Liver transplantation became an accepted therapeutic option for end-stage liver disease after the National Institutes of Health Consensus Development Conference in 1983. Since then, its applications have expanded so that now there are 16,219 patients on the United Network for Organ Sharing waiting list (data as of September 30, 2000), with 4,698 transplants performed in 1999 and an expected increase of 6% per year.* Although liver transplantation was once almost exclusively the domain of a few large teaching centers, now it is more widely offered, with 115 centers in the United States performing this procedure. Overall patient survival rates are 94% at 30 days and 86% at 1 year (n = 6,755, January 1997 to December 1998).* Several factors have contributed to this, including advances in organ preservation, immunosuppressive therapy, surgical technique, and anesthetic management.

Optimal anesthetic management of these complex, frequently critically ill patients requires not only anticipation of the physiologic changes associated with the surgical procedure but also management of the multisystem abnormalities associated with end-stage liver disease. Although the purpose of this chapter is primarily to describe management for the transplant procedure, it is important to first discuss management of other organ system derangements. In fact, in some instances (notably pulmonary hypertension), the hepatic disease may be overshadowed by the severity of the coincident extrahepatic disease.

**Cardiac**

A hyperdynamic circulation develops in 30% to 60% of all patients with cirrhosis.1 Typically, the cardiac index is elevated and the systemic vascular resistance is low, with a low blood pressure and elevated heart rate. Elevated levels of both circulating vasoconstrictors and vasodilators are found in patients with end-stage liver disease, although the clinical balance favors vasodilation. This is thought to be the basis of the observed pressor resistance in these patients.

Cardiomyopathy with overt congestive failure is uncommon in patients with cirrhosis. However, it appears that these patients show ventricular dysfunction with volume and hemodynamic stress,2,4 such as may occur during reperfusion of the graft. As transplant recipients age, the incidence of coronary artery disease increases. Reported incidences of significant coronary artery disease in liver transplant candidates older than 50 years range from 5%4 to 27%,5 with diabetes identified as an independent risk

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factor. This suggests the need for aggressive initial and continued cardiac evaluation for patients with this history.

**Pulmonary**

Pulmonary disorders in end-stage liver disease involve both the parenchyma and the vasculature. Common parenchymal manifestations are those that occur frequently in other debilitated patients and include atelectasis, obstructive airway disease, pneumonia, aspiration, and effusion. Patients with ascites, particularly those with a large volume and tense abdomen, will show early airway closure and decreased lung volumes on pulmonary function studies. There may additionally be pulmonary involvement related to the underlying cause of liver failure such as interstitial pneumonitis and granulomatous disease.

Vascular disease includes apparent shunting caused by intrapulmonary vasodilations (IPVDs), true shunting, and pulmonary hypertension. Transplantation of patients with severe manifestations of these complications is controversial because resolution after transplant is unpredictable and, in the case of pulmonary hypertension, intraoperative and perioperative death is common.

Hepatopulmonary syndrome is the diagnosis given to hypoxemia in the setting of hepatic disease that is thought to be caused by vascular abnormalities, most often the presence of IPVDs. The defect is one of oxygen diffusion at the capillary level. The driving force of oxygen across the alveolar membrane into the widely dilated capillaries of patients with IPVDs cannot adequately penetrate the entire stream of blood, leaving a central stream that is essentially shunted (Fig. 1). The hypoxemia of hepatopulmonary syndrome paradoxically improves in the supine position and worsens in the upright (orthodeoxia). This is because reclining shunts blood away from the lung bases, where IPVDs predominate, and toward the apices, which are better ventilated.

