Intraoperative Care of the Transplant Patient

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KEYWORDS

- Transplantation
- Anesthetic management
- Liver
- Kidney
- Pancreas
- Comorbidities

KEY POINTS

- Patients presenting for abdominal organ transplantation often have significant comorbidities, including cardiovascular and pulmonary disease, posing numerous challenges to the anesthesiologist in the perioperative period.
- Intraoperative management for abdominal organ transplantation is highly variable between transplant centers and depends on factors such as experience of surgical and anesthesia teams as well as available resources.
- Abdominal organ transplantations are major surgeries involving multiple vascular anastomoses. Patients may have advanced disease at the time of surgery, increasing the risk for morbidity and mortality.
- Adequate preparation including preoperative workup and risk stratification, planning of vascular access, blood product management, and preparation for possible complications is important to minimize the risk of perioperative morbidity and mortality. Standardization of protocols within a transplant center is important in that aspect.
- In this article we try to provide background and practical information helpful in establishing or improving protocols for intraoperative management. However, the management will have to be adapted to the practices of each particular transplant center and established protocols cannot simply be transferred to a new setting.

RENAL TRANSPLANTATION

Brief Overview

Patients presenting for renal transplant have extensive comorbidities, most importantly cardiovascular disease, posing numerous challenges to the anesthesiologist in the perioperative period. Organs from living donors confer the best short- and long-term outcomes. The 3-year graft survival is 88% with cadaveric organs and 93% from living organ donation.
Transplant Recipient—Anesthetic Management

Transplant recipients undergo extensive preoperative workup to optimize the intraoperative course. However, waiting times for transplant can be extremely long and a thorough preoperative review is necessary. In addition, the fluid status should be assessed in detail. Patients would frequently have undergone recent dialysis and may be significantly fluid depleted resulting in potential cardiovascular instability after induction of anesthesia. If dialysis has been recently performed, residual effects of anticoagulants can be problematic. Patients often know that their “dry weight” and current weight on the day of surgery may aid assessment. Recently drawn laboratory test results are also required with particular attention to the serum potassium level, which is frequently high in end-stage renal failure. Potassium levels greater than 6 mmol/L may warrant a delay in surgery while this is corrected. Patients are also expected to be relatively anemic secondary to chronic kidney disease despite many having erythropoietin supplementation.

Coagulation studies (prothrombin time and partial thromboplastin time) are routinely performed before surgery. Uremia causes platelet dysfunction, and therefore hemostatic clot formation can be hindered (prolonged bleeding time). This effect may also be secondary to the effects of anemia in end-stage renal failure; correction of anemia to packed cell volume greater than 30% reduces the bleeding risk dramatically.

A medication history should be taken, with particular attention to antihypertensive drugs. Evidence suggests that β-blockade should be continued in the perioperative period to reduce the risk of myocardial infarction, although no rigorous studies have been conducted in the kidney transplant population. Consideration should be given to withholding angiotensin-converting-enzyme inhibitor (ACE-I) and angiotensin II receptor blocker (A2RBs) on the day of surgery because of the risk of severe and refractory hypotension postinduction.

Anesthetic Choice

The initial renal transplants were performed exclusively under spinal anesthesia, and there are recent reports of centers using regional techniques with good outcomes. More commonly, however, endotracheal intubation is performed and anesthesia is maintained with volatile anesthetics, although total IV anesthetic techniques have also been shown to be effective and safe. When maintenance with volatile anesthetic has been compared with total intravenous anesthesia (TIVA) techniques, no difference in outcome has been shown. Concerns exist around the use of sevoflurane because of its metabolism to potentially nephrotoxic fluoride ions and the production of Compound A in a reaction with sodium or barium hydroxide lime. No study has shown a clinically relevant risk to renal function regardless of fresh gas flow rates, even in patients with preexisting renal insufficiency. However, controlled studies have not been performed in patients undergoing renal transplant.

