

Chapter 25: Anesthesia for Liver Transplantation

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INTRODUCTION

FOCUS POINTS

1. Most common etiology of end-stage liver disease (ESLD) in children is cirrhosis secondary to biliary atresia.
2. ESLD involves nearly every organ system.
3. The primary pulmonary manifestation of ESLD is arterial hypoxemia.
4. The most common cause of fulminant hepatic failure (FHF) is acute viral hepatitis.
5. Indications for the highest priority status (1A) for liver transplantation include FHF and hepatic arterial thrombosis or primary graft nonfunction post-transplant.
6. There are three surgical phases in liver transplantation: preanhepatic, anhepatic, and neohepatic.
7. Postreperfusion syndrome (PRS) during the neohepatic phase is associated with increased perioperative morbidity and mortality.
8. Postoperative complications following liver transplantation include bleeding, vascular occlusion events, rejection, and primary nonfunction.

CASE

A 9-year-old boy with history of biliary atresia post Kasai procedure presents with hyperbilirubinemia, transaminitis, and altered mental status. Acute hepatic failure with hepatic encephalopathy is diagnosed and he is placed on the highest priority status (1A) for liver transplantation.

HISTORY

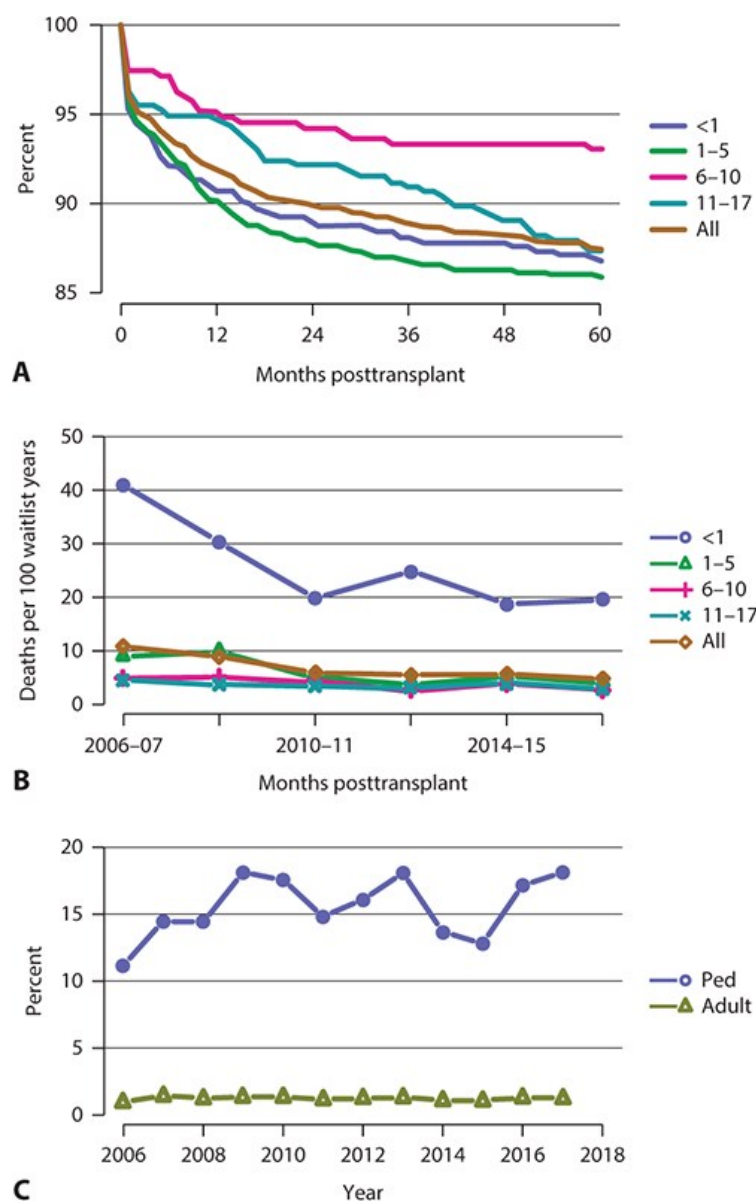
Dr. Thomas Starzl performed the first pediatric liver transplant (LT) in a 3-year-old girl with biliary atresia in 1963. The recipient expired in the operating room secondary to intraoperative bleeding. In 1967, the first successful pediatric LT was performed.¹ Prior to the introduction of cyclosporine, 2-year survival following LT was less than 30% with rudimentary immunosuppression regimens consisting of corticosteroids and azathioprine.²⁻⁴ Following the introduction of cyclosporine in 1979 survival rates increased. Current 1-year survival rates exceed 80%.⁵ Initially few centers performed pediatric LTs, but this has increased significantly over the past three decades. Currently, there are more than 100 centers approved to perform pediatric LT in the United States; however, only 16 centers perform more than 10 pediatric LT annually.⁶