![Diagram of Pulmonary Vascular Abnormality](image)

**Fig. 1.** Pulmonary vascular abnormality considered likely in a patient with hepatopulmonary syndrome. This schematic presumes that abnormal vessels are present at precapillary level and exist close to gas exchange units in the lung, thereby participating in diffusion of oxygen molecules from the alveolus. Some vascular dilatations or communications may be larger, not in proximity to gas exchange units or have vascular walls that preclude transfer of oxygen molecules into venous blood flow. (From Krowka MJ, Cortese DA: Severe hypoxemia associated with liver disease: Mayo Clinic experience and the experimental use of almitrine bimesylate. Mayo Clin Proc 1987; 62:164–73.)
Increasing inspired oxygen fraction will also improve oxygenation by increasing the
driving force of oxygen through the capillary. In fact, failure of 100% O₂ to markedly
increase arterial oxygen tension raise should raise suspicions that a true shunt exists.
True anatomic shunts are much less common vascular abnormalities and are most
often a portopulmonary communication. Although these shunts are usually small,
sometimes they are severe enough to warrant obliterative intervention.

Pulmonary hypertension is defined as a mean pulmonary artery pressure (mPAP) of
25 mmHg or greater with a pulmonary capillary wedge pressure (PCWP) less than
15 mmHg. An alternate definition is a pulmonary vascular resistance (PVR) greater
than 120 dynes · cm⁻¹ · s⁻³. Because the formula for PVR is

\[
\text{PVR} = \frac{\text{mPAP} - \text{PCWP} \times 80}{\text{CO}}
\]

it can be seen that an elevated mPAP with normal pulmonary capillary wedge pressure
is no guarantee of an elevated PVR if the cardiac output (CO) is also elevated. This is
a common scenario in end-stage liver disease. Therefore, some clinicians feel a diag-
nosis of portopulmonary hypertension requires that all three criteria be met. Which
portopulmonary hypertension patients may undergo transplantation safely and who
may expect resolution of their portopulmonary hypertension after transplantation is
unclear. A recent review of reports of portopulmonary hypertension patients who
underwent transplantation led to the following recommendations for proceeding with
transplant based on reported survival (Table 1).

These recommendations were made using untreated PAP measurements. They do not
differentiate between patients who respond to pharmacologic therapy and those who
do not. There remains a controversial set of patients whose mPAP values are
35 to 50 mmHg and PVR values are 250 dynes · cm⁻¹ · s⁻³ or more, and whose mortality
rate is greater than 50%. If these patients are lucky enough to be diagnosed before trans-
plantation, oral vasodilator or long-term epoprostenol therapy (constant infusion via
implanted pump)⁶ may improve their survival at transplantation. Unfortunately, many
patients are not diagnosed until they present for transplantation, and then a decision
must be made while an anesthetized patient and a harvested organ await.

In this situation, a rapid evaluation of patient responsiveness to pharmacologic ther-
apy may aid in the decision. Such therapy includes intravenous nitroglycerin, dopamine,
dobutamine, prostaglandin E₁, and inhaled nitric oxide. Most recently, aerosolized

<table>
<thead>
<tr>
<th>Mean Pulmonary Artery Pressure (MPAP)</th>
<th>Intraoperative Guideline</th>
<th>Reported Mortality Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 mm Hg</td>
<td>Proceed with OLT</td>
<td>0/14 (0)</td>
</tr>
<tr>
<td>35–50 mm Hg</td>
<td>If PVR &lt;250 proceed with OLT</td>
<td>0/6 (0)</td>
</tr>
<tr>
<td></td>
<td>If PVR ≥250 cancel OLT</td>
<td>7/14 (50)†</td>
</tr>
<tr>
<td>≥50 mm Hg</td>
<td>Cancel OLT†</td>
<td>6/6 (100)</td>
</tr>
</tbody>
</table>

*PVR in dynes · s · cm⁻³.
†If untreated, refer for additional pulmonary hypertension evaluation/therapeutic considerations and
reevaluate for orthotopic liver transplantation (OLT).
‡One patient died post-transplantation hospitalization of right cardiac failure.

(Reprinted with permission from Krowka MJ: Pulmonary hemodynamics. Liver Transplantation 2000; 6: 448.)
epoprostalenol has been reported to decrease PAP without peripheral effects. Many clinicians look for a 20% or greater decrease in mPAP or PVR to define a favorable response.