Monitoring

Depending on the patient’s comorbidities, renal transplantation may be performed with standard American Society of Anesthesiologists (ASA) monitoring alone. Invasive monitoring is institution and patient specific and not always routine. Central line insertion is reserved for patients with specific indications, such as poor peripheral IV access or need for monitoring of cardiac filling pressures. No benefit has been shown in graft function by targeting a specific central venous pressure (CVP) or fluid management based on venous pressure. If venous pressure measurement is required,
peripheral venous pressures (transduced via a peripheral IV) have been shown to have a tight correlation to CVP without the need for central venous access.\textsuperscript{17}

Similarly, arterial line insertion is only truly indicated in patients who are anticipated to have significant cardiovascular instability under general anesthesia, for example, those with severe coronary artery disease (CAD), uncontrolled hypertension, poor cardiac function, or significant valvular lesions. In these patients, it may be prudent to site the arterial line awake, before induction. Severe cardiac arrhythmias are rare in this patient population.\textsuperscript{18}

**Vascular Access**

Patients may have had multiple fistulae for dialysis and recurrent hospital admissions with attempts at IV access. Consequently, these patients may present significant challenges when attempting to obtain IV access. A well-functioning 20-gauge IV is usually adequate for induction with a second, larger IV sited under anesthesia.

**Induction**

Patients with uremia and other risk factors, such as gastroparesis secondary to diabetes, are at high risk of gastric aspiration. A rapid sequence induction (RSI) with cricoid pressure should be considered along with sodium citrate pretreatment to increase gastric pH, thereby reducing pulmonary damage should aspiration occur. RSI can be performed with caution using rocuronium or suxamethonium. Rocuronium can be anticipated to give a prolonged block because of the reduced renal elimination (49 minutes for 25% first twitch (T1) recovery vs 32 minutes in patients with normal renal function), although predominant hepatic metabolism occurs allowing for safe use at induction.\textsuperscript{19,20} Suxamethonium will cause an increase in plasma potassium levels to a similar extent (0.5 mmol/L) to that seen in the general population.\textsuperscript{3} This drug can be used safely as long as the preoperative potassium level is below 5 mmol/L.\textsuperscript{3} About 20% of patients with end-stage renal failure (ESRF) have been shown to have below normal plasma cholinesterase activity. Prolonged neuromuscular blockade is only seen to occur in patients with an atypical form of plasma cholinesterase.\textsuperscript{21}

Hypnosis is usually induced with a judicious dose of propofol. In studies, patients with end-stage renal failure have been shown to require significantly more propofol to achieve hypnosis and target bispectral index (BIS) values than healthy controls, probably because of a hyperdynamic circulation and increased intravascular volume and hence volume of distribution.\textsuperscript{22} However, cautious induction dosing remains advisable in these patients because of their cardiovascular comorbidities. Maintenance of muscle relaxation should be provided with nonrenally excreted drugs such as atracurium or cisatracurium, which rely predominantly on Hofmann degradation.

In some institutions, the pressor response to intubation is attenuated with esmolol, 0.5 to 1 mg/kg, rather than high-dose opioids to minimize postinduction hypotension. Once fascia is dissected, the surgery is relatively unstimulating, and titrating a short-acting cardioselective β-blocker allows for precise heart rate control and maintenance of adequate diastolic pressure in patients at high risk of myocardial ischemia. Opioid analgesia is often titrated toward the end of surgery, which aids in the maintenance of adequate perfusion pressures throughout the procedure without the need for exogenous vasopressors, which may contribute to reduced renal blood flow and graft vasoconstriction. Fentanyl is typically used because of its limited renal elimination (7%) and is therefore less likely to accumulate.

After induction, meticulous attention to positioning of the patient is required and, in particular, to protecting arteriovenous (AV) fistulae. AV fistulae should also be monitored.
periodically throughout surgery. Perioperative loss of fistula function can be problematic because a proportion of patients have delayed graft function and require dialysis postoperatively.

Immunosuppressive medications to prevent graft rejection are administered by the anesthesiologist intraoperatively and should be discussed with the surgical team. Methylprednisolone is often given and may modulate the patient’s pain response and hence analgesic requirements postoperatively.

**Fluid Management**

Controversies exist regarding the appropriate volume and constitution of IV fluid administered during renal transplantation. As discussed earlier, these patients are often fluid deplete on arrival to the operating room because of recent dialysis and preoperative starvation. Adequate fluid loading is required to improve immediate graft function and prevent intraoperative hypotension. A blood volume of 70 mL/kg has been shown to correlate with immediate graft function in living related renal transplantation.23

When a CVP line is inserted, targeting a CVP of 10 to 15 mm Hg has been advocated to optimize cardiac output and renal perfusion.

Concerns regarding hyperkalemia have led to the widespread administration of potassium-deplete fluid, for example, 0.9% saline. Recent surveys show that this is the practice during transplantation in 90% of cases in 49 centers across the United States.24 However, O’Malley and colleagues25 demonstrated that hyperkalemia (>6.0 mmol/L) and metabolic acidosis were significantly increased in patients undergoing renal transplant who received saline rather than Ringer lactate. Intraoperative albumin administration has been shown to be beneficial for graft function in a dose-dependent manner, presumably because of effective intravascular volume expansion optimizing graft perfusion and minimizing tissue hypoxia.23

Blood transfusion in renal transplantation is rare; however, it is prudent to have the recipient’s blood typed and screened.

