- Preoperatively
- Every 30 min after induction
- Immediately after clamping the major veins
- The end of the anhepatic phase
- Release of the venous clamps
- Release of the hepatic artery clamp
- Hourly until closure
- Additional samples as clinically indicated

Hypocalcemia is common due to chelation with unmetabolized citrate. Intravenous infusion is given to avoid hypotension, protect against hyperkalemia, and aid coagulation. Local protocols should be followed.

Metabolic acidosis may be due to poor tissue perfusion, optimized as above. Worsening in the anhepatic phase is common, and immediately post reperfusion, with resolution by a working graft over the next few hours postoperatively. Worsening acidosis with hyperlactatemia post-operatively may indicate poor graft function. Medical management is initiated, and the surgical team consulted.

Hyperkalemia is usually transient on reperfusion and doesn’t require treatment. A normal ionized calcium will protect the myocardium after cross clamp release. Routine medical management of clinically significant hyperkalemia is standard. Potassium replacement should be avoided in hypokalemia before the graft is functioning.

Monitoring blood glucose levels will direct appropriate management and patients may rarely require a glucose infusion.

Point of care (POC) coagulation testing, full blood count (FBC), and laboratory coagulation testing is performed preoperatively. Our unit repeat the hemoglobin and POC testing:

- At the end of heptatectomy
- Ten minutes post reperfusion
- Sixty minutes post reperfusion
- End of surgery
- Additional testing if clinically indicated, such as excessive surgical bleeding

Laboratory coagulation tests are sent intra-operatively if significant blood loss.

Hypercoagulability should be avoided, and platelet transfusion avoided unless necessary to reduce the risk of hepatic artery thrombosis.

Close monitoring of blood loss will guide appropriate fluid strategies, and patient identification information should be easily seen for cross checking blood products.

After reperfusion hyperfibrinolysis may occur and variable heparin-like substances are released from the newly perfused graft. This makes the coagulopathy complex and relies on clinical judgement and timely performed coagulation testing, as well as close cooperation with laboratory staff. Antifibrinolytics, such as tranexamic acid, are not routinely used, but may play a role and calcium replacement is also required.

Major hemorrhage treatment:

- Correct hypothermia, acidosis and hypocalcemia
- Cell salvage operative field
- Targets hemoglobin >70 g/L or > 80 g/L if the patient has ischemic heart disease
- Other blood products where indicated by POC test algorithm

Our local unit uses ROTEM:

- Target FIBTEM >8 mm
- FFP used first line for fibrin deficiency
- Cryoprecipitate is second line where: 6 units FFP infused and ROTEM suggests persistent fibrin deficiency; CVP >10 cm H O and ROTEM suggests persistent fibrin deficiency; FIBTEM A10 < 5 mm
- Factor concentrates are rarely used
19.21.4.4  Neurology
Continuous ICP monitoring +/- jugular bulb oxygen saturation is used locally in patients with fulminant hepatic failure.

19.21.4.5  Temperature and Pressure Areas
Temperature maintenance is paramount, from the moment the patient arrives in the anesthetic room. Under mattress warmers should be instigated in the anesthetic room before induction and continued intraoperatively. Hot air top blankets are also used away from the surgical field. Fluid warmers, heat and moisture exchangers in the anesthetic circuit and continuous temperature monitoring is used.

Temperature management may differ in fulminant hepatic failure and should be discussed at the surgical brief.

Arms are wrapped in Gamgee and positioned as per team preference in a neutral position to avoid peripheral nerve or nerve plexus injury.

Eyes are taped closed, monitoring leads checked, and final pressure point check made before draping the patient.

19.21.4.6  Infection Prophylaxis
Local protocols exist for antibiotic prophylaxis. These may need re-dosed during the procedure depending on duration.

19.21.4.7  Veno-Venous Bypass
New surgical techniques mean that VVB is less frequently used. The piggyback technique no longer requires this. When it is indicated, the bypass cannulas are sited to decompress the splanchnic circulation, passing through a centrifugal pump before being returned to the patient.

19.21.4.8  Miscellaneous
Air embolism is a complication usually associated with VVB. Management is early recognition and communication to the team/VVB technician, and supportive care.