Central Nervous System

Portosystemic encephalopathy is a common feature of patients undergoing transplantation. Frequently, it will be severe enough to warrant intubation for airway protection. Although it was once assumed that the encephalopathy of chronic liver disease was not associated with intracranial hypertension (as it is in acute hepatic failure), a study from the University of Nebraska warns against that blanket assumption. In this study, 12 deeply comatose patients who also showed signs suggestive of increased intracranial pressure were further evaluated. The signs of increased intracranial pressure included absent corneal reflexes, decerebrate and decorticate posturing, and anisocoria. All 12 were found to have cerebral edema by head computed tomography, intracranial pressure monitor, or both. Therefore, an index of suspicion must be maintained for intracranial hypertension even in patients with chronic disease. Consideration should be given to empirically instituting cerebral decompressive measures and avoiding cerebral vasodilators if diagnostic studies are unavailable by the time of transplant.

Renal

The hallmark effect of hepatic failure on the kidneys is to promote inappropriate salt and water retention via several mediators, including antidiuretic hormone, the renin-angiotensin-aldosterone system, prostaglandins, and the sympathetic nervous system. Progression of this process leads to profound renal vasoconstriction and renal insufficiency, a state termed “hepatorenal syndrome.” Therapy includes large volume paracentesis, transjugular intravenous portocaval stent, and selective V1 splanchnic vasoconstrictors. Dialysis may be necessary to support the patient until transplantation and in the perioperative period.

Gastrointestinal

Although it is uncommon for a patient to arrive for transplantation while undergoing cure for an acute bleeding episode, many come with a history of gastroesophageal variceal bleeding. Frequently these patients are receiving β-blocker therapy that continues until the day of surgery. Unfortunately, β blockade compromises or eliminates major compensatory mechanisms for these patients, who will likely experience intraoperative decreases in systemic vascular resistance (SVR), acute blood loss, or acute decreases in venous return because of surgical manipulation. For well β-blocked patients, it is prudent to have vagolytic and β-agonist drugs prepared in advance.

For patients who arrive for transplantation with a splanchnic vasopressor infusing for treatment of acute bleeding, discussion with the surgeon about the earliest appropriate time to discontinue this is recommended. Left infusing too long, these drugs may decrease blood flow the new graft, compromising its viability.

Although the placement of an nasogastric tube is accompanied by the theoretic risk for precipitating upper gastrointestinal bleeding, that fear is largely unfounded. However, nasal bleeding from nasogastric tube placement is a real possibility and is not triv-
ial in this coagulopathic population. Placement of a nasogastric tube should be preceded by nasal vasoconstriction and generous lubrication.

**Coagulation**

With the notable exceptions of factor VIII, tissue plasminogen activator (tPA), and plasminogen activator inhibitor, the liver is the major site of synthesis of the procoagulants and anticoagulants in the body. The liver is also the site of the clearance of tPA and activated coagulation factors. In hepatocellular disease, the factor levels of both systems are decreased, but the clinical balance tends toward a bleeding rather than a clotting diathesis. Diffuse intravascular coagulation, a clotting diathesis, can occur in the setting of liver disease, but whether it is a regular feature is controversial. Diagnosis is confounded by the fact that the usual laboratory markers of diffuse intravascular coagulation may be elevated in cirrhosis because of liver failure *per se*. In cholestatic disease, synthesis of the vitamin K–dependent factors (II, VII, IX, and X) is hampered by poor absorption and inadequate levels of this fat-soluble vitamin. Unless there is coexistent cirrhosis, improvement in coagulation may be expected with the administration of vitamin K.

Transplant patients are frequently thrombocytopenic for several reasons, chief among them sequestration of platelets by the enlarged spleen that is a consequence of portal hypertension. Other causes include bone marrow suppression and immune-mediated platelet destruction. Although the platelet count ideally should be maintained at more than 50,000/mm², sequestration or immune-mediated destruction may make this goal difficult to achieve.