**Hemodynamic Management**

Intraoperative hypotension can be minimized via adequate fluid administration and judicious use of induction agents and opioids. Reperfusion injury may occur on unclamping of the iliac vessels and perfusion of the graft.

Potent vasoconstrictors with α-adrenergic activity, such as phenylephrine, should be avoided during renal transplantation because of concerns regarding vasoconstriction in the graft and should only be used as a last resort. Vessels within the transplanted organ are more sensitive to vasoconstriction than the systemic arterioles, hence blood flow in the graft could become compromised.26 Dopamine infusion can be used as an inotropic agent to improve mean arterial pressure if hypotension becomes problematic.

**Discussion of Adjuvant Drugs**

In addition to ensuring adequate perfusion of the kidney with fluid loading, osmotic and loop diuretics are frequently administered to enhance urine output. A recent survey demonstrated extensive variation in intraoperative diuretic use between different transplant centers, and an evidence base for their use remains controversial.27

Typically, furosemide and mannitol are used to promote diuresis and dopamine is infused to enhance renal blood flow in an attempt to optimize graft function.

Mannitol is freely filtered at the nephron and exerts an osmotic effect increasing urine volume. Mannitol may protect the renal tubules from ischemic injury, and in
transplanted cadaveric kidneys, it has been demonstrated to reduce delayed graft function.\textsuperscript{20}

Furosemide, by blocking the $\text{Na}^+$/K$^+$ pump in the ascending limb of the Loop of Henle, may prevent oliguric renal failure. No difference in immediate graft function or function at 1 year could be seen between the use of mannitol or furosemide and no diuretic at all.\textsuperscript{27}

Use of renal dose dopamine (2–3 $\mu$g/kg/min) has been questioned because denervated renal transplants do not respond to dopamine-like native kidneys. No improvement was shown in graft function, and length of intensive care unit (ICU) stay was prolonged in patients receiving dopamine infusions.\textsuperscript{28} A small study by Sorbello and colleagues\textsuperscript{29} compared dopamine versus fenoldopam infusion (a selective dopamine receptor type 1 [DA-1] agonist) in living donor renal transplantation. Significant improvement in postoperative renal function (diuresis and electrolyte excretion) was seen with fenoldopam. Further rigorous randomized controlled trials are needed to clarify this effect.

Brauer and colleagues\textsuperscript{30} investigated whether furosemide, dopamine, and prostaglandin E1 were beneficial in preventing delayed graft function. The investigators demonstrated that renal function was actually worse in the intervention group (with higher urea and creatinine levels).

**Emergence**

At the conclusion of surgery, muscle relaxation should be reversed and the patient should be extubated if appropriate. Postoperative ICU admission in patients undergoing renal transplant is unusual (<1% in one case series), most commonly occurring because of fluid overload, respiratory distress, or infectious complications.\textsuperscript{31} Postoperative pain is typically of mild to moderate intensity and frequently controlled with fentanyl titrated to effect, followed by patient-controlled analgesia (PCA).

**The Living Donor**

Living donors are intensively screened before surgery.\textsuperscript{32} Donor health assessment can significantly prolong the time from organ requirement to donation but is necessary to prevent harm to an otherwise healthy patient. As such donors are almost exclusively healthy ASA 1 or 2 patients.

Surgical technique has moved away from the traditional “open” approach to the laparoscopic hand-assisted donor nephrectomy. The latter technique has the advantage of reducing postoperative pain, allowing earlier mobilization and a shorter hospital stay. Graft function and safety has been shown to be comparable to organs harvested via open nephrectomy.\textsuperscript{33}

**Induction**

Standard ASA monitoring is sufficient for most donor nephrectomies. Anesthesia is induced with IV propofol, judicious opioid use, and neuromuscular blockade. Endotracheal intubation is then performed. The patient is then positioned in the lateral position with a break in the table to allow surgical access. Either kidney may be used; however, the left kidney is preferable because of a longer vascular pedicle. Meticulous care must be taken to prevent pressure areas or nerve injury.

