

Surgery in the Patient With Liver Disease

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Patients with liver disease often undergo surgery. With the increasing prevalence of liver disease and improved survival due to newer medications and treatments, a growing number of patients with liver disease will require preoperative assessment. Because of the multiple physiological roles of the liver, hepatic dysfunction places these patients at an increased risk of perioperative morbidity and mortality. The precise risks associated with specific liver dis-

eases are poorly understood but are greater with increased impairment of hepatic function. Identifying preexisting problems that could be optimally and appropriately managed before surgery (eg, coagulation status, intravascular volume, renal function, electrolytes, cardiovascular status, and nutrition) may reduce these risks and decrease mortality in patients with liver disease undergoing surgery.

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Patients with liver disease often undergo elective surgery, and up to 10% of patients with end-stage liver disease may have surgery during their last 2 years of life.¹ Patients with unsuspected liver disease may also undergo surgical procedures. Indeed, patients with advanced liver disease may be asymptomatic despite alterations in hepatic function. In 1 study, abnormal results on liver-related tests were noted in 11 of 7620 otherwise-healthy surgical candidates, all of whom were subsequently shown to have underlying liver disease.² With the increasing prevalence of liver disease and improved survival due to newer medications and treatments, a growing number of patients with liver disease will require preoperative assessment. These patients are at an increased risk of perioperative mortality due to the effects of surgery and anesthesia on the liver and alterations in the unique metabolic and synthetic functions of the liver. Identifying preexisting problems that could be managed before surgery may reduce these risks. The purposes of this review are to (1) describe the effects of liver disease on surgery; (2) discuss the risks associated with anesthesia and surgery in the patient with liver disease; (3) outline an approach to perioperative risk assessment, evaluation, and management of the patient with known or suspected liver disease who is a surgical candidate; and (4) delineate an approach to patients with postoperative liver dysfunction.

EFFECTS OF LIVER DISEASE ON ANESTHESIA AND SURGERY

Several pathophysiological factors contribute to increased perioperative mortality in patients with liver disease. Be-

cause multiple hepatic functions are important during surgery and administration of anesthesia, understanding derangements of hepatic function in disease will help in the preoperative evaluation. Major functions of the liver include metabolism, detoxification, and excretion of endogenous compounds, drugs, and toxins as well as synthesis of plasma proteins, glucose, and blood coagulation factors. Because of its reserve and regenerative ability, the liver can sustain considerable damage before hepatic dysfunction becomes clinically manifest, and therein lies the challenge to preoperative assessment.

As the liver is a major site of drug metabolism, alterations in hepatic function may result in a prolonged duration of action of agents that are predominantly metabolized by this organ. For example, agents such as methoxyflurane and halothane should be avoided in patients with known hepatic dysfunction. Drugs such as sedatives or narcotic analgesics that affect the central nervous system may cause a prolonged depression of consciousness and may even precipitate hepatic encephalopathy if administered to patients with severe liver disease and marked impairment of hepatic function. Because hepatic biotransformation has a minor role in the elimination of the halogenated agents (except halothane), these agents are well tolerated in patients with liver disease. The metabolism of drugs dependent on enterohepatic circulation will also be altered during cholestasis. Moreover, the liver is susceptible to injury from a wide range of xenobiotics, and postoperative hepatic dysfunction may result from an effect of the anesthetic agents used. Anesthetic agents with known direct hepatotoxicity, such as chloroform or halothane, should be avoided in patients with known hepatic dysfunction.

Advanced hepatic disease often results in hemodynamic abnormalities. Patients with advanced hepatic disease may have an increased cardiac output and decreased systemic vascular resistance.³ Despite the large cardiac output, tissue

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perfusion may be decreased because of shunting. Most inhalational anesthetic agents reduce hepatic blood flow, and the result is decreased oxygen uptake by the liver and splanchnic organs.⁴ Although these effects seldom result in overt liver hypoxia, this outcome is more likely in the patient with preexisting liver disease. Postoperative hepatic ischemia often occurs in situations in which other factors such as hypotension, hypoxemia, hemorrhage, and use of vasoactive drugs have further reduced hepatic oxygenation. Stresses due to surgery, with concomitant catecholamine release and neurohormonal responses, may also induce changes in liver hemodynamics that lead to hepatic dysfunction.

Pulmonary dysfunction may be present in patients with liver disease.⁵ In patients with the hepatopulmonary syndrome, intrapulmonary arteriovenous shunting may result in hypoxemia. Some patients with portal hypertension also have coexistent pulmonary hypertension, which can contribute greatly to increased morbidity and mortality. The presence of ascites and pleural effusions results in atelectasis and restrictive pulmonary disorders. In addition, ventilation-perfusion mismatch or interstitial or restrictive disease may be present in patients with liver disease.