Between 10% and 20% of patients with end-stage liver disease show baseline enhanced fibrinolysis. This is believed to be caused by elevated tPA activity as a consequence of inadequate tPA clearance by the diseased liver. Because hyperfibrinolysis is also a common feature of the transplant process, many centers routinely use antifibrinolytic agents to minimize bleeding. Caution should be exercised in administering these drugs because relative and absolute contraindications exist. These include diffuse intravascular coagulation, a history of thrombosis (Budd-Chiari syndrome, portal venous thrombosis), the presence of antiphospholipid antibodies, and malignancy.

**Liver Transplantation Procedure**

The liver transplantation procedure is commonly divided into three phases: the preanhepatic phase or dissection phase, the anhepatic phase, and the postreperfusion or neohepatic phase. The preanhepatic phase extends from abdominal incision to vascular isolation and removal of the native liver. The anhepatic phase begins with portocaval cross-clamp and ends with perfusion of the graft. The neohepatic phase begins with reperfusion and ends with closure of the abdominal incision.

Patients may arrive in the operating room from home having been admitted solely for their procedure. They also may be already hospitalized; some in the intensive care unit with invasive monitoring lines in place, and even intubated. The blood bank should already have been alerted about the impeding transplant. A common preoperative set up at many centers is 10 units of erythrocytes and 10 units of fresh frozen plasma. Platelets and cryoprecipitates are not routinely set up in advance, as their need is not universal. A rapid infusion device that efficiently heats and delivers large volumes of fluid is a must for this procedure.
Most patients who arrive in the operating room without invasive monitors already in place do not need them for induction. Their anesthetic may be induced with the aid of standard monitors consisting of electrocardiogram, noninvasive blood pressure, pulse oximeter, and capnography. Most of these patients can be considered to have full stomachs because of the presence of ascites, recent upper gastrointestinal bleeding, congestive gastropathy, and gastritis, which are a consequence of portal hypertension, and idiopathic nausea and vomiting that accompany end-stage liver disease.

Unless there are preinduction concerns about hypotension or volume status, barbiturates or propofol may be used for induction. Although the metabolism of succinylcholine may theoretically be expected to be prolonged because of reduced production of pseudocholinesterase in patients with liver disease, this is not of clinical significance for a single intubating dose and certainly not for a long surgical procedure. For similar reasons, although some newer nondepolarizing muscle relaxants that do not rely on hepatic or renal excretion seem advantageous, the reality is that the length of the procedure plus the practice of titrating to clinical effect allows the use of older and less expensive drugs. The vagolytic action of pancuronium may, in fact, be desirable in some patients on β-blocker therapy, as discussed previously.

Maintenance of anesthesia is usually achieved with a combination of inhaled agent and narcotics. The chief mechanism by which inhaled anesthetics compromise the liver is by reducing hepatic blood flow and therefore hepatic oxygen delivery. Although isoflurane has a long history of use, desflurane has some potential advantages. Desflurane appears to decrease splanchnic blood flow less than isoflurane. The fact that desflurane also undergoes less oxidative metabolism may make it the more desirable agent.

In centers that aggressively try to extubate transplant patients in the operating room, the rapid offset of desflurane is an added advantage. Nitrous oxide is not used, both because of its effects on the bowel and because of the risk for venous air embolism, particularly in patients on whom veno-venous bypass (VVB) is used during caval clamp.

After the patient is intubated and anesthesia is induced, lines are placed. Minimum lines include one arterial line and two large-bore venous access lines, one of which is used for placement of a Swan-Ganz catheter. Some centers will establish two arterial lines, one of which may be femoral. A femoral arterial line will be compromised in the event of aortic clamping, if an aortic graft is needed for the hepatic artery anastomosis. However, it is thought to provide more accurate blood pressure measurements when the patient is in a widely vasodilated state, such as may happen during and after reperfusion. Transesophageal echocardiography is used variably in transplant centers, and there are some that advocate its routine use.