**Maintenance**

Anesthesia is usually maintained with volatile anesthetic agents, and care is taken to ensure deep neuromuscular blockade to prevent damage to vascular structures while organ harvest is performed.
Fluid management
Care is taken to ensure adequate renal perfusion and urine production during surgery so as to optimize graft function posttransplantation. The pneumoperitoneum established during laparoscopic surgery has adverse effects on hemodynamics, reducing cardiac output and renal perfusion. Often, generous volumes of IV crystalloid are infused to ensure adequate kidney perfusion and to stimulate urine production, typically 10 to 20 mL/kg/h. Mertens zur Borg and colleagues demonstrated that overnight IV hydration before surgery followed by intraoperative colloid bolus administration improved intraoperative urine output and stroke volumes when compared with aggressive intraoperative fluid administration alone.

Direct-acting vasopressor agents should be avoided if possible to prevent graft vasoconstriction. If required, dopamine or low-dose ephedrine should be used for hemodynamic support.

In many institutions, the surgical team, in addition to providing a target for fluid loading, also asks for the administration of diuretics to promote urine production. Typically, furosemide, 20 mg, as a bolus, and mannitol, 12.5 g, are given to improve diuresis. Before clamping of the renal vasculature, 3000 to 5000 units of heparin are administered to prevent coagulation in the graft, which is commonly reversed with protamine after harvest of the kidney.

Laparoscopic donor nephrectomy is typically not unduly painful and does not warrant the use of epidural catheter insertion. Intraoperative pain relief is provided with a balanced simple analgesic and opioid technique. Fentanyl is most commonly used and is titrated to effect. Transversus abdominal plane (TAP) block has been shown to be efficacious in this setting. Parikh and colleagues demonstrated a prolonged analgesic effect and reduced requirement for breakthrough pain relief with ultrasound-guided TAP block.

Postoperative care can be provided in the postanesthetic care unit except in rare circumstances.

LIVER TRANSPLANTATION
Brief Overview
Liver transplantation has become the treatment of choice for eligible patients with end-stage liver disease (ESLD) and has overall excellent outcomes with a nationwide 5-year graft survival rate of over 70%. Most liver transplants are isolated liver transplants from deceased donors. Transplantations of split liver grafts or pared down grafts as well as living donor transplants or transplantation of organs recovered donation after cardiac death (DCD) represent only a small fraction of the volume. Also, combined liver-kidney transplantation is performed only infrequently because patient and graft survival are inferior when compared with single-organ transplantation.

Transplant Recipient—Anesthetic Management
The anesthetic management for liver transplants may be standardized at each liver transplant center, but it varies widely between centers. The management highly depends on the surgical approach (bicaudal cross-clamp, piggyback, or venovenous bypass [VVBP]), on the experience of surgeons and anesthesiologists, as well as on the case volume. In a survey of 62 transplant centers in the United States performed by Schumann, a pulmonary artery catheter was used in approximately 30%, transesophageal echocardiography (TEE) in 11.3%, and VVBP in roughly half of adult transplants. A tendency toward decreased use of pulmonary artery catheters and VVBP was shown with increasing case volume. Similarly, the intraoperative resource and
personnel utilization also varies widely between liver transplant centers and is influenced by the same factors.

**Anesthetic Choice**

Because no anesthetic technique has been established as optimal, balanced techniques using volatile anesthetics in an oxygen/air mixture and opioids as well as IV techniques with combination of opioids, benzodiazepines, and propofol have been used successfully for liver transplantation. With the exception of halothane, all volatile anesthetics are suitable for liver transplantation. Isoflurane and desflurane are the most frequently used. Nitrous oxide should not be used to avoid intestinal distention. The use of epidural catheters is discouraged in this type of procedure because a severe and prolonged perioperative coagulopathy may persist.

**Monitoring**

In addition to the standard ASA monitors, invasive arterial blood pressure should be measured. This monitoring will also allow measurement of levels of arterial blood gases, blood glucose, and electrolytes (sodium, potassium, and ionized calcium) and the hematocrit value, which is considered routine in most transplant centers. Additional hemodynamic monitoring may consist of pulmonary artery catheter, TEE, simple CVP monitoring, or a combination with the choice being determined by institutional practice. Although guidelines have generally improved preoperative assessment of pulmonary hypertension, there may still be cases with inadequate workup or suspicion for newly developed or worsened pulmonary hypertension prompting placement of a pulmonary artery catheter for preincision diagnostics.\(^\text{39,40}\)

Recently, TEE has been used more frequently for fluid management, monitoring of cardiac function, and identification of intraoperative complications (eg, pulmonary embolus). Transfusion to correct severe coagulopathy may be considered before line placement, but there are no generally accepted guidelines for this patient population, especially because the use of ultrasound guidance for central vein cannulation has become the standard of care.