The most common causes of perioperative mortality include hemorrhage, sepsis, liver failure, and the hepatorenal syndrome. Specific complications of liver disease such as coagulopathy, malnutrition, or ascites may influence outcomes after surgery, and their specific management is outlined later in this review. Coagulopathy may be present due to vitamin K deficiency associated with cholestasis or impaired hepatic synthesis of vitamin K-dependent factors. During portal hypertension, splenic sequestration may result in thrombocytopenia. Thus, it is not surprising that hemorrhage is a common cause of mortality. Patients with cholestatic jaundice are at an increased risk of postoperative renal failure. The pathophysiological processes leading to this outcome are unknown, but a high degree of renal afferent arteriolar vasoconstriction may contribute to renal insufficiency. Increased bilirubin (>3 mg/dL) and creatinine levels and a decreased albumin level are associated with greater mortality.⁶

RISKS ASSOCIATED WITH SURGERY IN PATIENTS WITH LIVER DISEASE

The effect of liver disease on perioperative risk may lead to unnecessary concern and testing in patients at low risk of perioperative mortality. Furthermore, inappropriate surgery may be performed in those at high risk of perioperative mortality. Thus, appreciation of the risks of surgery is essential for optimal preoperative evaluation. The risk of perioperative mortality and morbidity in patients with liver disease depends on the type of surgery, nature

and severity of the underlying hepatic disease, and extent of hepatic dysfunction. Unfortunately, assessment of perioperative risk remains an inexact science due to the paucity of large prospective studies of the operative risk in patients with liver disease. The available data are primarily derived from retrospective studies of cirrhotic patients undergoing abdominal studies or from case series. Nevertheless, surgical risk may be estimated on the basis of the available data.

The perioperative mortality associated with cholecystectomy in patients with liver disease was examined in a large retrospective study. After the investigators had corrected for comorbidity that is known to be associated with increased perioperative mortality, the odds ratio for perioperative mortality for patients with liver disease vs that for patients without liver disease was 8.47 (95% confidence interval, 6.34-11.33).⁷

Acute Hepatitis

Patients with acute hepatitis are believed to have increased operative risk and perioperative mortality. Although the cause may vary (viral, toxic, alcohol, ischemia, thrombosis, or drugs), the mainstay of management is supportive care for most patients, and improvement in their overall condition will diminish the perioperative risk. Thus, elective surgical procedures should be postponed in the presence of acute hepatitis.

Acute viral hepatitis is historically associated with a high mortality rate. Harville and Summerskill⁸ reported a 10% mortality rate in patients with acute viral hepatitis undergoing laparotomy and major postoperative complications in another 11% of patients. Other subsequent studies have confirmed this high mortality.⁹ Distinguishing between medical jaundice (acute hepatitis with intrahepatic cholestasis) and surgical jaundice (extrahepatic cholestasis) was a major clinical challenge before advanced imaging techniques became available. Laparotomy was often performed for jaundice but was associated with high mortality attributed to unrecognized hepatic parenchymal disease. Because of advances in imaging capabilities, laparotomies for this purpose are seldom performed. In addition, advances in nonoperative management of extrahepatic biliary obstruction have further reduced the need for surgery. The perioperative mortality associated with acute liver disease may be lower than that in the conventional, somewhat dated literature because of advances in surgical and therapeutic techniques, better understanding of drug actions, and improvements in perioperative nutrition. Nevertheless, delaying elective surgery until the problem has resolved would be prudent.

The risk associated with drug-induced acute hepatitis has not been evaluated, but the risk due to acute alcoholic

hepatitis is believed to be worse than that for acute viral hepatitis. In 1 series, mortality was increased 5-fold in patients in whom the diagnosis of alcoholic hepatitis was made by open biopsy compared with those made by closed biopsy.¹⁰ Some series report a surgical mortality rate of 100% in patients with alcoholic hepatitis.¹¹ Thus, patients with acute alcoholic hepatitis should not undergo surgery until their hepatitis has diminished and their clinical condition improved. Fulminant hepatic failure is a medical catastrophe, with marked destruction of hepatocytes and impairment of hepatic function. Patients are encephalopathic and have severe metabolic derangements. Treatment involves intensive supportive care and transplantation.

Chronic Hepatitis

Chronic liver disease can result from a wide range of diseases with multiple causes. Data are scant regarding the surgical risk in patients with chronic liver disease. The major predictor of mortality is likely to be the extent of hepatic dysfunction. Patients with mild chronic hepatitis and well-preserved hepatic function tolerate surgery well, whereas those with decompensated disease are at a much higher risk.⁶ The nature of the liver disease may also pose specific, unique risks that increase operative morbidity, such as malnutrition in patients with alcoholic liver disease or chronic cholestasis.