Citrate toxicity results from high volume blood transfusion with excess circulating citrate not metabolized by the liver. It may lead to hypocalcemia with associated electrophysiological changes and hypotension. Calcium replacement is the treatment, until the functioning graft is metabolically active.

Post Reperfusion Syndrome (PRS) is an exaggerated hemodynamic compromise post graft perfusion. The mean arterial blood pressure, SVR, and heart rate fall, with increased pulmonary artery pressure and CVP suggesting myocardial depression and vasodilation secondary to biochemical disturbances and hypothermia. Adequate flushing of the liver and VVB may reduce the risk, and active management during the anhepatic phase influences the severity.

Graft non-function is always a possibility, up to 5% of cases [22]. Persistent acidosis, hypoglycemia, worsening coagulopathy and thrombocytopenia, hypotension, renal failure and encephalopathy point to primary graft non-function, a post-transplant emergency. General Considerations can be found in Table below (Table 19.5).

19.22  Postoperative Management

Patients are transferred to the intensive care unit (ICU) postoperatively, with routine and invasive blood pressure monitoring. Postoperative care will follow local protocol and be guided by clinical need. Early extubation is often achievable once all metabolic disturbances have normalized and may improve graft flow due to negative intrathoracic pressure in spontaneous ventilation.

Maintenance postoperative fluids should be via the naso-jejunal tube if able with continuous assessment of coagulopathy and fluid balance, avoiding high CVP to reduce hepatic congestion. An appropriate fluid regime is 1–2 ml/kg/h of crystalloid, and albumin or blood products used if indicated.

Postoperative pain relief is usually patient controlled analgesia since regional techniques are contraindicated in coagulopathy.

Immunosuppression is continued, and the patient is monitored closely to identify any complications early.
Renal Transplantation

Renal transplants are the treatment of choice for end stage renal failure (ESRF) [23]. The procedure is carried out in many centres and are predominantly cadaveric renal transplants. The authors will focus on cadaveric renal transplant, as organ procurement is beyond the scope of this chapter.

Patients receiving renal transplants show an almost immediate improvement in quality of life, morbidity, and mortality compared with dialysis [24]. It provides cheaper care for renal failure than ongoing dialysis but is a complex surgical procedure and the outcomes can be attributable to intraoperative physiological status, thus the anesthetic team contribute significantly to improved clinical outcomes.

The main cause of renal failure in the United Kingdom is diabetes mellitus. Many effects of renal failure impact on anesthetic care, in addition to the impact of the underlying cause.

These patients are high risk, particularly diabetic patients with ESRF [25]. Hypertension is very common, whether cause or effect of renal failure, and may be difficult to control. Accelerated atherosclerosis means that there is significant risk of ischemic heart disease that may be silent, again, particularly in diabetic patients. The incidence of valvular heart disease and left ventricular dysfunction is increased, and autonomic neuropathy is common. However, only irreversible ventricular dysfunction with low cardiac output should be considered a contraindication to transplant, because graft viability is endangered [26].

The sequelae of renal failure pose problems intraoperatively:

- Hypovolemia
- Abnormal electrolytes
- Altered acid-base status
- Reduced drug clearance
- Anemia
- Arterio-venous fistulae and difficult intravenous access, central and peripheral
- Delayed gastric emptying

Patients are usually dialyzed prior to theatre, causing hypovolemia which may be exaggerated by general anesthesia. Serum potassium may be high requiring treatment or monitoring, in addition to dictating neuromuscular blocking drugs. Altered acid-base status affects drug handling and clearance, and reduced doses of drugs may be necessary. Anemia is common but well tolerated, with increased cardiac output and low systemic vascular resistance (SVR) to compensate. The oxyhemoglobin dissociation curve is shifted to the right to facilitate oxygen supply at tissue level.