Less than 10% of all LTs are performed in children. According to the United States Organ Procurement and Transplantation Network (OPTN) more than 145,000 LTs were performed in the United States between 1998 and 2016, and approximately 1600 were performed in children.⁵ Current survival rates for deceased donor LT (DDLT) are greater than 90% in some centers (Figure 25-1A), with higher survival rates for live donor LT.⁵ Inadequate cadaveric organ supply has resulted in unacceptably high pretransplant waitlist mortality (Figure 25-1B). Innovative techniques to optimize hepatic graft supply for pediatric LT include reduced liver, split liver, and live donor LT (Figure 25-1C). However, split and reduced LTs have lower graft survival compared to

whole organ cadaveric and live donor transplants.⁷

Figure 25-1

A. Patient survival among pediatric liver transplant recipients: deceased donor. **B.** Pre-transplant mortality rates among pediatric patients waitlisted for a liver transplant, by age. **C.** Percentage of split liver transplants compared to total transplants performed among pediatric and liver transplant recipients. (Reproduced with permission, from Kasiske BL, Israni AK, Snyder JJ, et al. OPTN/SRTR 2017 Annual Data Report: Liver: *Am J Trans.* 2019; 19(S2): 184-283.)



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Pediatric anesthesiologists are key members of the multidisciplinary teams needed to ensure optimal pediatric LT outcomes. Pediatric anesthesiologists must participate in all phases of perioperative care including patient selection, preoperative optimization, intraoperative management, and postoperative care. This essentiality is highlighted by a United Network for Organ Sharing (UNOS) mandate requiring all LT centers (including pediatric centers) to designate a Director of Liver Transplant Anesthesia (UNOS Bylaws, Appendix B, Attachment I, Section XIII). This chapter will focus on the perioperative management of pediatric LT.

INDICATIONS

Indications for pediatric LT include end-stage liver disease (ESLD), metabolic disorders, hepatic malignancy, and fulminant hepatic failure. The most common form of pediatric ESLD is cirrhosis secondary to biliary atresia. This disease is caused by obstruction or agenesis of the extrahepatic biliary tree resulting in cholestasis and progressive cirrhosis. Prior to introduction of the Kasai hepatoportoenterostomy 2-year survival for children born with biliary atresia was less than 10%.⁸ The Kasai procedure increased survival rates, but most patients will still develop hepatic failure requiring LT by age 10.^{8,9} Other indications for pediatric LT include metabolic disorders (22%), fulminant hepatic failure (11%), hepatic neoplasms (9%), autoimmune diseases (4%), and other miscellaneous conditions (13%).⁵

PATHOPHYSIOLOGY OF END-STAGE LIVER DISEASE

End-stage liver disease is defined as irreversible hepatic fibrosis and cirrhosis resulting in portal hypertension and the loss of synthetic function and toxin clearance. Complications of ESLD involve nearly every organ system.

Patients with ESLD typically exhibit hyperdynamic circulatory physiology with high cardiac output and low systemic vascular resistance. Cardiac output is increased secondary to both stroke volume and heart rate. Systemic vascular resistance is reduced as a consequence of vasodilatory splanchnic peptide release and systemic arterial shunt (intrapulmonary, portopulmonary, etc.) development. Patients with ESLD typically have maldistributed systemic bloodflow and abnormal oxygen utilization with elevated systemic venous oxygen saturation.¹⁰ Low-resistance splanchnic bloodflow is increased, stealing bloodflow from vital organs. Compensatory increases in sympathetic nervous and renin-angiotensin-aldosterone tone decrease responsiveness to exogenous and endogenous vasoactive agents. In rare instances, children with ESLD develop cirrhotic cardiomyopathy with reduced ejection fraction and diastolic dysfunction.¹¹ Congenital heart malformations associated with progressive hepatic failure are common with biliary atresia or Alagille syndrome.¹²