Cirrhosis

The published data for operative risk in patients with cirrhosis are more extensive than for other liver diseases. However, the published studies are small, retrospective, and heterogeneous with regard to cause and have usually examined a limited range of risk parameters. Nevertheless, the risk of surgery is clearly increased in patients with cirrhosis, being greater for emergency surgery or abdominal procedures. Patients with cirrhosis may be asymptomatic or have clinically overt hepatocellular dysfunction or portal hypertension. In the presence of coagulopathy, cholecystectomy in patients with cirrhosis was associated with a greater than 80% mortality rate.¹² Although reduced mortality (8%) has been reported in recent series of abdominal surgery in patients with cirrhosis, the risk remains considerable.¹³ Perioperative mortality correlates with the degree of hepatic dysfunction or severity of cirrhosis.

ASSESSMENT OF PERIOPERATIVE RISK

Few efforts have been made to quantify the risk of perioperative mortality in patients with liver disease. Most reported studies have been retrospective, have involved small numbers of patients, and have included groups that were heterogeneous with regard to cause of liver disease

Table 1. Modified Child-Pugh Score

Presentation	Points*		
	1	2	3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International			
normalized ratio	<1.7	1.7-2.3	>2.3
Bilirubin (mg/dL)†	<2	2-3	>3
Ascites	Absent	Slight- moderate	Tense
Encephalopathy	None	Grade I-II	Grade III-IV

*Class A = 5-6 points, B = 7-9 points, and C = 10-15 points.

†For cholestatic diseases (eg, primary biliary cirrhosis), the bilirubin level is disproportionate to the impairment of hepatic function, and an allowance should be made. For these conditions, assign 1 point for bilirubin level <4 mg/dL, 2 points for bilirubin 4-10 mg/dL, and 3 points for bilirubin >10 mg/dL.

and type or urgency of surgery. Furthermore, comorbid conditions were often not considered.

The risk of perioperative mortality or morbidity is related to the extent of hepatic dysfunction. However, conventional biochemical markers of hepatobiliary disease correlate poorly with the degree of hepatic dysfunction because of the lack of individual specificity (except for the prothrombin time). Nevertheless, these markers may be helpful in combination or in monitoring hepatic abnormalities. Hepatic synthetic function may be better evaluated by albumin, prothrombin time, or pseudocholinesterase determinations, whereas hepatic excretory function can be evaluated by the bilirubin level. Tests of global liver function such as the indocyanine green test, galactose elimination capacity, and the aminopyrine breath test may have a role in predicting the outcome of surgery but are not routinely used and are not universally available.¹⁴

The most commonly used approach for the prediction of perioperative risk is based on the system developed by Child and Turcotte¹⁵ to predict mortality after portocaval shunt surgery. However, this system has never been prospectively validated in patients undergoing other types of surgery. Furthermore, it involved subjective assessments of nutrition and encephalopathy and thus could not be reliably used for retrospective studies. A modification proposed by Pugh and associates¹⁶ (Table 1) replaced nutritional status with the prothrombin time (an independent predictor of mortality) in the assessment of patients undergoing esophageal transection. The Child-Pugh score has been shown to correlate with perioperative mortality in patients undergoing nonshunt surgery and in cirrhotic patients undergoing abdominal procedures. In a retrospective analysis of risk variables of survival after abdominal surgery in cirrhotic patients, Garrison and colleagues¹⁷ reported that the serum