Electrolyte, acid-base, and metabolic derangements as well as significant blood loss and coagulopathy are monitored with frequent intraoperative blood samples for point-of-care and laboratory testing. Aside from guiding transfusion and interventions to correct other derangements, monitoring of base deficits and lactate levels after reperfusion of the new graft can be used to assess function of the donor liver. Although considerable controversy exists regarding the benefits of using thrombelastography or similar techniques to monitor coagulation during liver transplantation, like other point-of-care tests, it provides faster results than the average laboratory turnaround time for coagulation studies.

**Vascular Access**

Line placement should include a radial arterial line for invasive blood pressure monitoring, some form of central venous access, and 2 to 3 large-bore IV catheters, ideally including a rapid-infusion catheter. As mentioned before, the choices for central and large-bore peripheral venous access are highly variable between institutions. Similarly, practices for arterial access differ widely between transplant centers with some placing femoral arterial lines or routinely placing 2 arterial lines.

**Induction and Maintenance**

Patients selected for liver transplantation usually have preserved cardiac function, although the cardiovascular physiology in ESLD is significantly altered with often severe
peripheral vasodilation and increased cardiac output. However, it is usually not necessary to place an arterial line or a central line/pulmonary artery catheter for invasive monitoring before induction. Because ascites, encephalopathy, or uremia frequently present in ESLD, cricoid pressure and RSI should be strongly considered. Induction can be accomplished with any IV anesthetic such as propofol or etomidate, with or without opioids. The choice of opioid depends on institutional preference, and several drugs such as fentanyl, sufentanil, or remifentanil have been used successfully. A short- or intermediate-acting neuromuscular blocking agent should be used to facilitate endotracheal intubation. Given the reduced peripheral vascular resistance in ESLD, hypotension after induction is common and can mostly be treated with administration of small boluses of vasoconstrictors (eg, phenylephrine). An orogastric tube should be placed to improve surgical exposure through decompression of the stomach. The benefit of placing of a nasogastric tube, if desired, should be carefully weighed against the risk of bleeding in the setting of coagulopathy. Before the incision is made, appropriate antibiotic coverage should be ensured.

Pharmacokinetics and pharmacodynamics are significantly altered in ESLD affecting the action of drugs commonly used in anesthesia including benzodiazepines and nondepolarizing neuromuscular blockers. It is very difficult to predict the pharmacokinetics and pharmacodynamics of any given drug in the setting of liver transplantation because the dysfunctional native liver is going to be removed and replaced by a new graft. Initial graft function is difficult to predict and measure, and only secondary indicators such as lactate levels are available to assess function. However, in the case of neuromuscular blockers, it seems reasonable to choose cisatracurium and atracurium because they are cleared independently of liver function.

**Fluid Management and Transfusion**

The surgical procedure can be divided into 3 major parts, dissection phase, anhepatic phase, and reperfusion phase. It is useful to consider these different phases when thinking about specific goals of fluid administration and hemodynamics. The surgical approach (bicaval clamp, piggyback, or VVBP) also has a major impact on fluid and hemodynamic management.

In general, close communication with the blood bank before and during surgery is crucial. A standard protocol should be established that will guide the setup for blood products. While center volume and experience play a major role, a typical setup may include 10 units of packed red blood cells (PRBC) and 10 units of fresh frozen plasma (FFP) to be brought to the operating room, with 4 units of single-donor platelets available on request. A high-volume transfusion device is typically used and should be connected to a large-bore IV line. These devices include efficient warming systems that will help together with other fluid warmers and warming blankets to maintain the patient’s temperature as close to normal as possible.

The fluid requirement during a liver transplantation is significant because of bleeding and fluid shifts. In addition to blood products from the blood bank, the use of intraoperative cell salvage is common unless there are contraindications (eg, malignancy). Furthermore, most centers use a combination of crystalloid (preferred is normal saline) and colloid (preferred is albumin) to maintain intravascular volume. The practices in US transplant centers have recently been surveyed and results published by Schumann and coworkers.

Early in the dissection phase, acute decompression of ascites frequently unmasks intravascular volume depletion and might result in significant hypotension. Adequate volume replacement before or in addition to vasoconstrictor use is crucial at that time. Unless anemia and/or coagulopathy are also present, colloids are frequently the first
choice for fluid therapy at that time. Overall, during the dissection, relative normovolemia should be maintained while replacing blood loss and avoiding excessive dilution of coagulation factors. Depending on the underlying cause of the liver disease and the degree of portal hypertension, bleeding can vary dramatically from minimal in some patients to severe blood loss at the other end of the spectrum.

