INTRODUCTION

Patients are admitted to the intensive care unit (ICU) for a variety of reasons following hepatopancreaticobiliary (HPB) surgery, including maintenance, or restoration, of normal physiology immediately after extensive surgery and the subsequent management of complications that develop. Many of the issues that require ICU management are common to all ICU patients and will not be discussed in this chapter; however, there are recurring issues that are relatively specific to HPB surgery patients that will be discussed. The role of normal liver physiology and its alteration during HPB surgery and disease states will be discussed as well as the management of common problems that arise after HPB surgery.

HPB surgery is a surgery of the liver, bile duct, and pancreas, and may include portal decompressive procedures for complications of portal hypertension. Surgical procedures on the pancreas and bile duct alone generally do not require care in a critical care setting immediately after leaving the operating room unless complications occur. Liver resections, particularly when extensive, can require admission to a critical care unit immediately following surgery due to the alterations in normal physiology that occur during the procedure itself. An understanding of normal liver physiology and the alterations it undergoes during liver surgery is important when managing these patients.

LIVER ANATOMY AND PHYSIOLOGY

The liver is approximately 2% of total body weight and has multiple complex functions. The anatomy of the liver has been described using various methods (1–5); however, surgical anatomy is based on the segmental nature of vascular and bile duct distribution. The liver receives a dual blood supply from both the portal vein and hepatic artery that run, along with the bile duct, within the Glissonian sheath or main portal pedicle. The portal pedicle divides into right and left branches and then supplies the liver in a segmental fashion. Venous drainage is via the hepatic veins, which drain directly into the inferior vena cava. Hepatic segmentation is based on the distribution of the portal pedicles and their relation to the hepatic veins (Fig. 60.1). The three hepatic veins run in the portal scissurae and divide the liver into four sectors, which are in turn divided by the portal pedicles running in the hepatic scissurae. The liver is divided into right and left hemi-livers by the middle hepatic vein. The right lobe is divided by the right hepatic vein into anterior and posterior sectors. The anterior sector is divided by the plane of the portal pedicle into an inferior segment 5 and a superior segment 8. The posterior sector is divided by the plane of the portal pedicle into an inferior segment 6 and a superior segment 7. The left lobe lies to the left of the middle hepatic vein and is divided into anterior and posterior sectors by the left hepatic vein. The anterior sector is divided by the umbilical fissure into segment 4 medially and segment 3 laterally. The segment posterior to the left hepatic vein is segment 2. Segment 4 can be divided by the plane of the portal pedicle into a superior segment 4a and an inferior segment 4b. Segment 1 is the caudate lobe which lies between the inferior vena cava and the hepatic veins. The caudate lobe has variable portal venous, hepatic arterial, and biliary anatomy, and is essentially independent of the portal pedicle divisions and hepatic venous drainage. Segmental anatomy becomes important in considering surgical resection when essentially any segment or combination of segments can be resected if attention is paid to maintaining vascular and biliary continuity to remaining segments. Common liver resections that are performed that might require ICU admission after surgery are left or right hepatectomies in which approximately 50% of liver volume is removed or more extensive procedures such as right or left trisectionectomy in which up to 80% of the liver is removed (see Fig. 60.1). If less than 40% of the liver is resected in patients with normal underlying liver function, relatively little derangement of liver physiology is noted.

The liver performs many functions, including uptake, storage, and eventual distribution of nutrients from the blood or gastrointestinal (GI) tract and synthesis metabolism and elimination of a variety of endogenous and exogenous substrates and toxins (including narcotics and other drugs). Although the liver is only 4% to 5% of body weight, it is responsible for 20% to 25% of body oxygen consumption and 20% of total energy expenditure (6). The liver receives a dual blood supply with 75% of flow from the portal vein and 25% from the hepatic artery. Total blood flow to the liver is approximately 1.5 L/min/m² (7). Decreasing portal venous flow causes a subsequent increase in hepatic arterial flow; however with complete portal occlusion or diversion, hepatic arterial flow does not completely compensate and total liver blood flow is diminished (8). The opposite is not true, however. That is, decreasing flow in the hepatic artery does not increase flow in the portal vein; there is auto-regulation of hepatic arterial flow but not the portal venous system. Portal flow is increased by food intake, bile salts, secretin, pentagastrin, vasoactive intestinal peptide (VIP), glucagon, isoproterenol, prostaglandin E1 and E2, and papaverine. Portal flow is decreased by serotonin, angiotensin, vasopressin, nitrates, and somatostatin.

Bile, composed of inorganic ions and organic solutes, is formed at the canalicular membrane of the hepatocyte as well as in the bile ductules and is secreted by an active process that is relatively independent of blood flow (9). The major organic
developed. During PVE the portal vein of the side of the liver to be resected is embolized percutaneously. Diversion of portal flow and its hepatotrophic factors to the future liver remnant (FLR) causes growth and hypertrophy of the FLR of about 30% (Fig. 60.2) over a 6-week period and has been shown to reduce the complications associated with subsequent extended liver resections (12).

Patients with biliary obstruction may require preoperative drainage prior to surgery. For patients with obstruction of the common hepatic duct or bifurcation, scheduled to undergo a major liver resection (most commonly diagnosed with cholangiocarcinoma [CCC]), we recommend preoperative percutaneous drainage of the remnant liver until the total bilirubin is less than 2 mg/dL, this decreases the risk of postoperative liver dysfunction (13), although this is controversial. For patients with obstruction of the distal common bile duct, intrapancreatic bile duct, or ampulla (most commonly diagnosed with a pancreatic malignancy), drainage is only recommended for severe jaundice, cholangitis, or severe malnutrition (14,15).

**FIGURE 60.1** Diagrammatic representation of liver segments with standard liver resections demonstrated.

**FIGURE 60.2** Portal vein embolization of the right portal vein preoperatively allows an increase of functional liver remnant of approximately 30% from prior to embolization (A) to postembolization (B). (Reproduced with permission from Hemming AW, Reed AI, Howard RJ, et al. Preoperative portal vein embolization for extended hepatectomy. Ann Surg. 2003;237(5):686–691.)