The primary pulmonary manifestation of ESLD is arterial hypoxemia. Cyanosis in liver failure is multifactorial due to intrapulmonary shunt, restrictive lung disease, and abnormal hypoxic pulmonary vasoconstriction. Severe pulmonary complications of ESLD include hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PPH). Hepatopulmonary syndrome is defined as liver dysfunction and arterial hypoxemia in the presence of intrapulmonary arteriovenous malformations.¹³ The diagnosis is established by ruling out intracardiac shunt and demonstrating intrapulmonary arteriovenous shunt on bubble echocardiogram or ventilation perfusion scan.¹⁴ The development of HPS has been linked to increased mortality.^{15,16} There are no specific treatments for HPS, but LT is curative. Increased portal and pulmonary vascular resistance (PVR) are diagnostic of PPH. This entity may be complicated by acute right ventricular ischemia and sudden cardiac death. For severe PPH, pretransplant pulmonary vasodilator therapy (inhaled nitric oxide, prostacyclin, and sildenafil) may be indicated and has been linked to reduced pulmonary artery pressures allowing for successful LT.^{17,18}

Coexistent renal dysfunction (prerenal azotemia, acute tubular necrosis, or hepatorenal syndrome) is common with ESLD. Intravascular volume depletion due to ascites, hypoalbuminemia, and diuretic therapy frequently results in prerenal azotemia. Treatment involves fluid administration and decreased diuretic administration. Acute tubular necrosis (ATN) may occur due to acute alterations in renal blood flow (RBF) and renal ischemia, especially with increased intraabdominal pressure from ascites. Management of ATN includes optimization of RBF and in severe instances renal replacement therapy (RRT). Hepatorenal syndrome (HRS) is the rapid development of acute kidney injury (AKI) that may progress to acute renal failure requiring RRT.¹⁹⁻²¹ Oliguria with arterial hypertension and low urinary sodium is diagnostic of hepatorenal syndrome. The etiology of HRS is not completely understood but is thought to be secondary to renal arteriolar vasoconstriction and maldistribution of renal blood flow. An inciting stressor (infection, bleeding, etc.) generally precedes HRS. Liver transplantation has been shown to reverse HRS; however, patients may require intraoperative dialysis during LT.

Gastrointestinal complications of ESLD included portal hypertension, gastrointestinal bleeding, dysmotility, malabsorption, malnutrition, and growth failure. Portal hypertension is associated with the development of varices, prone to acute bleeding, and may require transfusion and sclerotherapy. Abnormal gastrointestinal motility and delayed gastric emptying increase the risk of aspiration during anesthesia. Ascites development is a source of protein loss with loss of plasma proteins and increased risk of peritonitis.

The neurological sequelae of liver disease are life-threatening. Hepatic encephalopathy (HE) is common in acute and chronic liver failure. Symptoms

range from altered sensorium to obtundation with decorticate and decerebrate posturing, cerebral edema, intracranial hypertension, and uncal herniation (Table 25-1).²²⁻²⁴ The etiology of HE is likely multifactorial. Neurotoxins (ammonia, false neurotransmitters) exerting GABA-like effects are thought to play a role.²⁵ Similar to HRS, precipitating events (sepsis, bleeding) frequently precede the development of HE. Treatment includes supportive therapies (ICP monitoring, temperature regulation) and gastrointestinal decontamination (lactulose, rifaximine).²⁶

Table 25-1

Grades of Hepatic Encephalopathy and Associated Clinical Findings

Grade	Clinical Signs	Asterixis	EEG Findings
I	Altered sleep-wake cycle	Minimal	Minimal
II	Drowsy, irritable, altered mood	Obvious	Generalized Slowing
III	Unresponsive to verbal stimuli, hyperreflexia, positive Babinski	Reduced	More pronounced slowing
IV	Obtunded, decerebrate or decorticate posturing to painful stimuli	Absent	Generalized slowing with reduced amplitude to flat EEG

Hematological changes in ESLD include thrombocytopenia due to hypersplenism, and reduced synthesis of coagulation factors. Hepatically derived procoagulant and anticoagulant factors are decreased in ESLD affecting both the intrinsic and extrinsic coagulation pathways. Children with ESLD have increased risk of both bleeding and thrombosis.

