Anesthetic management of the pediatric patient undergoing solid organ transplantation

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Solid organ transplantation is now commonly performed in pediatric patients at many institutions throughout the world. Although kidney, heart, and liver transplants still dominate the field, new inroads are being made in the arena of small bowel, lung, heart-lung, and multivisceral transplants. Multiorgan transplants, although still rare, are being performed with increasing frequency. These endeavors are still considered experimental and have not achieved survival rates comparable to single-organ transplants; nonetheless, survival rates are improving and research will continue to improve outcomes.

The multitude of differences between pediatric patients and their adult counterparts lends itself to special anesthetic considerations that may not be readily evident to the anesthesiologist. Anatomic, physiologic, pharmacologic, and psychologic differences compounded with the technical expertise required to care for these children make for unique and difficult challenges to the pediatric anesthesiologist.
Liver transplantation

Indications for liver transplantation

The first successful pediatric liver transplant was performed in 1967 [1]. Of the 61,442 liver transplants performed in the United States from January 1988 through October 2003, 8414 were performed in patients under 18 years of age [2]. Centers across the country annually perform approximately 500 pediatric liver transplants. Organ availability continues to be a limiting factor in the number of liver transplants that are performed. The introduction of split and reduced-sized livers, as well as the use of living related donors has increased the donor pool, but there is nonetheless an overall shortage of available organs, and a significant number of patients still perish while awaiting organs.

Biliary atresia continues to be the most common indication for pediatric liver transplantation, comprising over 50% of patients in reported series (Table 1).

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic failure</td>
<td></td>
<td></td>
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<tr>
<td>Biliary atresia</td>
<td>62</td>
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<td>α1-Antitrypsin deficiency</td>
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<tr>
<td>Progressive intrahepatic cholestasis</td>
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<td></td>
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<tr>
<td>Fulminant hepatic failure</td>
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<td></td>
</tr>
<tr>
<td>Ductular hypoplasia syndromes</td>
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<td></td>
</tr>
<tr>
<td>Chronic active hepatitis</td>
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<td></td>
</tr>
<tr>
<td>Neonatal hepatitis</td>
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<td></td>
</tr>
<tr>
<td>Post necrotic cirrhosis</td>
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<td></td>
</tr>
<tr>
<td>Tyrosinemia</td>
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<td></td>
</tr>
<tr>
<td>Secondary biliary cirrhosis</td>
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<td></td>
</tr>
<tr>
<td>Wilson’s disease</td>
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<td></td>
</tr>
<tr>
<td>Nonprogressive liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arteriohepatic dysplasia</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Primary therapy for inborn errors of metabolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycogen storage disease</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Urea cycle defects</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Crigler-Najjar syndrome</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Secondary liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Langerhans’ cell histiocytosis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Primary hepatic malignancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>&lt;1</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>&lt;1</td>
<td></td>
</tr>
</tbody>
</table>

A Kasai portoenterostomy is commonly performed before transplantation. After undergoing a Kasai procedure, approximately one third of patients will have long-term success, one third will require urgent transplantation, and the remaining one third will require nonurgent transplantation [6–8]. The incidence of hepatocellular carcinoma and cirrhosis is significantly lower in the pediatric population than in adults.

Preoperative considerations

Pediatric liver transplant recipients often have a multitude of associated medical problems. Preoperative evaluation of the patient begins with the patient’s indication for transplantation. Patients with Alagille syndrome, for example, may have underlying structural heart disease. Patients with cystic fibrosis have varying degrees of underlying lung disease. A thorough assessment of these underlying end-organ complications must be performed before placing the patient on the transplant list. As in other specializations, a team approach is critical for a successful transplant program. Anesthesiologists must be available for consultation should a question arise regarding the patient’s medical condition or suitability to undergo as potentially life-threatening a procedure as liver transplant.

The general medical condition of the patient should be assessed, beginning with overall health and nutritional status. Poor preoperative nutrition may result in prolonged recovery and mechanical ventilation [9–11]. A low serum albumin coupled with ascites may be observed. Preoperative total parenteral nutrition (TPN) may contribute to preexisting hepatic dysfunction. Intraoperative and perioperative glucose management may be difficult in patients with fulminant hepatic failure [12,13].