Preanhepatic Phase: Surgical Events (Standard Transplant Procedure Assuming Veno-venous Bypass Use)

1. Cutdown and cannulation of axillary and femoral bypass sites
2. Bilateral subcostal incision with upper midline extension
3. Drainage of ascites
4. Dissection of porta hepatis, division of hepatic artery
5. Dissection of portal vein, clamp, and cannulation for decompression of splanchnic circulation by VVB; at this point the patient is functionally anhepatic, although further dissection remains before hepatectomy
6. Dissection of suprahepatic and infrahepatic cava, placement of clamps
7. Hepatectomy with _en bloc_ removal of the retrohepatic cava
The anesthesiologist’s goals during the prehepatic phase are to
1. maintain normothermia,
2. obtain baseline hemodynamic and laboratory values,
3. address and correct hemodynamic and laboratory abnormalities,
4. establish good urine output, and
5. replace losses with appropriate fluids and blood products.

Instituting warming measures early is important because regaining lost ground is very difficult. Fluids, breathing circuit, and nonsurgical areas of the body should be warmed by the best means available. Upper and lower body warming blankets are very effective. If these are unavailable, wrapping the extremities and head in plastic can help retard heat loss. The metabolic activity of the liver contributes a great deal to maintaining body temperature, so that losses early in the procedure will be compounded during the anhepatic phase. The good news, however, is that a good graft that functions immediately will warm the patient toward normothermia in the postreperfusion phase. Another option when VVB is used is the addition of a heat exchanger to the circuit, which can warm the patient to normothermia during the anhepatic phase.

Swan-Ganz data will commonly show a high CO and low SVR. Although PAP may be elevated, it is important to calculate a PVR because it may be a flow-related phenomenon. Patients with ascites may have impaired venous return with falsely low filling pressures and CO that increase on abdominal incision and drainage of ascites.1

Volume replacement should be tailored to the patient’s individual needs. A common practice is administration of fresh frozen plasma to achieve an international normalized ratio of less than 1.5, platelets to achieve a platelet count of greater than 50,000/mm², and cryoprecipitate to maintain a fibrinogen level greater than 100 mg/dl. Many centers use thromboelastography, a functional assessment of the coagulation of the patient’s blood, to guide replacement. Whether to use crystalloid or colloid is a personal choice, keeping mind that most patients have low oncotic pressures. The choice of crystalloid solution may be dictated by the patient’s serum sodium or potassium concentrations.

Whether a patient has enhanced fibrinolysis, absent a contraindication, many centers administer an antifibrinolytic agent prophylactically from the beginning of surgery because they feel that eventual hyperfibrinolysis is common and that the possible benefits throughout surgery outweigh the risks. Which agent to use and at what dose remains controversial. Aprotinin, a nonspecific serine protease inhibitor, and the lysine analog, aminocaproic acid and tranexamic acid, all have their champions. Although earlier studies were plagued by small numbers, historic controls, lack of randomization, and retrospective analyses, recent studies using aprotinin and tranexamic acid have shown statistically significant decreases in blood product usage.18–20 Historically, aminocaproic acid was the first agent to gain wide acceptance and continues to be commonly used.

Dose regimens for aprotinin used in liver transplantation studies range from a 2 million KIU loading dose followed by 1 million–KIU/h infusion18 to a 500,000 KIU loading dose followed by 150,000-KIU/h infusion.21 Dose comparison studies suggest that low-dose aprotinin may be as effective as high-dose aprotinin in the patient undergoing liver transplantation,18,21 possibly because plasmin inhibition is achieved at relatively low blood levels of aprotinin, and this may be its chief mechanism of action in liver transplant settings.

Aminocaproic acid is most commonly administered by infusion at 1 g/h, although Kang22 suggested that a single bolus dose of 250 to 500 mg is sufficient in response to documented postreperfusion hyperfibrinolysis.