FULMINANT HEPATIC FAILURE

The United Network for Organ Sharing (UNOS) defines FHF as the onset of HE within 8 weeks of the first symptoms of liver disease in the absence of preexisting liver disease. The most common cause of FHF is acute viral hepatitis (hepatitis A, B, C, D, E; EBV; CMV; enterovirus; etc.). Other causes include toxin exposure (acetaminophen), metabolic disease (neonatal hemochromatosis, Wilson disease), and idiopathic forms. Encephalopathy may be absent, late, or difficult to recognize. Patients with FHF with coagulopathy (INR > 2.0) and/or the presence of encephalopathy secondary to liver failure (grade II or greater) require higher level monitoring in the PICU.²⁴ FHF is a disease associated with significant mortality and is an indication for emergent Status 1A listing. Benzodiazepines should be avoided in FHF as they increase false neurotransmitters and may precipitate encephalopathy. Infection is a common cause of pre-transplant mortality. Children with FHF are at high risk of infection secondary to the impaired cellular and humoral immunity and empiric antimicrobial (bacterial and fungal) therapy is indicated.²⁷ Organisms responsible for life threatening infections in FHF include: *S. Aureus*, other Gram-Positive bacteria, *E. coli*, and *Candida*.²⁷

PRETRANSPLANT EVALUATION

The pretransplant evaluation process is an essential component of pediatric liver transplantation. In 2014, the American Association for the study of Liver Diseases, the American Society of Transplantation and The North American society for Pediatric Gastroenterology set forth “Guidelines for the Pediatric Patient Undergoing Evaluation for Liver Transplantation”.¹² These guidelines recommend that pediatric transplant centers develop multidisciplinary patient selection committees for the purpose of evaluating candidates for liver transplantation prior to listing. These teams will typically include transplant surgeons, hepatologists, anesthesiologists, intensivists, psychologists, social workers, nurses, dieticians, and pharmacists. The first task of these transplant evaluation teams is to identify the timing of initiation of the pretransplant workup, which may range from emergent to elective. Patients with fulminant or acute hepatic failure may be critically ill and at risk for death and permanent neurological injury. These patients will typically be listed in an emergent or urgent fashion.

These committees also serve to identify, evaluate, and manage comorbidities of ESLD. A comprehensive multiorgan system assessment is critical to the pretransplant evaluation process. Patients with malnutrition may require enteral or parenteral supplementation. Management of ascites includes diuretic therapy. Porto systemic shunt procedures may be recommended in the setting of respiratory compromise secondary to ascites.¹² Assessment

of cardiorespiratory status should include evaluation of HPS and PPH with room air pulse oximetry and trans thoracic echocardiogram. If concern for HPS is identified with pulse oximetry then agitated saline bubble test should be performed with TTE to evaluate for right to left shunt. If TTE shows evidence of right ventricular hypertension then PPHN evaluation with cardiac catheterization should be performed with direct pulmonary artery pressure measurements.

Following completion of the evaluation candidates will be listed and stratified according to severity of illness. Patients who are most critically ill with acute liver failure receive the highest priority status (Status 1A). Indications for status 1A listing include FHF, or hepatic artery thrombosis or primary graft nonfunction following liver transplantation. Status 1B is reserved for chronically ill children with life threatening comorbidities who receive special exceptions. All other patients with chronic liver disease awaiting cadaveric livers have been stratified according to the Pediatric End-Stage Liver Disease (PELD) score and Model for End-Stage Liver Disease (MELD) scoring systems. The PELD score is applied to children age less than 12 years and incorporates age, weight, height, bilirubin level, albumin level, and international normalized ratio (INR). The MELD score is for children older than 12 years and incorporates serum bilirubin, creatinine, and INR, as well as the need for renal replacement therapy. The MELD and PELD scores were designed to reduce pretransplant mortality without increase in posttransplant outcomes.²⁸ These scoring systems, implemented in 2002, predict pretransplant waitlist mortality and assist with organ allocation better than the previously used Child-Turcotte-Pugh Score, which incorporated subjective measures.^{29,30} The observation of elevated waitlist mortality in hyponatremic adults with ESLD candidates has led to the recent application of the MELD Na score.³¹