A multitude of factors combine to cause coagulopathies in the patient with end-stage liver disease (ESLD). Poor synthetic function of coagulation factors, inadequate absorption of vitamin K-dependent factors, and dysfibrinogenemia are the most common contributing factors [14]. Variceal bleeding may occur in patients with portal hypertension, resulting in anemia; anemia may also be the result of bone marrow suppression, decreased erythropoietin production secondary to renal impairment, or malnutrition. Thrombocytopenia may exist in patients with splenomegaly from portal hypertension. Portal hypertension can significantly contribute to intraoperative blood loss. Patients may have been treated with a portosystemic shunt in the form of a transjugular intrahepatic portosystemic shunt [15].

Renal impairment may accompany hepatic failure and is multifactorial in origin. In some instances, renal insufficiency occurs as a result of the patient’s underlying medical condition, such as in Wilson’s disease or in primary oxaluria. Chronic liver disease is accompanied by an increase in antidiuretic hormone and aldosterone and a decrease in prostaglandin synthesis [16–18]. Prostaglandins are potent renal arteriolar vasodilators. Intravascular hypovolemia from blood loss or from therapy for ascites can contribute to renal failure. Finally, patients may develop hepatorenal syndrome, with its concomitant oliguria and sodium
Retention. Renal function may return to normal with a successful liver transplant, but occasionally patients progress to frank renal failure despite normal hepatic function. Preoperative hyponatremia or hyperkalemia may be difficult to manage and may require preoperative continuous hemofiltration or, in severe cases, preoperative hemodialysis. Should either be the case, provisions must be made to have these modalities available in the operating room (OR) during the transplantation procedure if necessary.

Ventilatory impairment may occur in the presence of massive ascites coupled with hepatosplenomegaly. Pleural effusions, poor nutritional status, and myocardial dysfunction may further compromise ventilatory function. Hepatopulmonary syndrome is a result of pulmonary arteriovenous and portopulmonary shunts leading to a left-to-right shunt [19]. Fortunately, resolution often occurs following successful liver transplantation [20]. Pulmonary hypertension may be present, which requires pulmonary vasodilator therapy. Perioperative mortality appears to be higher in patients with preexisting pulmonary hypertension [21]. Either of these conditions often results in prolonged postoperative ventilatory requirements. The exact cause of these processes is unknown.

Patients with liver failure typically exhibit a high cardiac output along with a low systemic vascular resistance because of peripheral vasodilatation. Fortunately, pediatric patients rarely have concomitant coronary artery disease. Circulating blood volume, however, can be deceptively low and patients may exhibit greater degrees of hypotension than expected with release of ascitic fluid shortly after surgical incision. Some practitioners have speculated that pediatric patients with ESLD may have an increased incidence of myocardial dysfunction, but no conclusive evidence has been produced at this time. Finally, patients with Alagille syndrome often have accompanying structural congenital heart disease.

Hepatic encephalopathy occurs as a consequence of elevated serum ammonia levels and increased γ-aminobutyric acid agonists in the brain [22]. Encephalopathy can be life threatening or cause obtundation associated with cerebral edema and increases in intracranial pressure, occasionally requiring intracranial pressure monitoring. Hepatic encephalopathy is graded according to severity (Table 2) [23]. In patients with severe Grade III or IV encephalopathy, measures

<table>
<thead>
<tr>
<th>Grade</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>Normal</td>
</tr>
<tr>
<td>Grade I</td>
<td>Altered spatial orientation, sleep patterns, and affect</td>
</tr>
<tr>
<td>Grade II</td>
<td>Drowsy but arousable, slurred speech, confusion, asterixsis</td>
</tr>
<tr>
<td>Grade III</td>
<td>Stuporous, responsive only to painful stimuli</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Unresponsive, with decorticate or decerebrate posturing</td>
</tr>
</tbody>
</table>

customarily undertaken to decrease the intracranial pressure should be instituted as necessary, including hyperventilation, osmotic therapy, and the use of barbiturates or diuretics.