As mentioned earlier, the utilization of VVBP during the anhepatic phase to improve hemodynamic stability as opposed to a bicaval clamp without bypass is center dependent. Some transplant centers use VVBP routinely, whereas others routinely proceed without it. The risk-benefit assessment probably depends on training, expertise, and volume. Based on a study by Schwarz and colleagues, the outcome (mortality, graft function, and kidney function) is not different between a group with a drop in cardiac output of more than 50% after caval clamping and a group with a less-pronounced effect, arguing that VVBP might not provide any outcome advantage even if the cardiac output can be better maintained. Recently, the use of the piggyback technique seems to become more popular with good outcomes. Using this approach, the inferior vena cava is only partially occluded during the anhepatic phase allowing improved venous return and better hemodynamics, although the surgical technique might be more difficult and may lead to more complications.

The dissection ends and the anhepatic phase begins with excision of the native liver and control of bleeding. The ice-cold liver donor graft is placed into the surgical field after being flushed to remove the organ preservation solution. The suprahepatic and infrahepatic caval and portal vein anastomoses are then completed in that order. In the piggyback approach, only one caval anastomosis needs to be completed. The hepatic artery anastomosis is often performed after restoration of blood flow.

Before the anhepatic phase, especially when a complete caval occlusion is anticipated, a combination of products as indicated by blood count and coagulation parameters should be infused to increase the patient’s intravascular volume and preload so that partial or total caval occlusion and portal vein occlusion are better tolerated. A target CVP between 10 and 20 mm Hg should be achieved to minimize hemodynamic instability when complete occlusion of the vena cava is used. The surgeons should perform a test clamp so that the hemodynamic impact can be better anticipated and the fluid and vasoconstrictor therapy can be optimized before the anhepatic phase. One should avoid aggressive fluid administration during this phase because of possible fluid overload after release of the clamps.

In addition to monitoring laboratory values to assess coagulation, close attention should be paid to the surgical field. Laboratory parameters will be helpful in the underlying mechanism for the coagulopathy (dilution/consumption of clotting factors, platelet entrapment, endogenous heparinoid-like substances, and primary fibrinolysis), but moderate abnormalities in laboratory parameters should probably not be treated in the absence of clinical bleeding with the possibility of a rapid trend to abnormal values. One difficulty in the assessment is the slow turnaround time for laboratory tests. The approach to correct coagulopathy and achieve hemostasis in the absence of surgical bleeding depends on the method of coagulation monitoring and institutional preference. However, the administration of PRBC, FFP, platelets, and cryoprecipitate seems to remain the preferred method to treat blood loss and coagulopathy during liver transplantation.

Postsurgical care of the patient undergoing liver transplant is generally in the ICU, although selected patients (eg, after transplant for hepatocellular carcinoma) may be candidates for an intermediate care setting depending on the setup. Extubation in the operating room is possible in a large percentage of patients depending on volume and experience in the transplant center.
Hemodynamic Management

Patients with ESLD often have very low peripheral vascular resistance and high cardiac output, which may be associated with intravascular volume depletion, especially in the setting of refractory ascites. Patients frequently present with a low normal blood pressure or even with hypotension and may require blood pressure support as early as during induction. Careful attention should be paid to ensure adequate fluid therapy in addition to vasoconstrictor therapy. Commonly used agents are phenylephrine and norepinephrine as well as vasopressin, mostly in combination. Dopamine and dobutamine are also used but less frequently. Phenylephrine is the most common drug administered as bolus. Vasopressor support often increases significantly during the anhepatic phase, especially when complete caval occlusion is used. As mentioned earlier, a temporary “test clamp” on the inferior vena cava may help guide management before vascular clamps are permanently placed for the anhepatic stage. If VVBP is used to blunt the hemodynamic consequences of vascular exclusion, bypass is usually accomplished by cannulation of the femoral and portal veins with diversion to the suprahepatic vena cava through the axillary, subclavian, or jugular vein.