Tranexamic acid, although not widely used, is 6 to 10 times more potent than aminocaproic acid. Studies on its use in liver transplantation have also used widely
varying doses and have not shown consistent results. However, a recent study comparing 10 mg · kg\(^{-1}\) · h\(^{-1}\) tranexamic acid and 16 mg · kg\(^{-1}\) · h\(^{-1}\) of aminocaproic acid to placebo did show a significant decrease in perioperative blood replacement with tranexamic acid, but not with aminocaproic acid.\(^{19}\)

Thrombotic complications have been described during use of all antifibrinolytic agents in liver transplantation. However, they have also been documented in liver transplantation in the absence of antifibrinolytic therapy and have not been found to occur more frequently with antifibrinolytic use.\(^{10,18,19}\) Some feel that because aprotinin inhibits the intrinsic coagulation pathway (prolonging partial thromboplastin time) and because it selectively inhibits unbound plasmin, it is theoretically less likely than the lysine analogs to promote pathologic thrombosis.

The electrolytes that are followed most carefully during transplantation are Na\(^+\), K\(^+\), Ca\(^{++}\), and Mg\(^{++}\). Transplant patients often present with significant hyponatremia. Elevated aldosterone and antiuretic hormone impair their ability to excrete free water. In addition, these patients are often on low-sodium diets but not water restriction. Limitation of large acute changes in serum sodium is particularly important in this population because they are associated with the development of central pontine myelinolysis, a devastating neurologic complication.\(^{23,24}\) Although banked blood products contain obligate sodium in the form of sodium citrate, this can be balanced by the use of lower-sodium crystalloid solutions, 25% albumin, and tromethamine (a nonsodium buffer) to treat acidosis. In extreme cases, dialysis may be necessary.

Hyperkalemia is a more common and difficult to manage problem in adults than is hypokalemia. Potassium from banked blood products, cellular shifts, and reperfusion of the new graft can increase concentrations high enough to provoke electrocardiograph changes, arrhythmias, and arrest. Treatment should begin early in the procedure and be somewhat anticipatory as most of these methods take time. These include loop diuretics, insulin–glucose administration (1 unit regular insulin per 2 g glucose), correction of acidosis or hypocalcemia, and dialysis. Of these, only the administration of a buffer such as sodium bicarbonate and calcium will shift potassium intracellularly quickly enough to treat acute electrocardiograph changes such as occur during reperfusion.

Banked blood products contain citrate that, failing to be adequately metabolized by the diseased liver, binds calcium and produces hypocalcemia.\(^{25}\) Fresh frozen plasma contains the most citrate, and calcium replacement requirement tends to be proportionate to the amount of fresh frozen plasma administered.

Magnesium, like calcium, is bound by citrate. Low levels are associated with arrhythmias\(^{26}\) and myocardial depression.\(^{27}\) Although studies have shown mixed results, some have shown hypomagnesemia at some point during the transplant procedure that tends to resolve during the neohepatic phase.\(^{28,29}\) Although rapidly measured ionized magnesium concentrations may not be easily obtained, consideration should be given to replacing magnesium for baseline hypomagnesemia, and empirically for large blood loss cases, resistant arrhythmias, and prolonged myocardial dysfunction after reperfusion.

Veno-venous bypass usually drains the portal and left femoral circulations and returns the volume to the central circulation via the left axillary vein (Fig. 2). As much as 40% of the CO can be returned this way, and hemodynamic stability on caval cross-clamp can be expected with pump flows of 25% of CO.\(^{30}\) The institution of VVB is not without risk, however, and complications such as massive air embolism,\(^{16}\) thromboembolism\(^{31}\) and vascular injuries\(^{32}\) have been described. Universal benefit to patients has not been demonstrated, and practice and criteria for use vary by center.

A surgical technique that can largely make hemodynamic stability possible without the use of VVB is the piggyback technique.\(^{33}\) Although not universally applicable, it allows hepatectomy without caval cross-clamp and division, largely maintaining venous
return. The liver is mobilized off of the inferior vena cava, and the outflow clamp is placed across the hepatic veins rather than the suprahepatic cava, minimizing caval compromise (Fig. 3).