Adequate supplies of packed red blood cells, fresh frozen plasma, and platelets should be available before induction of anesthesia. A routine protocol should be established to guarantee adequate blood product availability. Blood products should be checked before surgical incision. The hospital laboratory should be capable of providing rapid results of blood counts and coagulation tests. If this is not possible, portable on-site systems are currently available that can provide blood gas analysis, and assessments of electrolytes, hemoglobin, hematocrit, and glucose. Some system must be available for expedient transportation of samples to the laboratory and for transportation of blood products from the blood bank to the OR.

Anesthetic management

Infants rarely require any preoperative sedation. Older children often benefit from the administration of midazolam intravenously (IV) (0.05–1.5 mg/kg) or orally (0.5–1.0 mg/kg) to provide amnesia and to allay anxieties. Intramuscular injections are avoided in the presence of underlying coagulopathies.

The OR should be warmed before the patient enters the room. A forced-air warming device should be available throughout the operative procedure. Following placement of routine monitoring devices, an inhalational induction may be performed in elective living related donor cases or in patients who are hemodynamically stable and who have been nil per os (NPO) for an appropriate length of time. Sevoflurane is usually administered for induction along with nitrous oxide, depending on the nature of the patient’s underlying cardiopulmonary status and the discretion of the anesthesiologist.

In patients with venous access, an intravenous induction should be performed. The choice of induction agents will, again, be dictated by the patient’s medical condition and the preference of the anesthesiologist. In patients with a full stomach, a rapid sequence induction should be performed. There is no contraindication to the use of succinylcholine. High-dose rocuronium may be used in place of succinylcholine. Nasal intubation is avoided in patients with coagulopathies. Nasogastric tubes should also be softened and lubricated before insertion.

No studies have documented the superiority of one anesthetic technique or particular anesthetic agents. The general philosophy of this author is to use a narcotic-based anesthetic with a supplemental volatile agent as the primary anesthetic drugs. At our institution, we typically administer a loading dose of fentanyl (10–20 μg/kg) followed by a continuous infusion throughout the procedure. A variety of muscle relaxants may be used. Our protocol uses an intubating dose of pancuronium (0.1 mg/kg) followed by a continuous infusion at 50 μg/kg/hour. We have not found the use of pancuronium to result in prolonged postoperative ventilation. In fact, we have been able to extubate several patients intraoperatively
using this technique. Low renal doses of dopamine are used in some centers. Isoflurane in air/oxygen is typically used for the maintenance of anesthesia.

Invasive monitoring usually includes a Foley catheter, an arterial line, and central venous pressure (CVP) monitoring. Arterial access should be obtained in the upper extremities if possible because the hepatic artery anastomosis may require partial clamping of the aorta. Pulmonary artery catheters are rarely required in the pediatric population and should be reserved for specific indications. Placement of invasive monitoring devices may be technically challenging and surgical intervention may be required in some instances.

Massive blood loss may occur during liver transplantation. With this in mind, venous access must be adequate to allow the anesthesiologist to fluid-resuscitate the patient. Catheters ideally should be placed above the diaphragm because the vena cava may require cross-clamping. Ideally, two large-bore catheters should be dedicated for volume replacement. A double-lumen central line is useful for both CVP monitoring and for infusion of medications. We avoid the subclavian route in patients with underlying coagulopathies. Another option is to have a percutaneous intravenous catheter (PIC) line inserted preoperatively that can be used for CVP monitoring. This will allow the placement of a single-lumen large-bore central venous catheter for volume replacement. The presence of a hemodialysis catheter may further limit the patient’s central venous access.

Massive blood loss should be anticipated in retransplantation cases or in patients with a history of multiple intra-abdominal procedures [24]. It is critical that some form of rapid volume infusion device be available. Several of these devices are currently available on the market. An ideal device should be able to administer large volumes over a short period of time at or above body temperature and with sufficient safeguards against the possible infusion of large quantities of air. We usually reserve the use of these devices for patients over 40 kg or in patients over 30 kg who are at risk for excessive blood loss.