Components of bile are the conjugated bile acids, cholesterol, phospholipid, bile pigments, and protein. Under normal conditions, 600 to 1,000 mL of bile is produced daily (10). Bile secretory pressure is approximately 10 to 20 cm H$_2$O, with maximal secretory pressures of 30 to 35 cm H$_2$O in the presence of complete biliary obstruction.

Bilirubin is a degradation product of heme and is eliminated almost entirely in the bile. It circulates bound to albumin and is removed from the plasma by the liver by a carrier mediated transport system. In the hepatocyte, bilirubin is bound to glucuronic acid before being secreted in bile. While the liver maintains the ability to clear bilirubin with partial duct obstruction, complete obstruction of one of the right or left hepatic ducts alone will cause marked liver enzyme abnormalities, but rarely causes jaundice.

The liver synthesizes many of the major human plasma proteins including albumin, gamma globulin and many of the coagulation proteins. Liver dysfunction can have a profound effect on coagulation by decreased production of coagulation proteins or, in the case of obstructive jaundice, a decreased activity of factors II, V, VII, IX, and X secondary to a lack of vitamin K-dependent posttranslational modification. Reversal of coagulation abnormalities by exogenous administration of vitamin K differentiates between synthetic dysfunction and lack of vitamin K absorption secondary to obstructive jaundice.

After hepatic resection, liver function is altered through both a reduction in functional liver mass as well as potential ischemia/reperfusion injury to the liver remnant. With extensive liver resection in patients with normal underlying liver function, reduction of functional liver volume below 25% has been associated with increased risk of both liver failure and mortality (11). To reduce the risk of liver failure in this setting, preoperative portal vein embolization (PVE) has been...
Surgical Procedures

Liver Resection

As the liver is a tremendously vascular organ, intraoperative or postoperative complications are often related to excessive blood loss (16); thus a number of techniques have been developed to achieve presection vascular control and decreased bleeding. While liver resection can often be performed without the need for interruption of blood flow to the liver, in many cases some degree of reduction of flow is required to prevent excessive blood loss.

Selective inflow control can be established by division or occlusion of the vascular structures supplying the segment(s) of liver to be removed. The right or left portal pedicle containing the respective portal vein, hepatic artery, and bile duct are controlled with a vascular clamp. This technique has the advantage of preserving blood flow to the segment of the liver being preserved but is generally only useful in smaller resections.

Total inflow occlusion (Pringle maneuver) results from clamping the entire inflow of the liver at the hepatoduodenal ligament; this has been shown to reduce blood loss during the parenchymal transection phase of the resection (17). While there is some concern regarding warm ischemic injury, abundant data shows that the normal liver can tolerate inflow occlusion for up to 1 hour, and there are reports suggesting that some cirrhotic livers can safely tolerate 60 minutes of inflow occlusion as well (18). We use total inflow occlusion when selective occlusion provides insufficient control. Clamp times are expected to be less than 30 minutes for formal hepatectomies, but may be higher for more complex parenchymal transections. In such cases, total occlusion is carried out in 15-minute increments with 5-minute reperfusion intervals. An alternative to the intermittent clamping technique is to use ischemic preconditioning, during which the liver inflow is occluded for 10 minutes, after which it is allowed to reperfuse for 15 minutes prior to clamping again for a sustained time period up to 1 hour. Intermittent clamping is associated with more blood loss than ischemic preconditioning; however, the protective results of ischemic preconditioning in ischemia reperfusion injury have not been uniform across age groups and may not be as effective in livers that have been exposed to preoperative chemotherapy (19).

Total vascular isolation of the liver, with both inflow occlusion and occlusion of the supra- and infrarenal vena cava, can be useful for technically demanding cases where the vena cava or proximal hepatic veins are involved with tumor (Fig. 60.3). Total isolation has been shown to be safe for up to 60 minutes in normal liver, but can be accompanied by varying degrees of hemodynamic instability (20). In cases where this is required, we carry out as much of the operation as possible prior to isolation of the liver to reduce the ischemic time and the period of hemodynamic instability.

Hemodynamic Monitoring during Liver Resection

Central venous pressure (CVP) monitoring has traditionally been used to minimize blood loss during hepatectomy. During liver resection, hepatic vein pressure and blood loss are linearly related to CVP, with a CVP of 2 to 3 mmHg optimal for hepatic resections (21,22). The most troublesome bleeding during liver resection is usually from branches of the hepatic vein; this can be minimized by maintaining the CVP of 5 mmHg or less during the period of hepatic transection. Cooperation of the anesthesiologist in minimizing volume loading, and occasionally using pharmacologic agents to reduce CVP is essential. However, if total vascular isolation is to be used, volume loading prior to caval clamping is required to avoid an acute decrease in cardiac output at the time the clamps are applied. Low CVP anesthesia can result in significant volume depletion postoperatively and needs to be considered as part of the differential of hypotension and low urine output in the ICU after liver resection.

Knowledge of the details of intraoperative conduct of the operation is, therefore, important to the physicians that are to manage the postoperative care of the liver resection patient in the ICU setting. Was inflow occlusion or vascular isolation required and for how long? Prolonged clamp times are associated with greater liver dysfunction. Was the patient maintained with a low CVP throughout the course of the surgery? If so then the patient may need volume expansion on arrival to the ICU. How much liver remains and is it normal? If the percent of liver is less than 25% in normal livers, or less than 40% in cirrhotic livers or livers with bile duct obstruction, the chance of liver failure and the need for its management is higher. Was there significant blood or fluid requirements? Patients may need a period of ventilation while fluid shifts and equilibrates.
**Pancreatic and Bile Duct Surgery**

The majority of patients undergoing pancreatic or bile duct surgeries do not require admission to an ICU setting immediately postoperatively because of issues specific to the pancreatico-biliary surgery itself. In general, procedures on the pancreas or biliary tree should not be associated with major intraoperative hemodynamic changes or alterations in physiology. Tumors of the head of the pancreas or bile duct may involve the portal vein or cause extensive fibrotic reaction in the area. Technical difficulties can arise in which damage occurs to, or resection is required of, the portal vein (Fig. 60.4). If portal vein resection or repair is required, it is more likely that the patient will require ICU care. Portal vein resection, when planned, requires variable durations of portal venous outflow obstruction from the gut, which are usually short and well tolerated, but can increase the amount of fluid third spaced in the bowel wall. Portal vein injury, however, can lead to massive transfusion requirements and hypotension that can require postoperative ICU care. The more common indications for admission to the ICU after pancreatic or biliary surgery are either an underlying medical condition or the development of a complication postoperatively. Pancreatic or bile leaks can lead to sepsis but will be discussed later in the chapter.