The decisions of whether to perform hepatectomy leaving an intact cava (“piggyback procedure”), and whether to use VVB during the anhepatic phase, present different management concerns. A caval cross-clamp alone, without VVB, decreases venous return by 50%. If VVB is not planned, preclamp augmentation of intravascular volume to target central pressure is undertaken. A common end point is mPAP 18 to 20 mmHg. Test clamping is often performed before hepatectomy. Failure to maintain hemodynamic stability during the test can be treated with further volume loading, pressor support, or the institution of VVB.
Anhepatic Phase: Surgical Events

1. Retroperitoneal hemostasis and peritoneal closure
2. Anastomosis of graft: suprahepatic cava, infrahepatic cava, portal vein, possibly hepatic artery
3. Reperfusion

The anesthesiologist’s goals are as follows:
1. Prepare for reperfusion with the following conditions:
   - Adequate intravascular volume
   - Acceptable K
   - Ca\(^{++}\) and base-deficit corrected
2. Decide whether to “vent” graft
3. Support the patient through reperfusion

Once the hepatectomy is complete, there is usually little further blood loss in the anhepatic phase. Most therapy in this phase is aimed at achieving a stable reperfusion and avoiding or minimizing postreperfusion syndrome (PRS). PRS has been defined either as a greater than 30% decrease from baseline mean arterial pressure lasting at least 1 minute and occurring within the first 5 minutes of reperfusion,\(^{36}\) or a mean arterial pressure less than 60 mmHg meeting the same criteria.\(^{35}\) Reported rates of occurrence vary from 8%\(^{35}\) to 30%.\(^{36}\) The common hemodynamic lesion is a profound
decrease in SVR. Acute pulmonary hypertension with right ventricular dysfunction, arrhythmias, and relative hypovolemia have been observed to coexist and exacerbate the hypotension in some studies.

The cause of PRS is unclear, but there appear to be both graft and recipient factors. Although many potentially causative conditions occur during transplantation, none have been shown to be of more significance in a PRS group than in a non-PRS group. Thus, the anesthesiologist’s role is to optimize things that could potentially exacerbate PRS before reperfusion and support the patient hemodynamically should it occur. This means aggressively correcting hyperkalemia, hypocalcemia, acidosis, hypovolemia, and hypothermia.

Hyperkalemic complications from the addition of acidotic, potassium-rich reperfusate to the central circulation have been well described. If hyperkalemia is a continued problem in the anhepatic phase, repeat or additional measures must be undertaken to reduce serum potassium. Although the liver is the major site of insulin-mediated potassium uptake, insulin administration still has value in the anhepatic phase. Concomitant glucose administration should be tempered by existing hyperglycemia, consideration of resistance to insulin-mediated glucose uptake in the anhepatic phase, and anticipation of glucose release from the new graft after reperfusion. Hyperglycemia is best avoided, particularly in the period of reperfusion when profound and prolonged hemodynamic instability is possible and the potential for cerebral ischemia exists.

“Venting” the graft is the process by which an initial volume of blood (roughly 500 ml) is allowed to reperfuse the liver but is then discarded. The intent of this is to reduce the sudden entry into the central circulation of vasoactive ischemic metabolites, potassium, and cold venous return from the graft liver. Although this has not been consistently shown to reduce PRS, one study did show a decrease in potassium increase on reperfusion after venting. Thus, venting may have value in the persistently hyperkalemic patient who is soon to be reperfused.

Anastomosis of the graft begins with the suprahepatic cava, followed by the infrahepatic cava and the portal vein. The hepatic artery may or may not be anastomosed before reperfusion. To perform the portal anastomosis, it must be excluded from the VVB system, resulting in decreased pump flow and decreased perfusion and filling pressures.

In anticipation of the hemodynamic instability associated with reperfusion, the patient is ventilated with 100% oxygen and the anesthetic agents decreased. Resuscitation drugs are drawn, and some may give an anticipatory dose of vasopressor before removal of the clamps.

Reperfusion begins with the release of the suprahepatic clamp, followed by the infrahepatic, portal, and hepatic artery (if anastomosis is complete) clamps. Immediate changes are an increase in central filling pressures and a decrease in temperature. It is particularly important to watch the electrocardiogram for changes suggesting hyperkalemia, for which immediate therapy is warranted. An accurate CO is difficult to obtain because of the varying temperature of the venous return as blood exits the cold graft, but hypotension can most often be attributed to SVR, as discussed previously. Although the hypotension associated with reperfusion tends to resolve over several minutes, an increased CO and decreased SVR persist through the neohepatic phase.