Stage I of liver transplantation is known as the preanhepatic stage and begins with surgical incision and ends with removal of the liver from the circulation. Massive blood loss may occur secondary to adhesions, large collateral vessels, coagulopathies, and portal hypertension. In patients with large amounts of ascites, hemodynamic instability may occur with the release of ascitic fluid. The goal is to achieve a relatively high preload just before Stage II because cross-clamping of the vena cava will result in an acute decrease in preload and cardiac outputs. A test clamp of the vena cava should be performed to ensure that the patient will tolerate caval cross-clamping. Should undue hypotension occur, the preload should be increased, and, if necessary, inotropic support should be initiated before caval cross-clamping.

Stage II is known as the anhepatic stage and begins with removal of the patient’s native liver from the circulation and ends with reperfusion of the new liver, customarily before hepatic artery anastomosis. Clamping of the vena cava results in a decrease in cardiac output, which is well tolerated in most children. Fluid management during this stage should aim to titrate the preload to maintain
cardiac output in anticipation of caval unclamping, which results in an acute increase in right-sided filling pressures.

Stage III commences with reperfusion of the new liver. Cardiovascular instability or reperfusion syndrome may occur, including hypotension, arrhythmias, and complete cardiac arrest [25]. Acute hyperkalemia, acidosis, air embolus, clot, cellular debris, acute hypocalcemia, and the introduction of vasoactive substances from the new liver may all play contributory roles. Pretreatment with calcium chloride, sodium bicarbonate, and lidocaine may have protective roles.

In the majority of cases, reperfusion-associated hypotension is transient and may be treated with small boluses of epinephrine. In rare instances, high right-sided pressures may result in systemic hypotension. Should hypotension or arrhythmias persist, treatment should include both inotropic and chronotropic support. The exact cause of this phenomenon is unknown. Thirty to forty percent of adult transplant recipients exhibit reperfusion syndrome [25]. Transesophageal echocardiography may be useful in diagnosing myocardial dysfunction and pulmonary hypertension [26].

Maintenance of hemostasis can be challenging. Prothrombin times (PT) of 18 to 20 seconds are acceptable, and no attempt should be made to normalize the PT or activated partial thromboplastin time (PTT) because this may increase the possibility of postoperative hepatic artery thrombosis. Fresh frozen plasma should be used to maintain the PT at or near control levels. In patients with underlying coagulopathies, 1 unit of fresh frozen plasma may be administered for every unit of packed red blood cells. This will also help to maintain the hematocrit level between 25% and 35%. Overtransfusion will increase blood viscosity, potentially predisposing the patient to hepatic artery thrombosis. High right-sided filling pressures will also adversely affect hepatic perfusion following reperfusion. Cryoprecipitate should be given when hypofibrinogenemia is present, despite fresh frozen plasma administration. Coagulopathies tend to worsen continuously throughout the procedure, with a marked increase in PT and PTT occurring immediately following reperfusion. Platelet administration should be withheld, if possible, until reperfusion is complete. Blood product administration can be guided by serial determinations of PT, PTT, and fibrinogen or by thromboelastography (TEG) [27]. TEG gives a measure of whole-blood clotting activity, platelet activity, and fibrinolysis. TEG may be more useful than standard measures of coagulation in identifying the specific cause of a coagulation defect, particularly in instances of fibrinolysis and hypercoagulability.

Prophylactic administration of ε-aminocaproic acid has not been shown to improve outcome; however, it is considered efficacious in cases of fibrinolysis. Prophylactic use of aprotinin [28] has been shown to decrease transfusion requirements during liver transplantation, but some controversy exists regarding the risk-benefit ratio of this practice, particularly in pediatric recipients, who are at greater risk for hepatic artery thrombosis compared with adult recipients. Hypotension is a common occurrence during pediatric liver transplantation. Hypovolemia, acute hypocalcemia, metabolic acidosis, and hypothermia, may contribute to hypotension. Hypotension following reperfusion may also be
caused by vasoactive substances from the new liver or by inadequate washout of the preservation fluid. Treatment of hypotensive episodes should be guided by the CVP, arterial blood gases, and ionized calcium levels. Slight metabolic acidosis should be tolerated because patients tend to develop progressive metabolic alkalosis following reperfusion, from citrate metabolism.

Virtually all patients will require postoperative ventilation, although intraoperative extubation has been performed in a limited number of cases, in our experience. Ideally the postoperative patient should be admitted to the pediatric intensive care unit (PICU) in hemodynamically stable condition, with normothermia, a hematocrit level of 25% to 30%, and a PT of 16-18 seconds.