INTRAOPERATIVE MANAGEMENT

Operating Room Set Up

The operating room configuration for LT should resemble other major blood loss procedures (cardiopulmonary bypass or trauma). Dual fluid warmers with Y type blood administration sets and multiple invasive pressure lines set up should be available. Rapid infusion devices should be available for infants greater than 20 kg. A balanced salt solution containing dextrose carrier should be attached to a manifold such that vasoactive and inotropic medications may be administered at a constant rate. Multiple syringe pumps must also be available for drips on a pump tree. Available vasoactive infusions should be able to support cardiac output ([epinephrine](#)) and vasomotor tone ([norepinephrine](#) and [vasopressin](#)). Bolus resuscitative drugs should include [epinephrine](#) and [phenylephrine](#) in 10 mcg/mL and 100 mcg/mL dilutions in 10-mL syringes as well as [atropine](#), calcium chloride, and sodium bicarbonate. Additional medications should include antibiotics (ie, ampicillin-sulbactam), immunosuppressants (ie, [methylprednisolone](#), basiliximab), and heparin (1000 U/mL).

The blood bank must be notified of the potential LT when the organ is accepted to ensure that blood products are available. The quantity required varies based on patient weight and on additional risk factors for bleeding (previous abdominal surgery, decreased synthetic function with coagulopathy, hypersplenism with thrombocytopenia). The minimum available products should be 2 adult packed red blood cell (PRBC) units/10 kg, 2 adult fresh frozen plasma (FFP) units/10 kg, and 1 single-donor platelet (SDP) unit/10 kg. Blood products should be pre-checked and placed in the room-specific refrigerator or cooler within the operating room. Platelets must not be refrigerated but placed on a rocker.

Patients undergoing LT have multiple risk factors for perioperative hypothermia including intraabdominal surgery, massive fluid shifts, and hypothermic graft implantation. The patients will lose heat rapidly after abdominal incision. Hypothermia increases the risk of coagulopathy, infection, and dysrhythmias. The operating room should be warmed prior to patient arrival. Additional warming methods should be employed such as forced air heating devices, circulating water heating blanket, heated, humidified circuits, heating lamps, and fluid warmers.

Anesthetic Induction

Preservation of cardiorespiratory homeostasis is essential during induction of anesthesia for LT. Premedication with midazolam is generally acceptable but should be avoided in patients with HE. Intravenous induction is preferred. Patients with ESLD are at risk for aspiration due to delayed gastric emptying as well as increased intraabdominal pressure from hepatomegaly and ascites. Rapid sequence induction with cricoid pressure is routinely performed to mitigate risk of aspiration. Placement of an appropriately sized cuffed endotracheal tube is recommended as dynamic changes in ventilatory mechanics are routine during dissection of the diseased liver. There may also be significant size discordance between the donor graft and the recipient abdomen, further contributing to reduced compliance postoperatively.

Standard monitors include electrocardiogram, two pulse oximeters (one upper extremity, one lower extremity in case of cross-clamping of the aorta),

capnography, and core body temperature. Advanced invasive and noninvasive monitoring should include arterial and central venous pressures (CVPs) as well as two-site (cerebral and somatic) near-infrared spectroscopy (NIRS), although NIRS may only be useful as a trend monitor with hyperbilirubinemia. Two large-bore IV catheters should ideally be placed in upper extremities in case of cross-clamping. If venovenous bypass (VVB) is to be potentially used, a discussion with the surgeon should take place regarding the extremity to be used or avoided for IV placement. Generally, the left side is preferred for VVB. Arterial access should be obtained in an upper extremity in anticipation of abdominal aorta cross-clamp during anastomosis of the hepatic artery with placement of the noninvasive blood pressure cuff on a lower extremity. Central venous access is generally placed in the internal jugular vein with ultrasound guidance. When long-term durable central venous access is required, the surgeon will place a tunneled Hickman or Broviac catheter. Care must be taken when placing an orogastric tube as these patients may have esophageal varices and are generally coagulopathic. Nasogastric tubes should be avoided in coagulopathic patients.

MAINTENANCE OF ANESTHESIA

Maintenance of anesthesia typically involves a balanced anesthetic technique consisting of a volatile agent (sevoflurane or **isoflurane**) along with an opioid (fentanyl or sufentanil). Cisatracurium is a neuromuscular blocking agent metabolized by Hoffman elimination and not dependent on hepatic metabolism, which may be useful in the setting of ESLD, particularly when early postoperative extubation is planned.