**Portal Decompressive Procedures**

Surgical portal decompressive procedures are becoming a rarity since the introduction of transjugular intrahepatic portosystemic shunt (TIPS) procedures. Decompressive procedures do, however, remain indicated in select patients with variceal bleeding with preserved liver function that have failed medical management and who are not transplant candidates. The myriad technical variations of surgical portosystemic shunts are beyond the scope of this chapter but certain commonalities exist.

Whether total or partial shunts, selective or nonselective patients will have had the high-pressure portal system surgically connected to the low-pressure caval circulation to lower the pressure in the portal venous system and stop variceal bleeding. Reduction of portal flow in patients that have borderline liver function can precipitate liver dysfunction or failure. Additionally, the fraction of portal flow diverted into the systemic circulation through the shunt is not cleared by the liver until it returns to the liver via the arterial circulation. This may induce encephalopathy, and shunts that divert most or all of the portal flow into the systemic circulation are more likely to induce encephalopathy than do those shunts that are selective or partial. One special case scenario is Budd–Chiari syndrome in which the hepatic venous outflow is obstructed, usually due to thrombosis secondary to a hypercoagulable state. In this disorder, blood flow perfuses the hepatic sinusoids from both hepatic artery and portal vein, but cannot exit through the blocked hepatic veins. A functional side-to-side shunt is performed (portacaval, mesocaval) that allows hepatic arterial blood to flow into the sinusoids and then exit via the portal vein, and through the shunt into the systemic circulation. It is not uncommon for liver function to deteriorate initially after the shunt is performed with subsequent gradual improvement and liver regeneration. Support of liver function may be required immediately after the shunt while liver function stabilizes. In some cases the shunt may precipitate acute liver failure making urgent liver transplantation the only option.

**Immediate Postoperative Management**

Postoperative fluid management is important in the care of patients after major hepatobiliary surgery. In particular, fluid shifts in patients who have had major liver resection can be difficult to manage after surgery. Intraoperatively, most liver resections are performed with low CVP and low intravascular volume. This practice minimizes bleeding during the hepatic parenchymal transection phase of the procedure, but may pose some difficulty in postoperative management. Postoperatively,
patients that have had a major liver resection may have signs of hypovolemia with low urine output and low blood pressure. Volume re-expansion should be gentle, as partial liver resection leads to hypoalbuminemia, and pulmonary edema and ascites can develop with aggressive resuscitation. Although the use of albumin infusions is generally frowned upon in critical care medicine, albumin and fresh frozen plasma (FFP) may be useful in the resuscitation of patients after liver resection as the physiology is similar to patients with cirrhosis. We will use albumin containing fluids for volume expansion if the serum albumin is less than 2.9 mg/dL. FFP can be used for volume expansion; however, it is generally reserved for abnormalities in coagulation. Serial lactate levels are helpful in the postoperative management of patients after liver resection. Elevated lactic acid levels may be a sign of hypovolemia, but the lack of response to volume can indicate liver dysfunction.

After liver resections, glucose metabolism is altered, due to both a reduction in functional liver mass and relative dysfunction of the remaining liver secondary to ischemia reperfusion injury, especially if vascular control has been used during the procedure. As glycogen stores are depleted, the liver uses gluconeogenesis to provide glucose. As a result, patients may become hypoglycemic, although lethal hypoglycemia is rare. It has become standard practice in most critical care units to tightly control blood glucose levels. While the advantages of this approach, particularly regarding reduced risk of sepsis, remains for patients after major liver resection, aggressive blood glucose control with insulin infusions requires closer monitoring and may require reduced insulin dosing to prevent hypoglycemia.

Patients who have undergone shunt surgery need a different approach than patients undergoing other hepatobiliary surgery. Patients need more aggressive fluid management immediately postoperatively to maintain circulating intravascular volume and reduce the risk of shunt thrombosis. Maintenance fluid should be D5 0.45% saline solution to provide the liver with carbohydrates. After the immediate postoperative period, patients are also at risk for ascites formation, hence excessive sodium should be minimized. Additional volume expansion should be with albumin or FFP. Diuretics can be reinstated after the immediate postoperative period. A general rule is to use furosemide and spironolactone in combination with 100 mg of spironolactone for every 40 mg of furosemide. Antibiotics should be administered for 24 hours postoperatively to minimize infection.

While encephalopathy is rare in patients after liver resection, unless they present in liver failure or have pre-existing liver disease, the presence of asterixis can be an early sign of encephalopathy. Encephalopathy is treated with lactulose and dietary protein restriction, as in other patients with end-stage liver disease. Infection, dehydration, and bleeding, as well as narcotic use, must be evaluated as they can trigger encephalopathy.

**Hypophosphatemia**

After liver resection, care must be taken to aggressively replace low serum phosphate.

The exact mechanism of the hypophosphatemia remains unclear, as both increased utilization during liver regeneration and renal wasting mechanism have been proposed (23).

Regardless of the etiology, the clinical consequences of hypophosphatemia are well established, and include respiratory depression, diaphragmatic insufficiency, seizures, and cardiac irritability. Additionally, hepatocellular regeneration is dependent on ATP and, after liver resection, regeneration may be impaired if phosphate is not repleted (24). In a series of 35 liver resections, 21% had significant postoperative hypophosphatemia (less than 2.5 mg/dL). This group had a significant increase in complications (80%) compared with the normophosphatic group (28%) (25). Phosphate should be replaced with potassium or sodium phosphate preparations, or added to parenteral nutrition solutions. Recent studies in living donor right hepatic lobectomies suggest that replacement up to two times the recommended daily allowance (60 mmol) is necessary to replete severe hypophosphatemia and prevent its complications.