At the end of the anhepatic phase, with the release of the vascular clamps, the preload improves after establishing unobstructed flow in the inferior vena cava and hemodynamics usually improves. The removal of the portal vein clamp marks the beginning of reperfusion. Blood from the splanchnic circulation perfuses the new donor liver. This part of the operation is often the most critical from an anesthesia management perspective because significant hemodynamic instability and cardiac arrest may occur immediately after reperfusion. Manifestation can include various problems such as decreased inotropy leading to profound hypotension, severely decreased chronotropy leading to arrhythmias or full arrest, as well as hyperkalemic arrest. Anesthetic management is directed at maintaining or recovering cardiovascular stability. This goal may require immediate pharmacologic intervention such as the administration of epinephrine, atropine, calcium, or occasionally sodium bicarbonate. In severe cases, methylene blue might be considered because it has been shown to attenuate hemodynamic changes of the reperfusion syndrome. Preoperative placement of external pacing/defibrillation pads may be helpful in cases of immediate postreperfusion cardiac arrest.

Discussion of Adjuvant Drugs

Octreotide as infusion can be used intraoperatively for the treatment of severe portal hypertension with the goal to reduce portal pressure and bleeding. Ionized calcium levels can be significantly decreased during liver transplantation, especially when large volumes of PRBC and/or FFP need to be transfused. The citrate load from these products can lead to significantly reduced calcium levels, in particular during the anhepatic phase when even the remaining capacity to metabolize citrate is removed. Administration of calcium chloride or calcium gluconate as infusion or bolus is often required, and calcium levels should be regularly monitored.

In addition, the glucose-insulin pathway is frequently impaired in patients with ESLD, and close monitoring of blood glucose levels is required. Administration of steroids for immunosuppression, enhanced glycojenolysis, and insulin resistance of the graft may all contribute to hyperglycemia requiring insulin treatment. Close monitoring of electrolytes is also essential, and hypo- or hyperkalemia are not uncommon and often require treatment. Interventions used for renal protection have not been
shown to provide improved outcomes.\textsuperscript{51} One possible benefit of diuretics despite lack of renal protection may be the promotion of diuresis, which could make volume management easier especially if coagulopathy needs to be treated.

Immunosuppressive therapy is crucial for the success of transplantation. Protocols vary between medical centers, and clear communication is crucial for intraoperative delivery of the appropriate immunosuppressant (eg, steroid).

Several drugs, such as aprotinin, tranexamic acid, aminocaproic acid, and recombinant factor VIIa (rFVIIa) have been used in liver transplantation to reduce transfusion requirements. The efficacy of these approaches from the view of a starting liver transplant program with an emphasis on affordability has recently been reviewed by Rando and coworkers.\textsuperscript{52} Caution seems to be advised, especially in patients at risk for thrombotic complications because a dose that effectively reduces blood loss may at the same time increase the risk for hepatic artery or portal vein thrombosis or other thrombotic complications. However, most evidence exists for a benefit of the use of tranexamic acid. In addition, rFVIIa, initially developed for the treatment of patients with hemophilia, has been advocated for use in liver transplantation among other surgical settings. Given the high cost of rFVIIa and the lack of benefit demonstrated in prospective randomized trials, routine use in liver transplantation cannot be recommended.\textsuperscript{52–54} However, there is probably enough data from case reports and series as well as noncontrolled trials that it is reasonable to consider rFVIIa in extreme situations.\textsuperscript{52,55}

The first successful liver transplants from living donors were reported almost 25 years ago and are today performed as adult-to-child and adult-to-adult transplants.\textsuperscript{56} The regenerative capacity of the liver allows for complete recovery in donor and recipient after both a left or right lobe transplant. The choice between right or left hepatectomy is made depending on the relation between size of the recipient and the estimated mass of the donor lobe.

### Induction

Living donors are thoroughly screened preoperatively and are ASA 1 or 2 patients without any medical problem, which would significantly increase their anesthetic or surgical risk. Otherwise, the considerations for anesthetic management of the donor are similar to those of patients undergoing hepatectomies. Preoperative placement of a thoracic epidural catheter for postoperative pain control is performed in some transplant centers, whereas others rely on PCA. A recent study argues that pain control is better with an epidural technique compared with PCA and that concerns about safety based on possible coagulopathy may not seem to be justified.\textsuperscript{57,58}

A standard IV induction can be performed using any IV anesthetic and neuromuscular blocker of choice. Intraoperatively, the patient is placed in a supine position, frequently with one arm tucked (right or left) at the side and the other abducted. Two large-bore IV catheters and invasive arterial blood pressure monitoring are used in most centers.\textsuperscript{59,60} An orogastric tube should be placed to improve surgical exposure through decompression of the stomach.

### Maintenance

The intraoperative care of patients undergoing donor hepatectomy for liver donation is similar to that of other patients having other hepatic surgery. General anesthesia is standard and may consist of a balanced technique or be combined with intraoperative supplementation of epidural analgesia. Paralysis is maintained throughout the
operation. While the liver is mobilized, there may be brief periods of hypotension because of temporary decrease in venous return to the heart. These episodes usually do not require treatment especially because the donors are usually healthy.