Coagulation Monitoring

The American Society of Anesthesiologists (ASA) recommends advanced viscoelastic coagulation monitoring during cases where major blood loss is expected.³² Preoperative coagulation assessment via routine hemostatic assays (PT, aPTT, INR platelet count) is not predictive of perioperative bleeding during liver transplantation.^{33–36} Goal-directed transfusion algorithms based on viscoelastic assays (thromboelastography, rotational thromboelastometry) have been shown to reduce blood product exposure. In addition to help diagnose the specific elements of clot formation that contribute to coagulopathy, these assays may also be useful for identification of hypercoagulable states and fibrinolysis that are known to occur in the setting of hepatic failure.^{32,37}

Surgery

There are three surgical phases: preanhepatic, anhepatic, and neohepatic.

Preanhepatic Phase

The preanhepatic phase involves abdominal dissection with ultimate removal of the diseased liver. Significant alterations in preload occur during this period secondary to bleeding and reduced systemic venous return with manipulation of the mesentery and liver prior to explantation. Bleeding is increased with adhesions from previous abdominal surgery (ie, Kasai procedure, liver transplant). Anesthetic goals during the preanhepatic phase include maintenance of a relatively low CVP without limiting cardiac output and perfusion.³⁸ Blood losses should be replaced, and coagulopathy corrected. **Vasopressin** may be used to redistribute splanchnic bloodflow to the central circulation and reduce portal venous pressure and bleeding.

Anhepatic Phase

The anhepatic phase begins with clamping of the infrahepatic and suprahepatic vena cavae. Thereafter the hepatic artery and portal vein are cross-clamped, and the liver is removed. Caval clamping decreases venous return such that cardiac output may be reduced by up to 30%; however, children with portal hypertension may have collaterals mitigating preload limitation. This is not the case in the setting of acute fulminant hepatic failure. Required interventions include volume resuscitation and vasoactive and inotropic medication administration. When cardiac output remains critically limited despite corrective measures, VVB (typically femoral—axillary) is indicated. Direct feedback to the surgeon from the anesthesiologist during test clamping is essential in this decision-making process.

Maintenance of cardiorespiratory, hematological, and metabolic homeostasis is essential during the anhepatic phase.³⁹ Labs should be checked regularly (every 30 minutes) and prior to reperfusion so that electrolyte and acid-base status may be optimized. Hypokalemia is generally not corrected prior to reperfusion, as potassium levels will increase with reperfusion. Transfusion of packed red blood cells (PRBCs) (hematocrit 60% to 70%) in isolation without reconstitution in FFP may lead to a higher-than-desired recipient hematocrit and associated hyperviscosity. We routinely reconstitute

packed PRBCs and FFP for all intraoperative transfusions after initiation of the anhepatic phase to maintain hemodilution (goal Hct 30 or less) and coagulation factor levels. Prior to reperfusion of the neohepatic graft, acid-base, electrolyte (calcium and potassium), and intravascular volume status should be optimized.

Neohepatic Phase

Reperfusion marks the end of anhepatic phase and the start of the neohepatic phase. Reperfusion of the liver occurs with release of the portal venous, infrahepatic, and suprahepatic vena caval clamps. Preservation fluid is typically flushed out of the graft prior to reperfusion; however, there is frequently residual cold, acidotic, hyperkalemic solution within the graft which may cause circulatory depression.³⁹ Cardiovascular instability may ensue with bradycardia, hypotension, elevated PVR and right heart failure, malignant ventricular arrhythmias, and circulatory collapse. Postreperfusion syndrome (PRS) is defined as a 30% reduction in baseline blood pressure for more than 1 minute within 5 minutes of reperfusion. PRS is associated with increased perioperative morbidity (transfusion, renal failure, hospital length of stay) and mortality.⁴⁰ Increased PVR with PRS may require pulmonary vasodilator therapy (inhaled nitric oxide). Metabolic abnormalities should be corrected immediately after reperfusion. Thereafter most metabolic derangements will self-correct if the liver is functioning properly.

Following reperfusion, the hepatic artery anastomosis is performed. Biliary drainage is constructed as either direct end-to-end anastomosis or Roux-en-Y hepaticojejunostomy. Depending on patient physiological status, the biliary reconstruction may be delayed in the setting of a staged abdominal closure. Abdominal closure will increase intraabdominal pressure, especially with large donor organs. Graft perfusion may be compromised in this setting. Ventilatory mechanics and renal somatic NIRS trends should be followed closely during closure. Loss of the lower extremity pulse oximeter tracing is a late finding of high intraabdominal pressures. Bladder pressure monitoring may be useful to detect abdominal compartment syndrome.