**Liver Function: Assessment and Support**

Liver function should be carefully monitored after major liver resections and shunt surgery, as liver failure is a risk in any major hepatobiliary surgery. The risk of liver failure increases with the extent of hepatectomy and in patients with preoperative liver disease or cirrhosis (27,28). Although standard liver function tests are helpful after major liver resection or shunt surgery, they may not show elevation until the patient has significant liver failure. Transaminases are frequently elevated in the 200 to 300 units/dL range postresection due to the direct effect of mechanical injury to the liver during transection, as well as to partial devascularization of areas of the liver. Measurements of liver function, including the prothrombin time and lactate, are more helpful in evaluating for early postoperative liver dysfunction.

Elevated total and indirect bilirubin are also useful indicators of postoperative liver dysfunction; however, isolated elevation of total bilirubin in the presence of normal liver function can have other etiologies. Perioperative blood transfusions can lead to hemolysis and hyperbilirubinemia with a predominance of direct hyperbilirubinemia, and can be diagnosed with a standard hemolytic workup. Bile leaks or obstruction can also lead to an elevated serum bilirubin. The diagnosis and treatment of bile leaks are covered later in this chapter. Many popular anesthetics, antibiotics, and other drugs can cause hepatotoxicity and elevation of the serum bilirubin, and need to be reduced or stopped if liver failure occurs.

When postoperative liver dysfunction does develop, it is important to exclude sepsis and anatomic causes of liver failure. A postoperative ultrasound can evaluate for portal vein, hepatic arterial, or hepatic vein thrombosis or obstruction, which may be amenable to surgical intervention. If the patient does not have sepsis, drug toxicity, biliary obstruction or leak, or vascular occlusion, the liver failure is likely related to a pre-existing liver disease and/or the extent of resection. Treatment is then supportive, with correction of coagulopathy, encephalopathy, and ascites, as above. Systemic antibiotics, or gut decontamination may be beneficial since the liver Kupffer cells play a role in decreasing bacterial translocation from the portal blood flow, and patients with liver failure or biliary leak or obstruction, may have an increased risk of bacteremia and sepsis. In some patients postoperative liver failure is fatal.

N-acetylcysteine has been shown to decrease liver injury after acetaminophen overdose (29) and lessen hepatic ischemia reperfusion injury (30). Intravenous infusions of prostaglandin have also been linked to improvement of ischemia reperfusion...
injury and liver damage (31). Although definitive clinical data are lacking, both N-acetylcysteine and PGE1 have been used to ameliorate postoperative damage in both liver resection and transplant patients. N-acetylcysteine is given over 16 hours as a continuous infusion of 40 mL of 10% solution mixed in 250 mL of D5W. Prostaglandin is also given as a continuous intravenous infusion, starting at 0.15 mcg/kg/hr. It is titrated up to 1 mcg/kg/hr based on systemic hypotension.

Coagulation Disorders

The liver synthesizes both procoagulant and anticoagulant proteins and, with liver dysfunction after liver resection, patients may be hypercoaguable, hypocoagulable, or both. Coagulopathy is more commonly associated with liver resection and dysfunction and can be particularly significant in the immediate postoperative period when excessive coagulopathy can lead to surgical bleeding and reoperation. Several studies have demonstrated and increase in prothrombin time directly proportional to the extent of liver resection (32,33). This coagulopathy has been attributed to impaired synthesis and clearance of clotting factors, inhibitors, and regulatory proteins (34,35). Patients with underlying liver disease and cirrhosis also often have thrombocytopenia and qualitative platelet defects. In addition, intraoperative hypothermia and perioperative transfections, which, while not routine, are not uncommon during major hepatobiliary surgery, and can contribute to postoperative coagulopathy.

Serial hemoglobin and prothrombin levels should be measured. Because of the vascular nature of hepatobiliary surgery combined with postoperative coagulopathy from decreased liver function, as well as the frequent need for intravascular volume expansion, serial hemoglobin levels should be followed to watch for postoperative bleeding. In general, we would obtain a hematocrit and international normalized ratio (INR) on ICU arrival and then repeat about 6 hours later. The surgeon should be notified of excessive bloody output from the drains, increasing abdominal distention, or hemodynamic instability. In the immediate postoperative period or if bleeding is suspected, the INR should be corrected if it goes above 2.0, unless specified otherwise by the surgeon (36). Vitamin K should be given in addition to FFP. Any patient who is bleeding should have their coagulopathy correctly corrected. For severe bleeding, both aprotinin and activated factor VII or 4-factor prothrombin complex are safe in patients during and after liver resection (35,37). A thromboelastogram may be helpful in these situations to determine the exact cause of the coagulopathy and is now routinely used in liver transplantation and hepatobiliary surgery. Patients who fail to stop bleeding after correction of their coagulopathy require return to the operating room. The surgical team should be made aware of any patient immediately post surgery that requires transfusion.

There is a common perception that patients post liver resection have some degree of auto-anticoagulation from physiologic liver dysfunction that is protective against venous thromboembolism (VTE) (38). In reality, patients undergoing major liver resection are considered at moderate to high risk for thromboembolic complications according to 2012 American College of Chest Physician (ACCP) guideline (39). It is imperative to start prophylaxis for VTE once the acute risk of hemorrhage has passed, especially in patients with malignancies. At our institution, we prefer low–molecular-weight heparin unless the patient has renal insufficiency or another contraindication to VTE prophylaxis. There are data suggesting VTE rate actually is increased in proportion to the extent of hepatectomy. Additionally, advanced age, higher BMI, male gender, high ASA classification (3 or higher), postoperative organ space infection, longer procedure times, as well as higher postoperative INR (1.5 or higher vs. less than 1.5), all increase the risk of postoperative VTE (38,40).

Pain Management and Sedation

The large subcostal incision needed for major hepatobiliary surgery can result in significant pain after surgery. However, altered pharmacokinetics and coagulopathy in particular after partial liver resection or shunt surgery can make postoperative pain management challenging. Patients with liver failure or compromised liver function secondary to hepatectomy have altered metabolism of many common medications, in particular, narcotics and sedatives that require clearance via the liver.

One of the more common problems that arises in the ICU after liver resection is oversedation of patients. A standard dose of narcotics given to a patient who has had 80% of the liver resected may well cause prolonged respiratory depression and signs and symptoms of encephalopathy. Narcotics and benzodiazepines should be used at the minimum dose required to achieve pain control/sedation. After liver resection, it is recommended that basal rates on patient-controlled anesthesia pumps be avoided, as metabolism of narcotics is difficult to forecast. Benzodiazepines also have altered clearance after liver resection, and thus should be dosed at lower levels or avoided altogether, if possible. In patients who require ongoing intubation we have found it useful to use sedative agents such as propofol, rather than narcotics, since the level of sedation can be more easily titrated and reversed.