Renal transplantation

Renal transplantation has been a successful treatment modality in children with chronic renal failure or end-stage renal disease (ESRD). One-year survival of grafts from living related donors has been reported to be 89% and 80% for 3-year survival. Survival data for cadaver grafts are 74% and 62% at 1 and

Box 1. Diseases leading to renal transplantation in children

- Alpert’s syndrome
- Anaphylactoid purpura
- Bladder neck obstruction
- Congenital nephrotic syndrome
- Corticosteroid-resistant nephrotic syndrome
- Cystinosis
- Glomerulonephritis
- Hemolytic uremic syndrome
- Hereditary interstitial nephritis
- Hypoplasia-dysplasia
- Lupus nephritis
- Medullary cystic disease
- Membranoproliferative glomerulonephritis
- Neurogenic bladder
- Oxalosis
- Pyelonephritis

3 years, respectively [29]. Some studies have reported decreased survival rates in recipients under 2 years of age [30]. There are a large number of indications for renal transplantation in children (Box 1) [31].

**Preoperative assessment**

The patient’s fluid and electrolyte status should be carefully evaluated. Postdialysis electrolytes should be obtained before transplantation. Hypovolemia may be present should transplantation occur shortly after hemodialysis. Hyperkalemia is a frequent finding that can contribute to cardiac conduction abnormalities. Hyperkalemia should be corrected before the induction of anesthesia. Patients with ESRD often have a hyperdynamic circulation but may also suffer from pericardial effusions, arrhythmias, hypertension, and cardiomyopathies [32,33]. Congestive heart failure may further compromise overall cardiovascular stability. Anemia has ceased to be a significant problem with the routine use of erythropoietin [34]. Platelet function is often abnormal, even though the platelet count may be normal. Other coagulopathies are not commonly found and if present should prompt an investigation for other underlying causes.

ESRD can cause neurologic dysfunction in the form of peripheral neuropathies. Central nervous system findings include somnolence, decreased intellect, memory loss, seizures, and in severe cases, coma.

**Anesthetic management**

Infants rarely require sedative premedication. Patients undergoing an elective living related transplant may receive oral midazolam. Should venous access be available, IV midazolam may be administered. A Foley catheter and CVP monitoring are used in addition to routine monitoring. Arterial pressure monitoring is not required for routine cases but may be indicated in patients with severe cardiovascular instability.

In elective cases, an inhalational induction may be performed. IV induction is preferred in patients in whom IV access is available and in those considered to have a full stomach. All of the currently available intravenous induction agents may be used. The choice of the drug should account for the patient’s cardiovascular and intravascular volume status and alterations in the pharmacokinetics and pharmacodynamics of these drugs in ESRD. Opioids are often administered during induction to minimize hemodynamic changes occurring with laryngoscopy and endotracheal intubation.

The diminished renal excretion characteristic of muscle relaxants is an important consideration. It may be prudent to choose a relaxant that does not rely on renal excretion. Nonetheless, all of the currently available relaxants may be safely used with careful monitoring. The use of succinylcholine in rapid sequence inductions is controversial. Succinylcholine will cause a rise of 0.5 to 0.75 mEq/L
in serum potassium levels, which could potentially cause transient hyperkalemia and its associated conduction abnormalities [35,36].

Maintenance of anesthesia often consists of a volatile agent in combination with opioids. Nitrous oxide may be used, but it is often prudent to avoid its use to prevent bowel distention. Epidural anesthesia in combination with general anesthesia may be helpful in maintaining hemodynamic stability and in providing postoperative pain relief. At our institution, we routinely place epidural catheters in renal transplant recipients without significant complications.

Fluid management should be guided by the patient’s hemodynamic status and CVP. Blood pressure should be maintained to within 10% of control values. Lactated Ringer’s solution is traditionally avoided because of the potassium concentration (4 mEq/L). Washed packed red blood cells should be used to minimize potassium administration. The CVP is often maintained at a high level just before release of the renal artery clamp. Special consideration should be given to the small child receiving an adult-sized kidney or in patients in whom the aorta is cross-clamped. The blood volume required to fill the new kidney may constitute a significant proportion of the child’s total intravascular volume. The anesthesiologist should be prepared to handle acute hypotension because poor graft perfusion may ultimately affect graft survival. Acidosis may accompany hypotension following release of an aortic cross clamp.