Blood loss intraoperatively is usually minor unless intraoperative complications arise and

| Table 19.5 Preoperative preparation for liver transplantation |
|-------------------------------------------------------------|
| Veno-venous bypass equipment                                |
| Blood warmer                                               |
| Bair hugger                                                |
| Cell saver                                                 |
| Rapid infusion device                                      |
| Infusion pumps                                             |
| Pressure transducer sets                                   |
| Cardiac output module, cable and equipment                 |
| SvO₂ monitor                                               |
| Transesophageal echocardiogram                             |
| Point of care coagulation test machine                     |
| Drugs should be drawn up in advance and include:           |
| Anesthetic                                                 |
| Propofol                                                   |
| Suxamethonium/rocuronium/ atracurium                       |
| Fentanyl/alfentanil                                        |
| Ranitidine                                                 |
| Vaporizer                                                  |
| Midazolam                                                  |
| Miscellaneous                                             |
| Prophylactic antibiotics: e.g. amoxicillin, gentamicin, metronidazole |
| Immunosuppression: e.g. methylprednisolone                  |
| Blood products                                             |
| Resuscitation                                             |
| Atropine                                                   |
| Epinephrine (adrenaline)                                  |
| Norepinephrine (noradrenaline)                            |
| Calcium chloride                                           |
| Metaraminol                                                |
| lignocaine 1%                                              |
| Sodium bicarbonate                                         |
| Infusions                                                  |
| Atracurium                                                 |
| Fentanyl/alfentanil                                        |
| Epinephrine (adrenaline)                                  |
| Norepinephrine (noradrenaline)                            |
| Calcium chloride                                           |

19.23 Renal Transplantation
compromise the anastomosis. Blood transfusion perioperatively is rare.

19.24 Preoperative Management

A full anesthetic history is mandatory and should then be targeted to issues that are ESRF and patient specific. Particular attention is paid to cardiovascular health, respiratory disease, and exercise tolerance. Any recent changes in symptoms may warrant further investigation as deteriorating cardiac function may be an indication of silent myocardial ischemia.

Dialysis assessment is important. Type and frequency of dialysis and when last dialyzed contributes to clinical care. Anuric patients will be fluid restricted and if recently dialyzed will have significant fluid shifts. Arterio-venous fistulae should be noted and must be protected intraoperatively.

The table documents preoperative investigations (Table 19.6).

Many drugs the patient is taking can alter their biochemistry, such as diuretics, or vasomotor tone, for example angiotensin converting enzyme inhibitors. They may also be on immunosuppression from previous transplants, and if this includes steroids then perioperative cover may be required.

Interrogation of diabetic patients’ regime and control, along with current blood sugar level, will guide the need for insulin therapy perioperatively.

Although renal transplantation is an urgent procedure it is seldom an emergency and there is usually time to obtain all the necessary preoperative information and results of investigations.

This also means that abnormal biochemistry can be corrected, and patients can be adequately fasted for theatre. The decision to use a RSI is based on individual patient need.

Premedication is rare but can be given if necessary.

19.25 Intraoperative Management

19.25.1 Surgical Brief

Surgical and anesthetic issues are discussed and planned, including the immunosuppression regime, in our unit. Anti-thymocyte globulin (ATG) is increasingly used in our clinical practice and there have been some adverse reactions secondary to the well-recognized cytokine release syndrome. Due to this we have developed protocols for the initiation of ATG that incorporates pre-infusion paracetamol, chlorphenamine and methylprednisolone, and the ATG is infused over 6 h through an infusion pump.

19.25.2 Monitoring and Equipment

Routine monitoring is initiated in the anesthetic room. Invasive blood pressure monitoring is rare and may impact on future fistula formation.

Intravenous access established, and our local unit advocate a 20 Gauge cannula is sufficient.

19.25.3 Lines

A central venous catheter is usually inserted asleep under aseptic conditions and real time ultrasound guided. The surgical team may request a dialysis central venous catheter as an alternative and this is discussed at the surgical brief. The target CVP is 12–14 cm H$_2$O, which may require significant volumes of fluid to establish. This optimizes graft perfusion, minimizing the risk of pre-renal hypoperfusion on graft function.

A urinary catheter is inserted when the patient is asleep.

| Laboratory investigations | Non-invasive and imaging |
|---------------------------|--------------------------|
| FBC                       | ECG                      |
| Urea & electrolytes       | CXR                      |
| Creatinine                | Echocardiogram           |
| eGFR                      |                          |
| Blood glucose             |                          |
| HbA1c                     |                          |
| Group & save serum sample |                          |
19.25.4 Drugs and Fluids

Emergency drugs to be drawn up include metaraminol, ephedrine, glycopyrrolate, and atropine. Additional drugs, such as epinephrine and nor-epinephrine should be readily available but seldom need made in advance.