Epidural pain management may be optimal after liver resection; however, it is contraindicated in many patients because of postoperative coagulopathy. Unfortunately, that includes many hepatic resections and shunt surgery. Recent literature has examined the use of epidural catheters in patients undergoing living donor partial hepatic resection. In one review of eight patients, good pain control was achieved with only one case of oversedation requiring naloxone. Although postoperative coagulopathy did occur, it was not to the extent that factor transfusion was needed prior to catheter removal, and there were no cases of hemorrhage (41). Epidural analgesia may be useful in select patients who do not have underlying liver disease and who are not undergoing extended resections.

Nutrition

Although nutrition plays an important role in the care of any critically ill patient, the role of the liver in protein and carbohydrate metabolism makes proper postoperative nutrition imperative in the management of patients after major hepatobiliary surgery, in particular, after partial liver resection when liver function is temporarily reduced. Patients with preoperative biliary obstruction, malignancy, and cirrhosis are at higher risk for nutrition-related complications after major liver or bile duct surgery. Preoperative nutritional risk factors that are associated with postoperative complications in hepatobiliary surgery include weight loss of over 14% lean body mass over 6 months, serum albumin less than 3 g/dL, hematocrit

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less than 30%, total body potassium less than 85% normal, less than 25th percentile for mid-arm circumference, and skin test anergy (42). Preoperative bilirubin, albumin, prealbumin, prothrombin time, transferring, and vitamin and trace mineral deficits may also be important preoperatively.

As with most critically ill patients, early enteral nutrition has been associated with improved outcomes. In hepatobiliary surgery, both enteral and parenteral nutrition have been associated with improved outcomes, especially in high-risk patients (42,43). However, parenteral nutrition has been clearly associated with an increased risk of infection (44). Enteral nutrition has been shown to improve gut flora, preventing gastrointestinal atrophy and loss of immunocompetence. A review of five prospective randomized trials on enteral and parenteral nutrition in patients after liver resection found a decrease in wound infection and line sepsis in patients on enteral nutrition (45). There were no differences in mortality.

In patients who have undergone routine liver resection or shunt surgery, low-volume enteral feeds can be started almost immediately postoperatively. In patients who have had hepatocojunostomies or pancreatic surgery, return of bowel function is necessary prior to starting feeds, unless the feeding tube is placed distal to the anastomosis. It is best to consult with the operating surgeon before starting enteral feeds in any patient, in particular those with enteric reconstruction. Patients with major pancreatic surgery (pancreatoduodenectomy [PD], subtotal or total pancreatectomy) may require pancreatic enzyme supplementation with enteral feeds or when resuming oral intake.

Patients with chronic liver disease or cirrhosis often have severe metabolic derangements that make nutritional management difficult. The depletion of the fat-soluble vitamins, in particular a loss of vitamin K, leads to coagulopathy and diminished antioxidant response. Chronic liver disease also stimulates a catabolic state with proteolysis and cachexia; protein loss can be exacerbated by dietary restriction to help decrease encephalopathy. Branched-chain amino acids, initially thought to reduce the development of encephalopathy in catabolic patients with advanced liver failure, have not borne out in clinical trials. Patients with cirrhosis also have abnormal glucose tolerance and insulin levels, along with elevated ammonia levels, hypophosphatemia, and hypoalbuminemia, all of which influence perioperative nutrition. All Child’s B or C cirrhotic patients should be fed enterally when hospitalized. Caloric needs of the patients are increased to a goal of 25 to 25 kcal/kg/d; protein requirements are 1 to 1.5 g/kg dry weight in those not encephalopathic, with a minimum of 0.5 g/kg dry weight if encephalopathy has ensued (45). Patients with ascites require sodium restriction of 2 g/d and a fluid restriction of 1 to 1.5 L/d, in combination with diuretics, if tolerated.

Patients with preoperative obstructive jaundice often have chronic, low-grade endotoxemia and sepsis. This can lead to weight loss and anorexia, often due to malabsorption of fat and fat-soluble vitamins related to the obstruction, which itself leads to coagulopathy and a diminished antioxidant response. Endotoxemia also results in decreased hepatic protein synthesis and catabolism (46). Patients with biliary obstruction require a low-fat diet, as absorption is impaired, as well as replacement of the fat-soluble vitamins. Medium-chain triglycerides may be helpful, because their absorption is not bile salt dependent and these may avoid diarrhea until bile flow is re-established.

Partial liver resections also cause metabolic abnormalities secondary to the regenerating liver. Hepatic mitochondria switch to fat from glucose as their preferred energy source in hepatic regeneration (47). As a result, hyperglycemia and insulin infusions should be avoided immediately after resection, as hyperglycemia and insulinemia suppress fatty acid release and decrease ketone body production by the liver. Some investigators have advocated administering fat and/or ketone bodies after liver resection to accelerate regeneration; conclusive evidence that this is beneficial is lacking. Similarly, infusions of glucose and insulin directly into the portal vein have also been looked at to improve regeneration although, again, conclusive evidence is lacking. Adequate liver regeneration is dependent on protein and calories; postoperative parenteral nutrition should be protein and fat supplemented, but low on glucose, to improve hepatic regeneration. General goals are 30 kcal/kg/d, with 1.0 to 1.5 g protein, glucose not to exceed 5 mg/kg/min, and fat making up 30% of the calories. Patients with cancer may need an increase of up to 35 kcal/kg/d and 2 g protein.

Well-nourished patients need no postoperative support, while malnourished patients will benefit from early enteral nutrition when possible, or parenteral nutrition until they are capable of taking enteral nutrition.

### Renal Failure

Acute renal failure occurs after major hepatobiliary surgery in 10% of patients (48) and, similar to other critically ill patients, significantly increases postoperative mortality (49). Risk factors for perioperative renal failure include postoperative sepsis, preoperative uremia, preoperative anemia, malignant disease, and preoperative jaundice (48,50,51). In particular, preoperative obstructive jaundice appears to be a significant risk factor, with an estimated 10% of patients developing postoperative renal failure (52). Both dehydration and endotoxin production from bile duct obstruction have been postulated to cause renal failure in these patients (53). Many studies have been performed trying to decrease this risk, including using mannitol, bile salts, hydration, and lactulose (52–55).