Neohpatic Phase: Surgical Events

1. Hepatic artery anastomosis (if not already complete)
2. Cholecystectomy
3. Biliary drainage procedure: choledochocholedochostomy *versus* choledochojejunostomy (roux-en-y)

4. Closure of cutdown sites and abdominal incision

The anesthesiologist’s goals are to

1. Optimize hemostatic parameters
2. Optimize fluids and electrolytes
3. Consider candidacy for operating room extubation
4. Plan postoperative pain control
5. Prepare for transport

Unless there is prolonged postreperfusion hypotension, the chief issue in the neohepatic phase is hemostasis. Contributing factors to the coagulopathy of this phase are as follows: (1) a dramatic increase in tPA activity with accelerated fibrinolysis; (2) release of heparin or heparin-like factors from the new graft; (3) consumption of factors I, V, and VIII by excess plasmin (generated by the increase in tPA); (4) generalized proteolytic activity; and (5) hypothermia, hypocalcemia, and acidosis.

In general, a well-functioning graft should be able to adequately metabolize citrate so that continued calcium administration in the neohepatic phase is unnecessary. Similarly, acidosis and hypothermia also improve with a functioning graft. Overzealous attempts to correct acidosis should be avoided lest the patient become alkalemic as liver function rapidly returns. Heparin-like activity tends to be limited, not usually requiring pharmacologic intervention.

The extent and duration of fibrinolytic activity after reperfusion is highly variable, sometimes severe enough to warrant completion of the biliary drainage as a staged procedure. Such severe fibrinolytic activity is highly suggestive of poor or delayed graft function and will often not improve unless or until the graft begins to function.

As mentioned previously, most centers use either conventional laboratory studies (including but not limited to prothrombin time, partial thromboplastin time, fibrinogen, and platelet count), thromboelastography, or both to assess the state of coagulation and guide therapy. Each method has its advantages and drawbacks. Although conventional studies can determine adequate levels or numbers of the components of clot, they cannot determine adequate function of those components. Thromboelastography produces a visual record of the formation of clot in a blood sample during controlled conditions and is thus a functional assay. Although standardized measurements on this visual record correlate with the function of certain coagulation components, they are not specific. However, thromboelastography has the added utility of being able to demonstrate the effect of pharmacologic intervention by allowing the addition of a standard amount of drug (e.g., aminocaproic acid) to a blood sample. Regardless of the method chosen, efficiency in performing the studies is important because delays in instituting therapy result in greater blood product use and duration of surgery.

Evaluation of graft function is an important part of the neohepatic phase. Evidence of good metabolic function includes the ability to maintain ionized calcium levels without supplementation, normalization of base deficit, implying hepatic acid clearance, and increasing patient temperature toward normothermia. The graft appearance should be uniform and purplish and the texture soft. Bile production can be noted before abdominal closure. Acute deterioration in urinary output with no other explanation, prolonged hypotension requiring pressor support, and recalcitrant hyperfibrinolysis are suggestive of poor graft function. The quality of the graft should particularly be considered in the decision to extubate a patient in the operating room.

Safe immediate postoperative tracheal extubation of liver transplant patients has been described at several institutions. Among the benefits of this approach are decreased
duration of intensive care unit stays and expenses. However, outcomes after discharge from the intensive care unit have not been evaluated. Adequate criteria for early extubation include normothermia, absence of significant preoperative encephalopathy or other extrahepatic disease, alveolar–arterial oxygen difference less than 150 mmHg, no requirement for hemodynamic support, and a well-functioning graft.44 Although some centers use additional criteria such as age less than 50 years, transfusion requirement less than 1 blood volume, and United Network for Organ Sharing status 3 before transplant, patients who have not met one or another of these have also been reported to be successfully extubated in the operating room.44–46

References


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