Induction of anesthesia is usually with propofol, but thiopentone can also be used. A recent review of anesthetic practice in our local unit revealed no advantage in using atracurium over rocuronium as the neuromuscular blocker in our clinical practice. Many anesthetists are more familiar with rocuronium, therefore the use of this is supported by our department, and sugammadex is used to reverse the block if required. If a RSI is deemed necessary then caution is exerted using suxamethonium in view of potential increase in potassium concentration, with 1.2 mg/kg of rocuronium an alternative.

Opioid use for induction and intraoperative analgesia is usually fentanyl, but there is increasing use of remifentanil infusions. Post operatively we use fentanyl patient-controlled analgesia (PCA), some units may use morphine or oxycodone.

Prophylactic antibiotics are given as per local protocol and patient allergy status.

Local protocols may exist to direct the type of crystalloid used intraoperatively. In our unit there is mixed practice with variable use of Hartmann’s solution and 0.9% saline. The postoperative protocol uses 0.9% saline, some institutes use Plasmalyte [27].

19.25.5 Maintenance

Maintenance of anesthesia is usually by vapor, typically sevoflurane. Isoflurane/Desflurane are alternatives. Remifentanil infusions are replaced by fentanyl bolus at the end of the procedure for post op analgesia.

If ATG is not used, then basiliximab is our alternative. In this instance the timing of methylprednisolone is at the surgeon’s discretion but is usually around the time of anastomosis/before removal of cross clamps.

Before the patient is woken the surgical team ultrasound the newly transplanted graft and assess for adequate blood flow.

Once the procedure is complete the muscle relaxation is reversed, and the patient is extubated. It is unusual for the patient to require ICU care postoperatively, and patients usually return to the specialist renal ward once recovered.

19.25.6 Temperature and Pressure Areas

Normothermia is important in the care of renal patients. Hypothermia may affect coagulation and drug metabolism, and postoperative shivering increases oxygen consumption. This increased oxygen requirement may unmask myocardial ischemia in vulnerable patients.

Hot air blankets are used intraoperatively to maintain temperature, and intermittent tympanic or continuous temperature probe monitoring used.

Pressure area care is of particular importance as the patients have fragile skin and may have fistula and dialysis grafts that need padding and protecting throughout the procedure.

19.25.7 Postoperative Analgesia

Regular paracetamol and fentanyl PCA are routine, and wound infiltration with local anesthetic by the surgeons is performed. Non-steroidal anti-inflammatory drugs are contra-indicated. Alternatives include regional anesthesia, for example transversus abdominis plane block, or wound infiltration catheters.

Opioids are metabolized by the liver and excreted by the kidney, therefore our PCA settings are altered, with a longer lock-out time, to account for this.
19.25.8 Complications

Surgical complications are infrequent, but sudden hemorrhage with significant blood loss may occur.

Patient complications are related to comorbidities and biochemical abnormalities, and postoperative blood tests are taken in recovery.

19.26 Postoperative Management

In the postoperative period oxygen is administered routinely. Fluid therapy should be guided by the CVP and urine output closely monitored. Postoperatively, potassium should be checked and appropriately treated.

Once the patient is stable they are returned to a specialist renal ward. Immunosuppressive therapy is continued according to local protocol.

19.27 Pancreatic Transplantation

Successful pancreatic transplant provides durable glycemic control and improves survival for patients with diabetes [28].

There are three types of pancreas transplants:

- Simultaneous pancreas and kidney transplant (SPK), most common
- Pancreas after kidney transplant (PAK), second most common, usually after a living donor renal transplant
- Pancreas transplant alone (PTA)

There are two main indications for pancreas transplants: type 1 diabetes with either severe metabolic complications and/or incapacitating problems with insulin therapy, or an eGFR <20 ml/min/1.73 m²; some type 2 diabetics, such as non-obese patients, are a minority. Most commonly pancreas transplants are in type 1 diabetics, and the nature of the pancreas transplant depends on the underlying difficulty. Patients with difficulties in insulin therapy or metabolic complications alone but normal or near-normal renal function are considered for PTA, and those with renal failure with or without the option for living kidney donor are considered for PAK and SPK respectively [28, 29].

Diabetes is a major health problem with a high incidence of vascular and degenerative complications. Additionally, diabetic patients are more at risk of peri-operative complications including infection and poor wound healing. Patient selection is greatly important, and particularly regarding cardiovascular fitness: absolute contraindications to pancreas transplant includes excessive cardiovascular risk, documented by the organ donation and transplant advisory group [29].