In all patients with acute renal failure, adequate hydration, treatment of sepsis, and avoidance of nephrotoxic drugs are mandatory. However, in patients with obstructive jaundice, lactulose and bile salts may decrease endotoxin absorption, and have been shown in some studies to be beneficial in the prevention of renal failure (51,52). Preoperative biliary drainage to help lessen the perioperative inflammatory response is also an important adjunct to prevent postoperative renal failure. Once acute renal failure does occur, supportive care and dialysis are needed until renal function returns.

Patients with advanced cirrhosis or postoperative liver failure may develop hepatorenal syndrome (HRS). This is more significant in the acute care of patients with liver failure or after liver transplantation. HRS is a diagnosis of exclusion, based on urine sodium less than 10 mEq/L combined with a urine osmolality greater than that of plasma osmolality that does not respond to volume. The cause of HRS is likely multifactorial, but is primarily related to circulatory disturbances in patients with advanced liver disease, reduced liver function, and portal hypertension. Systemic vasodilatation and low mean arterial pressure results in afferent renal arterial vasoconstriction and a reduction in glomerular filtration rate.
(56). Although liver transplantation remains the only cure for HRS, vasoconstrictors, albumin infusions, and transhepatic portosystemic shunts are able to reduce HRS, and may prevent its development in patients with spontaneous bacterial peritonitis (57).

**Postoperative Complications**

**Complications Following Liver Resection**

The morbidity associated with liver resection is reported to be between 30.7% and 47.7% (57–60). In addition to the standard complications associated with all major operations, liver resection is associated with specific problems including bleeding, bile leaks, liver insufficiency, ascites, pleural effusions, and infections.

Risk factors of complications following liver resection include increased blood loss, increased number of segments resected, increased preoperative bilirubin, increased prothrombin time, prolonged operative time, resection of segment 8, diabetes, and concomitant surgical procedures (60–65).

**Mortality.** In-hospital mortality due to liver resection has decreased over the past two decades and high-volume centers have reported rates of 0% to 5% (57,59,60,66–68). The decrease in mortality is attributed to improved surgical technique, intraoperative anesthesia management, and perioperative care. These changes have helped decrease in-hospital mortality in liver resection patients despite their increased mean age and comorbidities (57).

Risk factors associated with increased mortality include hypoalbuminemia, thrombocytopenia, preoperative total bilirubin greater than 6 mg/dL, elevated serum creatinine greater than 1.5 mg/dL, cholangitis, major hepatic resection, increased number of segments resected, synchronous abdominal procedure, major comorbid illness, diabetes, and blood transfusion requirements (57,59,62,68–71).

Specific surgical strategies to decrease mortality include minimizing blood loss and transfusions, and avoiding ischemic injury to the remnant liver. Specific posthepatectomy strategies include minimizing ongoing liver injury by maintaining tissue oxygenation, early support to facilitate liver regeneration by early feeding, and replenishing phosphate levels (66).

**Bleeding.** Bleeding, once the Achilles heel of liver resection surgery, has decreased dramatically over the last two decades due to a better appreciation of liver anatomy, surgical technique, and improved anesthetic management (66). As a result, centers routinely performing liver resections have noted a decrease in estimated blood loss of from 300 to 750 mL, and perioperative transfusion rates of 17.3% to 28.3% (57,59,68).

Risk factors for increased bleeding from liver resection include cirrhosis, portal hypertension, increased segments resected, coagulopathy, thrombocytopenia, and elevated CVP during resection (62,72). Strategies to minimize blood loss during liver resection include appropriate patient selection (especially avoiding resection in patients with portal hypertension), maintenance of CVP under 6 mmHg, Pringle maneuver, preoperative correction of coagulopathy and thrombocytopenia, use of fibrin sealant on raw liver surfaces, use of intraoperative ultrasound to locate the hepatic venous branches, and utilization of selective hepatic vascular exclusion (72–76).

**Bile Leak**

Biliary leaks occur in 3.6% to 17% of liver resections (77–80) and are associated with increased mortality and concomitant complications (78,79,81). Risk factors associated with biliary leaks following liver resection include older age, preoperative leukocytosis, left-sided hepatectomy, prolonged operative time, resection for peripheral CCC, and resection of segment 4 (77,79). When liver resection is performed for hepatocellular carcinoma (HCC), risk factors for bile leaks include central tumor location, and preoperative transarterial chemoembolization (TACE) (78).

Various strategies have been described to prevent bile leaks following resection. A few groups have shown that the use of fibrin glue on the cut surface of the liver reduces bile leaks (77). Others have combined fibrin glue with bioabsorbable polyglycolic acid to significantly reduce bile leaks (82). While these small studies may indicate some effect of fibrin glue in reducing biliary leaks, there are at least as many studies that show no difference in bile leak rate when fibrin glue is employed.

Most bile leaks following liver resections without biliary reconstructions are small and can be managed nonoperatively. A percutaneous drain is placed—if a drain placed at surgery is not present—to prevent abdominal sepsis from an undrained biloma and to control the leak (79) and broad-spectrum antibiotics initiated for fevers, leukocytosis, or positive bile cultures. Persistent drainage for 2 to 3 days of more than 100 mL of bilious fluid confirms an active leak, and is managed with endoscopic retrograde cholangiopancreatography (ERCP), sphincterotomy, and stent placement. This procedure may define the location of the leak and facilitate enteric biliary drainage and leak closure. When leaks are at the resected hepatic duct stump, a stent traversing the leak may further facilitate leak closure, although the main principle of treatment is to reduce the pressure in the biliary tree and allow spontaneous closure (79). Early endoscopic management of biliary leaks can minimize hospital length of stay and are not associated with late biliary complications (80). Others have used endoscopically placed nasobiliary tubes to decompress the biliary system as it allows easy repeat cholangiograms and later removal (80,83). Although most leaks will close with time with these measures, they may persist for months (28).