Anesthesiologists are often asked to administer immunosuppressant medication. Each patient should have an individual protocol clearly delineating the drugs, doses, and the appropriate time to administer these drugs. Most children can be extubated in the OR before transport to the PICU. These children should be hemodynamically stable, normothermic, awake, with normal neuromuscular strength, and have normal electrolyte levels and acid-base balance.

Heart transplantation

Indications

Children of all ages may be candidates for cardiac transplantation. The Registry of the International Society for Heart and Lung Transplantation reported a total of 4753 transplants performed in patients under 18 years of age, as of March 2001 [37]. Of these transplants, approximately 25% were performed in infants. Indications vary according to age with cardiomyopathies more commonly seen in older children. Table 3 lists the indications for children undergoing transplantation at Children’s Memorial Hospital from 1988 to 2001 [38]. Generally, candidates have structural congenital lesions that are not amenable to total correction or cardiomyopathies. Reported survival statistics vary from 80% to 90% at 1 year and 70% to 80% at 5 years. Early death occurs in approximately 8% of recipients [39,40].
Preoperative assessment

Assessment should begin with the indication for transplant. Many patients with structural congenital lesions will have undergone previous corrective or palliative procedures. One must understand the current anatomic structure of the heart as well its circulatory dynamics because each congenital lesion has its own set of anesthetic considerations. For example, there are considerable differences between a neonate with hypoplastic left heart syndrome and a teenager with a dilated cardiomyopathy.

Coexisting pulmonary hypertension should be noted. Although irreversible pulmonary hypertension is a contraindication to transplant, patients may have mild to moderate pulmonary hypertension that will have anesthetic implications. Renal insufficiency secondary to heart failure may also be present. Although it is rare for children to be in frank renal failure or to require dialysis, serum electrolytes should be evaluated before induction.

Patients requiring cardiac transplantation have extremely marginal myocardial reserve. A careful review of the patient’s current inotropic and vasoactive drug regimen should be conducted, and preparations should be made to ensure the

<table>
<thead>
<tr>
<th>Indications</th>
<th>No. of procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
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</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>19</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>8</td>
</tr>
<tr>
<td>Aortic stenosis with endocardial fibroelastosis</td>
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</tr>
<tr>
<td>Hypoplastic left heart syndrome s/p Norwood</td>
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</tr>
<tr>
<td>Unstable ventricular tachycardia</td>
<td>1</td>
</tr>
<tr>
<td>Children</td>
<td></td>
</tr>
<tr>
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<td>31</td>
</tr>
<tr>
<td>Cardiomyopathy, restrictive</td>
<td>7</td>
</tr>
<tr>
<td>Single ventricle s/p Fontan</td>
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</tr>
<tr>
<td>TGA s/p atrial repair</td>
<td>4</td>
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<tr>
<td>AV canal s/p repair</td>
<td>2</td>
</tr>
<tr>
<td>Single ventricle s/p shunt</td>
<td>1</td>
</tr>
<tr>
<td>Single ventricle s/p Glenn</td>
<td>1</td>
</tr>
<tr>
<td>Tetralogy of Fallot s/p repair</td>
<td>1</td>
</tr>
<tr>
<td>Truncus arteriosus s/p repair</td>
<td>1</td>
</tr>
<tr>
<td>Congenitally corrected TGA s/p MV replacement</td>
<td>1</td>
</tr>
<tr>
<td>Coarctation of the aorta s/p repair</td>
<td>1</td>
</tr>
<tr>
<td>Retransplant, transplant coronary artery disease</td>
<td>2</td>
</tr>
<tr>
<td>Retransplant, rejection</td>
<td>1</td>
</tr>
<tr>
<td>Retransplant, early graft failure</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>91</td>
</tr>
</tbody>
</table>

Abbreviations: AV, atrioventricular; MV, mitral valve; TGA, transposition of the great arteries.

continuity of these drugs during transportation to the OR and during the surgical procedure until cardiopulmonary bypass (CPB) is initiated.