In the USA there has been a decline in pancreas transplants over the last decade, which may be accounted for by improved medical care of patients, reduced quality of donors (increased obesity and older donors), and lack of consistent referral of transplant candidates from endocrinologists [28].

19.28 Preoperative Management

The patient will have been extensively reviewed and investigated by the referring and transplant teams when considered for the transplant list. Preoperative anesthetic assessment includes a thorough medical, surgical and anesthetic history, particularly focusing on diabetic control and associated complications.

Of importance to perioperative management:

- ischemic heart disease; increased risk of peri-operative cardiovascular event and surgery is contraindicated in those with myocardial infarction within the last 6 months
- evidence of autonomic neuropathy; risk of labile and difficult to manage intra-operative blood pressure and potential dysrhythmias
- dialysis history and biochemistry; causing hypovolemia or potassium abnormality
- blood glucose level; may require variable rate insulin infusion preoperatively and local protocols should be followed
- peripheral neuropathy; careful positioning in theatre to prevent pressure areas or peripheral nerve damage, and document existing deficits to exclude perioperative nerve damage
Airway assessment should be thorough as the incidence of difficult intubation is higher in type 1 diabetics due to atlanto-occipital joint stiffness [30].

Preoperative investigations are detailed in the table below (Table 19.7).

Premedication is not always required and is decided on an individual patient basis.

### 19.29 Intraoperative Management

The principles outlined can be adopted for all types of pancreas transplantation. They can be adapted to individual patient need and many units will have their own guidelines.

#### 19.29.1 Monitoring and Equipment/ Lines

Routine monitoring is attached in the anesthetic room. Consideration should be given to invasive blood pressure monitoring pre-induction in those with significant autonomic dysfunction but may be sited once anaesthetized. In particularly stable patients it may be considered unnecessary and could impact on future fistula formation, even if the patient is having a SPK or PAK transplant.

| Bloods | Non-invasive investigations and Imaging |
|--------|----------------------------------------|
| FBC    | ECG                                    |
| Group and save/cross matched blood according to local guidelines | Echocardiography if indicated, +/- stress testing |
| Coagulation screen | |
| Urea and electrolytes | |
| Creatinine and eGFR | |
| Calcium | |
| Phosphate | |
| LFTs | |
| Blood glucose and Hb A1c | |
| Additionally, preoperative testing should include blood borne virus screen and immunology screening, as per local protocols | CXR |
| Additional imaging such as CT or Ultrasound if required |

Table 19.7 Investigations for pancreas transplants

Intravenous access established for induction and further invasive lines, such as CVC, are sited asp in accordance to local policy and clinical need. These are ultrasound guided and performed under aseptic conditions. During SPK it may be necessary to insert a dialysis catheter.

There should be separate venous access for the dextrose/potassium/insulin infusion.

A urinary catheter is inserted once the patient is anaesthetized. A naso-gastric tube is also placed.

#### 19.29.2 Drugs and Fluids

Emergency drugs to be drawn up include metamizol, ephedrine, glycopyrrolate, and atropine, see Table 19.8. Additional drugs, such as epinephrine and norepinephrine should be readily available but seldom need made in advance.

Induction is usually with propofol, but thiopentone can also be used. Patients post dialysis may need dose adjustment or warmed fluid bolus during induction due to potential hypovolemia and therefore hypotension. Muscle relaxation is achieved with the anesthetist’s preferred drug(s), and RSI may be required in those with gastroparesis secondary to autonomic neuropathy. Suxamethonium may be considered if potassium level is normal, and rocuronium 1.2 mg/kg is an alternative.

Opioid use for induction and intraoperative analgesia is usually fentanyl, but remifentanil

| Anesthetic and analgesic drugs | Propofol/thiopental; anesthetic vapor; atracurium/rocuronium; Morphine/fentanyl; paracetamol |
|--------------------------------|-----------------------------------------------------------------------------------|
| Resuscitation                 | Ephedrine; metaraminol; atropine; glycopyrrolate; crystalloid fluids and cross matched blood |

Table 19.8 Drugs used in the anesthetic management of pancreas transplant

| Miscellaneous                  | Antibiotics Immunosuppressive agents according to local protocol Insulin/dextrose/potassium infusion(s) |
|--------------------------------|--------------------------------------------------------------------------------------------------|
intraoperatively is an alternative. Post operatively the patient is usually given a PCA, which may be fentanyl or morphine depending on renal function and unit preference.