From 10% to 32% of patients ultimately require reoperation because the leak cannot be controlled, and these procedures are associated with a high mortality rate (79,80,83). Biliary enteric drainage is performed on patients in whom ERCP cannot be performed for technical reasons, or who persist on leaking despite ERCP. Important factors contributing to a good outcome are early reoperation, control of the biliary fistula before surgery, and utilization of healthy bile duct edges for enteric anastomosis.

Hemobilia may complicate either bile leaks, liver resection, or occur secondary to trauma. Open communication from a branch of the hepatic artery to the biliary tree occurs and leads to intermittent and sometimes exsanguinating GI bleeding. Identification is made when blood is seen exiting the ampulla during endoscopy for upper GI bleeding. While CT scanning with arterial phase contrast can localize the bleeding within the liver, management is by angiographic embolization.

**Liver Failure/Dysfunction.** Liver failure complicates liver resection in up to 12% of cases (61), and occurs when inadequate functional liver volume is left after resection. This
complication occurs primarily in patients undergoing resection for HCC with underlying liver disease, and is often a consequence of patient selection and choice of operation.

Risk factors for hepatic insufficiency in cirrhotics include major resection—especially right lobectomy—portal hypertension, longstanding jaundice, Childs–Pugh–Turcotte (CPT) score greater than A, and hepatic steatosis (57). More recently, preoperative chemotherapy has become routine in patients with colorectal cancer metastatic to the liver. While there is no doubt that the addition of newer agents such as irinotecan, oxaliplatin, and bevacizumab have improved long-term results, they also cause an increase in hepatic steatosis as well as steatohepatitis, which can contribute to postoperative liver dysfunction.

By assessing the patient’s functional liver status, the surgeon can estimate the maximum amount of liver mass that can be resected while preserving adequate functional liver volume. In patients with normal livers, up to 75% of total liver volume can be resected safely. It is patients with abnormal livers, such as cirrhosis, that need careful assessment. In general, Childs–Pugh class C is a contraindication to any sort of resection. Early Child’s class B patients without portal hypertension may undergo minor resections from wedge resection to a single segmentectomy; however, these patients may be better served by nonoperative local ablation techniques. Childs–Pugh class A patients being considered for major hepatectomy (resection of 4 or more segments) should undergo assessment of both liver and physiologic status (84,85). Others have found that a model for end-stage liver disease (MELD) equal to or greater than 11 predicts liver failure following HCC resection (86). Portal hypertension, defined as a hepatic vein pressure gradient (HVPG) greater than 10 mmHg and suggested by signs such as esophageal varices, anatomic portosystemic shunts, and ascites (87), has been associated with increased morbidity and mortality following major resection (88). Thrombocytopenia with platelet counts less than 100,000 cells/µL is one laboratory indicator of portal hypertension and has been associated with in-hospital mortality following liver resection (84).

Although various tests exist to assess liver function in Childs–Pugh classes A and B patients before possible major liver resection (greater than or equal to four segments), none have been uniformly adopted. The indocyanine green (ICG) clearance test, commonly used in Asia, is one method of quantifying liver function (66,89,90). Early studies have shown that an ICG retention at 15 minutes (ICGR15) of less than 20% allows safe limited liver resection, and a value of less than 14% is associated with near-zero operative mortality (91–93).

In Childs–Pugh class A patients with right-sided lesions curable by major resection but whose liver reserve may be inadequate, preoperative ipsilateral PVE increases the remnant contralateral liver volume (92). Portal vein embolization is generally performed in patients with a predicted function liver remnant of less than 25% in noncirrhotics or less than 40% in patients with significant fibrosis and/or cirrhosis.

Liver failure following liver resection presents clinically with encephalopathy and asterixis. In severe cases, patients appear similar to fulminant liver failure patients with marked acidosis, jaundice, and hemodynamic instability. The patient ultimately succumbs to multiorgan failure and sepsis. In mild cases, treatment is supportive with judicious fluid management, optimizing tissue oxygenation, infection prophylaxis, and nutritional support if recovery is prolonged. The goal in the mild and salvageable cases is to promote immediate liver functional recovery from the insults inherent to liver resection, to promote liver regeneration with nutritional and electrolyte repletion (particularly phosphate), and to minimize the change of infections complications. With early studies demonstrating significantly improved hepatic oxygen delivery and extraction in patients receiving N-acetylcysteine for nonacetaminophen-induced liver failure (94,95), subsequent conflicting studies have failed to support a definite role in patient following liver resection (96). Nonetheless, many centers—including our own—selectively administer N-acetylcysteine in patients with marginal liver function following resection mainly based on favorable small-series and anecdotal benefits (97). This practice may be reasonable because of the sheer number of favorable outcome reports and the good drug safety profile, but controlled trials are needed.

Ascites and Pleural Effusion. Ascites occurs in up to 9% of liver resections (61) and is associated with decreased survival as it is a surrogate marker of liver insufficiency and because of its potential contribution to prerenal insufficiency (81). Pleural effusion usually occurs on the right side and frequently accompanies ascites. Pleural effusion following liver resection occurs in 3.8% to 21% of cases (61,98), is usually asymptomatic, and most often requires no treatment. Effusion may develop from underlying ascites that crosses the diaphragm. In addition, the same pathophysiologic processes of fluid overload and hypoalbuminemia that cause ascites also contribute to the development of pleural effusion.

Risk factors for both ascites and pleural effusion include right lobectomy, diabetes, poor nutritional status, and hypoalbuminemia, left-sided cardiac insufficiency, liver and renal insufficiency (57,99). In addition, risk factors specifically associated with pleural effusion have been found to include resection for HCC with underlying liver disease, subphrenic collections, postoperative liver insufficiency with ascites, and duration of inflow occlusion (98).

Strategies to prevent postresection ascites and pleural effusion include avoiding overhydration (including gentle diuresis), preventing renal insufficiency by avoiding nephrotoxic drugs and hypotension, early detection and treatment of infection, maintaining adequate nutrition, and the use of perioperative drains (99). The appropriate selection of patients and resection to maintain adequate liver function, especially in patients with hepatomas and underlying liver disease, will minimize the risk of liver failure and subsequent ascites.