Anesthetic management

The primary goal is to provide hemodynamic stability until CPB can be initiated. Preoperative sedation should be carefully titrated if given at all. Patients who are in the PICU should be transported with oxygen and monitoring. Emergency airway equipment should accompany the patient to the OR. Induction should proceed after placement of all monitoring devices and after ensuring that the patient is indeed receiving all cardiovascular infusions. In patients without intravascular access, it is prudent to start an IV line before induction rather than start with an inhalational induction.

Myocardial depressant agents should be avoided during induction. Ketamine (1–2 mg/kg), midazolam (0.1–0.3 mg/kg), fentanyl (30–100 μg/kg), or sufentanil (10 μg/kg) may be used for induction. Should a rapid sequence induction be required, succinylcholine or high-dose rocuronium may be used. Maintenance usually consists of an opioid-based anesthetic with low concentrations of volatile agents or benzodiazepines to provide amnesia. Any muscle relaxant may be used. Pancuronium is often used for long cases because the vagolytic-associated hypertension and tachycardia may be beneficial side effects in children.

Many patients will have undergone one or more previous surgical procedures. Prolonged dissection and potentially life-threatening blood loss can occur. A groin area is prepped and draped before surgical incision, should emergency femoral bypass be required. Venous access should be adequate to provide large volume transfusions.

The surgical procedure is relatively simple. Once complete, the patient is rewarmed. Acid-base status and potassium and ionized calcium levels should be assessed before discontinuing CPB. In patients without underlying pulmonary hypertension, the most common postbypass problem is bradycardia requiring chronotropic support or pacing. Inotropes, if required, are infused at low doses. Hypertension may be treated with afterload reduction. In patients with pulmonary hypertension, the new right ventricle may not be capable of sustaining work against an unfamiliar resistance. In these cases, hyperventilation and pulmonary vasodilators such as nitric oxide and prostaglandin E1 may be required [41,42].

The donor heart is completely denervated, resulting in delayed stress responses. Heart rate is dependent on circulating catecholamines [43]. Only direct-acting vasoactive drugs should be used. Should isoproterenol be used for chronotropic support, vasodilatation may cause hypotension requiring additional cardiovascular support. Particular attention should be paid during chest closure because hemodynamic decompensation can occur, especially if there is a considerable size mismatch between the donor and the recipient hearts.

Once complete, the patient should be transported to the PICU with full ventilatory support. Invasive monitoring and cardiovascular support should be
continued during transport. Analgesia and sedation should be provided in the postoperative period.

**Heart-lung and lung transplantation**

**Indications**

There has been very limited pediatric experience in both heart-lung and lung transplantation. Most children requiring heart-lung transplantation have irreparable complex congenital lesions or pulmonary hypertension with or without structural heart disease. Initial results have been encouraging but do not approach those of isolated heart transplantation [44]. Isolated lung transplantation has been performed primarily in children with cystic fibrosis, bronchiolitis obliterans, pulmonary arteriovenous malformations, and interstitial pneumonitis [45,46]. Single-lung transplantation is rarely performed in patients with cystic fibrosis because of the risk of contralateral infection. Unfortunately, reported 5 year survival rates are low for both procedures, on the order of 33% [47].

**Preoperative assessment**

In patients undergoing heart-lung transplantation, the assessment is virtually identical to those undergoing isolated heart transplantation. Special attention should be paid to the pulmonary system. In patients undergoing isolated lung transplantation, a determination should be made regarding the patient’s ability to undergo the procedure without CPB. This decision will be based on the patient’s underlying cardiovascular status and ability to tolerate one-lung ventilation and clamping of the pulmonary artery [48].

**Anesthetic management**

As in heart transplant recipients, the decision to premedicate should be based on the patient’s underlying condition. Midazolam has minimal effects on myocardial function, but it may compromise ventilation in a patient with marginal reserve. Virtually all patients require supplemental oxygen administration during transport and in the OR before induction. Nitrous oxide should probably be avoided during induction in these patients. Induction in heart-lung transplant recipients should take into account the same considerations as in patients undergoing isolated heart transplantation. Young children undergoing isolated lung transplantation may undergo an inhalational induction assuming an adequate NPO period and adequate myocardial function. Double-lumen endotracheal tubes are used in children large enough to accommodate them. Small children should have a bronchial blocker inserted. Patient positioning varies: lateral decubitus for single-lung, supine with the arms over the head for sequential double-lung, and supine for en bloc double-lung
transplants. Epidural catheters may be inserted in patients undergoing isolated lung transplantation off CPB. Blood loss is usually minimal, and fluid requirements are not excessive.