Prophylactic antibiotics are given as per local protocol and patient allergy status.

Crystalloid infusions perioperatively may be guided by unit preference, but a balanced solution is usual, for example Hartmann’s solution or Plasmalyte. Postoperative fluid management is in critical care and guided by biochemistry and clinical picture.

19.29.3 Maintenance

Maintenance of anesthesia is usually by vapor anesthetic agents, for example sevoflurane or desflurane. Isoflurane is an alternative, with minimal effect on cerebral blood flow and beneficial effects on renal blood flow [31].

Fentanyl boluses are required throughout the procedure for analgesia or at the end of the procedure for postoperative analgesia if remifentanil infusion is used.

Muscle relaxation is maintained by boluses of neuromuscular blocker and monitored using a peripheral nerve stimulator. This is reversed on completion of the procedure, and the patient is usually extubated and taken to recovery, after which they will be transferred to a critical care area.

Regular blood sugar monitoring is required with adjustment/instigation of insulin infusion as guided by results.

19.29.4 Temperature and Pressure Areas

Normothermia is important in the maintenance of normal metabolism of drugs and maintaining hemostasis. Intermittent monitoring of temperature or temperature probe for continuous monitoring may be used. Hot air blankets are also used, with gaps for surgical access.

Patients may be high cardiovascular risk by nature of their diabetes, and increased oxygen consumption if shivery may cause deleterious cardiovascular effects.

Pressure area care is important due to peripheral neuropathy and compromised peripheral perfusion in abnormal microvascular circulation. Any fistulae or dialysis grafts need protected.

19.29.5 Postoperative Analgesia

Regular paracetamol, no non-steroidal anti-inflammatory drugs, and a PCA are routine. Some centres report the use of epidurals for postoperative analgesia but it is generally avoided/unnecessary. Wound infiltration with local anesthetic by the surgeons is performed; alternatives include regional anesthesia, for example transversus abdominis plane block or rectus sheath blocks depending on incision used, or wound infusion catheters.

Opioids are metabolized by the liver and excreted by the kidney, therefore those with renal impairment may need dose or lock-out time adjusted on their PCA. Acute pain services may be involved.

19.29.6 Complications

Immediate intraoperative surgical complications include hemorrhage, where significant blood loss may occur, for example at the anastomotic site after reperfusion.

Metabolic disturbance may occur with release of arterial cross-clamps after anastomosis is complete: metabolic acidosis from reperfusion is common and may contribute to poor clotting and therefore blood loss; hyperkalemia can contribute to cardiac instability; hypotension is multifactorial with redistribution of blood volume and decreased SVR due to anaerobic metabolites and should be treated with fluid resuscitation and vasopressors and/or inotropic drugs.

After graft reperfusion the pancreatic beta cells begin secreting insulin with 5 min [30] and blood glucose monitoring is essential. The insulin infusion may need stopped because profound hypoglycemia may occur. Blood glucose levels should be monitored every 15 min for the following hour.
post reperfusion, then every 30 min thereafter for the remainder of the surgery. Good glucose control (between approximately 6–8 mmol/l or 120–150 mg/dl [30, 31] is required to prevent islet cell dysfunction secondary to hyperglycemia and rest the beta cells until the metabolic disturbance from reperfusion has resolved [30].

Patient complications are related to their comorbidities as well as the predictable abnormalities above.

19.30 Postoperative Management

Patients are admitted to critical care postoperatively. This provides close monitoring of metabolic status and glycemic control. Hypoglycemia is a common postoperative problem and may require dextrose infusion.

Postoperative critical care bundles are adopted as per the local unit protocol.

The patient’s own medications are reintroduced when able, but gut absorption may be impaired due to postoperative ileus.

19.31 Conclusion

The anesthetic management of patients presenting for organ transplantation is challenging yet rewarding. A thorough knowledge of the pathophysiological and pharmacological derangements associated with the various organ failures is essential. Careful pre-, intra- and postoperative management has a significant role to play in the successful outcome of such operations.

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