**Fluid management**

Intravenous fluid is administered cautiously until the graft has been isolated. This technique is generally advocated to maintain a low CVP to help minimize blood loss during transection. However, in a retrospective study, CVP monitoring did not seem to reduce blood loss when compared with patients without CVP monitoring. Fluid restriction without measuring the CVP seems to be sufficient. Although blood loss at most centers is usually well below 1000 mL, the nature of the procedure warrants vigilance and preparation. Therefore, liver donors usually donate 1 or 2 autologous units of blood before surgery. In addition, intraoperative cell salvage is utilized at most centers.

In most cases, the patient can be extubated in the operating room and transferred to the postoperative care unit, and ICU admission is rarely necessary. Nevertheless, in some institutions, living liver donors are routinely managed in the ICU during the early postoperative period.

**PANCREAS TRANSPLANTATION**

Successful pancreas transplantation can cure patients with diabetic mellitus. Pancreas transplant is frequently performed with simultaneous kidney transplantation, as nephropathy is extremely common in these patients. Recent advances in immunosuppressive therapy have allowed long-term graft survival to be possible. Long-term graft survival had been a significant problem because pancreatic grafts are a potent immunologic trigger.

**Intraoperative Management**

Pancreas transplant is usually performed under general anesthesia with endotracheal intubation. Surgical duration and the need for stable hemodynamics make a balanced general anesthetic the best choice. Full muscle relaxation is necessary to optimize surgical access. Patients with concurrent renal failure should be paralyzed in a similar way to those undergoing isolated kidney transplant, that is, the use of muscle relaxants that do not rely on renal excretion for the offset of action for maintenance of neuromuscular blockade. Cisatracurium infusion with train-of-four monitoring is the usual practice for these long cases, although intermittent vecuronium boluses have been successfully used. Patients undergoing isolated pancreas transplant (who have reasonable renal function) may be administered any nondepolarizing muscle relaxant provided the depth of blockade is monitored.

In addition to standard ASA monitoring, arterial and central venous line insertion are necessary. RSI is often indicated in this patient cohort. Diabetic gastropathy, secondary to autonomic dysfunction, puts these patients at a high risk of aspiration at induction of anesthesia. Nonparticulate antacid and cricoid pressure should be used.

An epidural catheter can be inserted before induction for intraoperative and postoperative analgesia. Postoperative pain can be significant because of the extensive abdominal exposure required for surgery.

Immunosuppressant and antimicrobial medication is administered in the operating room by the anesthesiologist after induction; clear communication with the surgical team is necessary.

During surgery, careful attention must be paid to maintaining adequate perfusion pressure to optimize graft function. Invasive monitoring allows for close control of
hemodynamics and cardiac filling pressures and also permits the ability to draw laboratory tests and arterial blood gas (ABGs). Monitoring the blood glucose level is of paramount importance. Before unclamping of the transplanted pancreas, blood glucose levels must be measure every hour along with monitoring for ketoacidosis. Insulin infusion should be instituted if blood sugar levels become deranged. Hyperglycemia is associated with worsened immune function and increases the risk of infection. After unclamping of the pancreas, glucose levels should be measured every 30 minutes because the blood glucose level typically falls by 50 mg/dL/h.

Autonomic neuropathy may increase the risk of cardiovascular instability under anesthesia; however, a study in uremic renal transplant recipients with diabetes and known autonomic dysfunction failed to illustrate any difference in hemodynamics when compared with uremic nondiabetic patients.66

Protracted surgery with extensive abdominal exposure results in significant insensible fluid losses. Choice and volume of fluid administration can be challenging and should be guided by central venous pressures, arterial pulse pressure variation, or where indicated, TEE. Blood products should be administered where necessary to optimize oxygen carriage or to correct coagulopathy. Crystalloid administration should probably be minimized; pancreatic edema seems to be less when colloids are given, although no trial data exists.

INTESTINAL TRANSPLANTATION

Intestinal transplantation is rarely performed, and its predominant indication is short gut syndrome, which accounts for 60% of cases.67 This technique can be performed as an isolated procedure or combined with simultaneous liver transplantation.

Graft failure is common, although long-term function has improved dramatically with newer immunosuppression. The 1-year graft survival is now 66%, whereas only one-fifth of grafts continue to function at 5 years.

No published trials exist regarding intraoperative anesthetic management and outcome.

REFERENCES