Maintaining arterial oxygenation during one-lung ventilation can be challenging. Strategies include increasing the inspired oxygen concentration, increasing minute ventilation, and applying positive end-expiratory pressure to the ventilated lung. It is impractical to attempt to apply continuous positive airway pressure to the nonventilated lung. The addition of pulmonary vasodilators may be helpful in patients with pulmonary hypertension. Cardiovascular instability or intolerance to these measures should prompt initiation of CPB.

Lung ventilation is initiated following completion of the bronchial anastomosis. The lung is reperfused shortly thereafter. The transplanted lung is denervated and lacks both bronchial blood flow and lymphatic drainage. The new lung has an abnormal response to arterial CO₂ with patients exhibiting a rise in resting PCO₂ to 45 to 50 mm Hg following transplantation [49]. The cough reflex has been noted to be absent following transplantation, and a rigorous regimen of self-induced coughing should be maintained. The double-lumen endotracheal tubes should be exchanged for a single-lumen tube before transport to the PICU.

**Intestinal and multiorgan transplantation**

**Indications**

The most common indication for a multiorgan transplant is the short-gut syndrome, which can result from a variety of causes. Short-gut syndrome invariably leads to the patient’s dependence on TPN. Long-term TPN therapy leads to steatotic liver disease and ultimately to hepatic failure requiring transplantation. These patients, therefore, become candidates to undergo combined liver-small bowel transplantation. Despite the relative success of isolated liver transplantation in children, results of isolated small bowel transplantation or combined small bowel-liver transplantation has not been as encouraging [50,51].

**Preoperative assessment**

In addition to the considerations for liver transplantation, intestinal transplant patients may be particularly malnourished. Venous access is a significant issue because central access may be exhausted resulting from the need for prolonged TPN. Access may require the involvement of interventional radiologists or our surgical colleagues. Intraoperative glucose management may be particularly difficult.

**Anesthetic management**

The anesthetic management of patients undergoing liver transplantation has already been discussed. Removal of the liver and evisceration of other organs
may cause significant blood loss because of adhesions from previous surgical procedures and underlying coagulopathies. Dissection can be lengthy, predisposing the patient to hypothermia. Fluid management, compounded with lability in serum glucose levels, can be difficult. Reperfusion of multiple organs may result in significant hemodynamic instability. Hyperkalemia, acidosis, release of vasoactive substances, bleeding, hypothermia, and possible air embolism may contribute to hypotension and arrhythmias.

Fatigue is an important consideration. These procedures are lengthy and often occur in the middle of the night. Provision should be made within institutions to provide relief for all OR staff on a timely basis.

Summary

Pediatric organ transplantation is being performed with increasing frequency and with improving survival rates. A scarcity of donor organs continues to limit the number of transplants being performed in the United States. The anesthetic management of these patients is complicated, and the potential for disaster is high. The complexity of the surgical procedure coupled with the fragile and tenuous condition of these patients can create an “anesthetic nightmare.”

These are extremely complicated procedures in extremely complicated patients. There are constant technical challenges in the placement of large IV catheters, invasive monitoring devices, and bronchial blockers. Children are more prone to hypothermia, a common problem during these long procedures. Blood loss can occasionally be massive, totaling multiple blood volumes. Maintenance of hemostasis is difficult in patients with coagulopathies and ongoing blood loss. Intraoperative fluid and glucose management require careful attention. The pharmacology and pharmacokinetics of anesthetic drugs are often altered in patients with ESLD and ESRD. Patients with congenital heart disease have completely abnormal anatomy and physiology. To devise an anesthetic plan, it is crucial to understand the underlying disease process and the intricacies of the surgical procedure. Only by doing so can one anticipate and adequately handle both expected and unexpected perioperative events thereby increasing the odds of a successful outcome.

References