POSTOPERATIVE MANAGEMENT

Hemodynamics

Hemodynamic support of the newly transplanted liver following reperfusion includes preservation of cardiac output and oxygen delivery through maintenance of adequate end-organ perfusion and avoidance of systemic venous hypertension. Maintenance of neohepatic perfusion without venous congestion is critical in the early postoperative period following LT. Hepatic perfusion pressure (HPP) is calculated by subtracting the CVP from the mean arterial blood pressure ($HPP = MAP - CVP$). The HPP should be maintained to at least 40 mm Hg. It is also critical to keep the systemic venous pressure within normal limits (less than 10 mm Hg) as systemic venous hypertension is associated with hepatic venous congestion and potential compromise of hepatic artery and portal venous blood flow, increasing the risk of thrombosis.

Anticoagulation

Pediatric LT is associated with an increased incidence of neohepatic thrombotic complications. Due to the high morbidity associated with neohepatic hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT), hepatic artery thrombosis anticoagulation is initiated early after hemostasis is achieved. Heparin infusions are started once adequate hemostasis has been established before exiting the operating room. The goal is therapeutic anticoagulation within the first 24 hours. Post-LT aPTT and anti-Xa levels are used to guide heparin management. Early initiation of antiplatelet therapy with aspirin is employed to reduce the incidence of HAT.

POSTOPERATIVE COMPLICATIONS

Postoperative complications following liver transplantation include bleeding, vascular occlusion events, rejection, and primary nonfunction. The overall incidence of post-LT complications approaches 10%. Surgical reexploration may be indicated for graft threatening lesions or for postoperative hepatic failure of unclear etiology. Bleeding and hemodynamic lability may be significant during these procedures requiring anticipatory planning by the anesthesiology team.

Postoperative vascular complications are more common following pediatric LT than in adults. Hepatic artery thrombosis (HAT) occurs in 1% to 2% of pediatric LTs and is associated with significant morbidity and mortality.⁴¹ The celiac trunk is the only arterial source of neohepatic arterial bloodflow. Risk factors for HAT include long donor-organ cold ischemic time, hypotension, mesenteric vasoconstriction, and hepatic venous congestion. Hepatic

arterial flow limitation from thrombosis may range from stenosis to occlusion. Persistent transaminitis [aspartate aminotransferase (AST), alanine aminotransferase (ALT)], elevated lactate dehydrogenase (LDH), or coagulopathy (INR) post-LT should prompt immediate imaging with Doppler ultrasonography. Early diagnosis and treatment are critical to graft and patient survival. Surgical reexploration is generally indicated for suspected postoperative hepatic artery stenosis. Fulminant hepatic failure following HAT requires urgent retransplantation.⁴¹

Portal vein thrombosis (PVT) is more frequent in children transplanted for biliary atresia due to portal vein hypoplasia.⁴¹ The overall incidence of PVT is 5% to 10%.⁴¹ Concern for post-LT PVT requires Doppler ultrasonography. Treatment for early PVT may involve surgical reexploration, anastomotic revision, and thrombectomy. Recrudescence of portal hypertension (GI bleeding, thrombocytopenia) is suggestive of late PVT. Catheter-based balloon dilation may be helpful for portal vein stenosis.⁴¹

Acute rejection is common following pediatric LT. There may be no symptoms, but a clinical presentation can consist of fever, right upper quadrant and back pain, irritability, and malaise. Transaminitis with leukocytosis and eosinophilia suggest rejection. Liver biopsy is the gold standard for diagnosis; however, donor-derived cell-free DNA offers the promise of noninvasive diagnosis of rejection. Treatment of rejection involves increasing immunosuppression. Antibody-mediated rejection may be treated with immunoglobulin, plasmapheresis, and CD-20 antibody (ie, [rituximab](#)).

Primary nonfunction (PNF) is suggested by signs of hepatic failure without evidence of vascular compromise or rejection. Persistent transaminitis, lactic acidosis, coagulopathy, and bleeding are common with PNF. Hyperammonemia with encephalopathy is life-threatening complications of PNF. Treatment is supportive initially, but urgent retransplantation is indicated in fulminant graft nonfunction.

CONCLUSION

The perioperative care of children undergoing LT requires a thorough understanding of physiology of ESLD and the unique challenges associated with each perioperative phase of care. Pediatric anesthesiologists possess the skills and training necessary to assume vital leadership roles on multidisciplinary pediatric LT teams allowing continued improvement in outcomes for this vulnerable patient population.

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