Complications Following Bile Duct Resection/Reconstruction

Perhaps the most extensive hepatobiliary operations are performed for proximal extrahepatic CCCs. With mounting evidence demonstrating significantly improved survival following extended liver and bile duct resections and reconstructions versus local bile duct resections, centers with experienced hepatobiliary surgeons are presenting series with improved outcomes (100–103). Nonetheless, significant complications remain associated with these procedures.

Perioperative mortality following extended liver and biliary resections ranges from 1.3% to 16% (102,104–106). Complications following these procedures occur in 51% to 81%, and many patients have multiple complications (100,102,105,106).
Complications include bile duct leaks, bleeding, liver failure, pleural effusions, wound infection, and sepsis (104,106–108). Each of these complications can also be found in liver resections alone and share the same risk factors. In addition, each complication can be approached with the same preventative strategy and treatment.

Lever failure following extended resections for obstructive CCC may have a unique pathophysiology and hence preventative strategy. Prolonged biliary obstruction causes significant hepatocellular dysfunction, and liver failure occurs in up to 27.6% of patients who undergo extended liver and biliary resections and reconstructions for CCC and is frequently fatal (106,108). Resection of up to 75% of the liver along with possible vascular reconstruction that requires an increased duration of ischemic injury to the liver is often necessary to resect hilar CCC and in the setting of pre-existing liver dysfunction liver failure can be problematic. Strategies to optimized functional liver volume prior to extended liver resections for hilar CCCs are essential to preventing postoperative liver failure. One strategy is to promote hepatocellular functional recovery by preoperatively decompressing the biliary tree using percutaneous transhepatic cholangiocatheterization. This practice is somewhat controversial as it may introduce infection into an otherwise sterile biliary tree, and so may be avoided in patients who can undergo surgery within 2 to 3 weeks after the onset of jaundice. Another strategy is to perform contralateral PVE to increase the remnant liver volume prior to resection. A number of centers have demonstrated decreased liver failure rates when these strategies are employed (103,104,109).

Complications Following Pancreatic Surgery

The mortality rate following PD ranges between 2.7% and 6.9% (109–114). Risk factors for perioperative mortality include elevated serum bilirubin, diameter of pancreatic duct, increased intraoperative blood loss, pancreatic fistulas, and older age (113).

Complications occur in between 22.1% and 30.2% of PDs, and include pancreatic fistulae, delayed gastric emptying, bleeding, abdominal abscesses, and wound infections (112,113).

Pancreatic fistulae are a dreaded complication of PD, occurring in 12% to 18% of patients (110–112,115–118). Pancreatic fistulae are associated with a mortality rate of 0% to 19% (104,111,112). These patients often die secondary to massive erosive bleeding from sepsis and pancreatic enzyme accumulation. These bleeding episodes occur in 1% to 8.8% of PD patients and carry a mortality rate of 47% to 50% (114,119,120).

Risk factors for pancreatic fistulae include small duct size, soft pancreas texture, duration of surgery greater than 8 hours, diabetes, lower creatinine clearance, preoperative jaundice, and increased intraoperative blood loss (112,116,118,121).

Despite numerous studies evaluating potential strategies to prevent pancreatic fistulae following PD, including the use of ocreotide, fibrin sealants, pancreatic stents, different methods, and sites of pancreatic anastomosis, none have proven effective (117,122–125). Pancreatic fistulae are initially detected on postoperative day 6, presenting with abdominal pain, fever, nausea/vomiting, and leukocytosis. Fistulae are then confirmed by CT scan which often demonstrates a fluid collection behind the pancreatic anastomosis, elevated serum amylase, and increased intraoperative blood loss (112,119,120).

Management is initially conservative with bowel rest, total parenteral nutrition, antibiotics, and monitoring of clinical signs and symptoms and drain output. If repeat imaging demonstrates increased accumulation of fluid and the patient does not respond to conservative measures, another drain may be placed percutaneously to prevent progression of abdominal sepsis. Eighty percent to 90% of patients seal pancreatic fistulae with these measures (110,115). However, those patients who develop uncontrolled leaks and abdominal sepsis may require surgery, usually for completion pancreatectomy. In addition, a smaller group of patients with fistulae will suffer life-threatening erosive intra-abdominal bleeding, usually from the stump of the gastroduodenal artery, small arterial branches to the pancreas, or rarely from the portal vein. These patients will present with signs and symptoms of sepsis and hypovolemia, such as fever, abdominal pain, hypotension, anemia, and bloody drain output; they are treated by rapid resuscitation and angiography for potential embolization of the bleeding arterial branch. If arterial bleeding cannot be controlled in this manner, or if the bleeding is venous, the patient is surgically explored for hemostasis and completion pancreatectomy. Surgery in this setting is associated with a high mortality: up to 36% of patients requiring surgery after PD for bleeding will not survive (114,120,123).

Key Points

- After hepatic resection, liver function is altered through both a reduction in functional liver mass as well as potential ischemia/reperfusion injury to the liver remnant.
- With extensive liver resection in patients with normal underlying liver function, reduction of functional liver volume below 25% has been associated with increased risk of both liver failure and mortality.
- Preoperative PVE diverts portal flow from the side of the liver to be resected to the FLR allowing for growth and hypertrophy over a 6-week period. This has been shown to reduce the complications associated with extended liver resections.
- A CVP of 5 mmHg or less during hepatic transection has been shown to decrease blood loss and improve outcomes, and can lead to hypovolemia postresection.
- Patients at an increased risk for liver insufficiency or complications post liver resection include liver remnant of less than 40%, cirrhosis, bile duct obstruction, vascular reconstruction, total vascular isolation or prolonged inflow occlusion, and significant intraoperative blood loss.
- Patients can develop significant hypophosphatemia post liver resection and need aggressive phosphorous replacement to facilitate liver regeneration and prevent the clinical consequences of low phosphate.
- PT/INR and lactate are the best postoperative indicators of liver function. AST and ALT are measurements of parenchymal damage and commonly elevated after major resection.
- Patients undergoing major liver resection are considered at moderate to high risk for thromboembolic complications and it is imperative to start prophylaxis.
for VTE once the acute risk of hemorrhage has passed, especially in patients with malignancies.

- Pancreatic fistula is a common and dreaded complication after PD. Most fistulae are managed nonoperatively with drainage, antibiotics, and bowel rest. A small percentage of patients develop uncontrolled leaks that lead to hemorrhage, sepsis, and death.

References