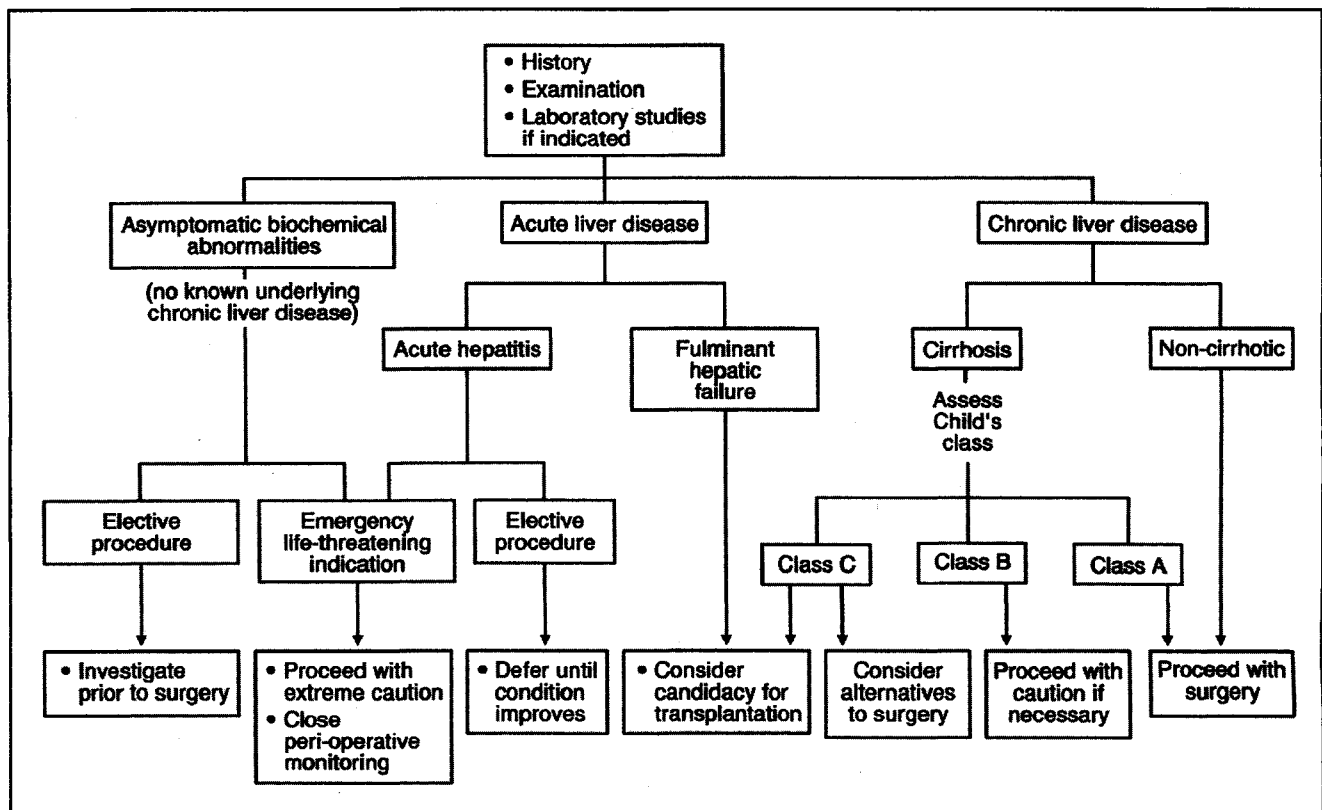


Figure 1. Preoperative approach to patient with known or suspected liver disease.

albumin level, leukocytosis, and an increased prothrombin time were the most sensitive indicators of perioperative mortality independent of the Child-Pugh score. In their study, patients with Child class A, B, and C cirrhosis had mortality rates of 10%, 31%, and 76%, respectively.

PREOPERATIVE EVALUATION OF THE PATIENT WITH SUSPECTED LIVER DISEASE

A suggested algorithm for the preoperative approach to the patient with known or suspected liver disease is outlined in Figure 1. The initial step in all preoperative evaluations should be a thorough history and physical examination. Inquiry should be made about risk factors for chronic liver disease and the presence of symptoms attributable to liver disease. Specific helpful information includes a family history of jaundice, anemia, or liver disease; travel history, occupational history, or exposure to hepatotoxins; alcohol or other drug exposure; and the use of prescription or over-the-counter medications. Physical examination should seek to ascertain evidence of chronic liver disease. Routine liver-related tests are not recommended unless underlying liver disease is clinically suspected. If, however, abnormalities are noted on liver-related test results, elec-

tive procedures should be deferred until an evaluation has been done for the presence, nature, and severity of liver disease.

Patients with acute, symptomatic liver disease should have elective surgery postponed, if possible, until they have recovered. However, if surgery is necessary because of life-threatening illness, it may be performed with close intraoperative monitoring to avoid hemodynamic instability and the use of known hepatotoxins. If chronic liver disease is evident, elective surgery should be deferred until the cause and severity of the liver disease are established. In the absence of cirrhosis, proceeding with surgery is reasonable. If, however, cirrhosis is present, an assessment of hepatic function and perioperative risk is necessary. The Child-Pugh score may help stratify risk in cirrhotic patients.

Patients with decompensated liver disease have a high risk of perioperative mortality. With the exception of procedures aimed at correcting the liver disease or its consequences (eg, transplantation or shunt), surgery should be deferred, if at all possible, until the patient's condition is stabilized. Nonoperative or less invasive management should be considered in these circumstances. The patient's

candidacy for liver transplantation should be assessed before any elective abdominal surgery.

Some surgical procedures, such as hepatic resection, shunt procedures for portal hypertension, and liver transplantation, are performed in patients with liver disease. Most patients undergo elective hepatic resection because of a primary or metastatic tumor; hepatic function is usually normal. However, liver function may be impaired postoperatively because of surgical trauma, ischemia, or loss of hepatocyte mass. Avascular planes do not exist for dissection, and thus more extensive procedures such as lobectomy may result in considerable blood loss. Furthermore, intraoperative clamping of the suprahepatic inferior vena cava or hilar vessels may result in warm ischemia of the liver. Liver transplantation is a unique and complex surgery, with its own risks and complications. Thus, pretransplantation evaluation and assessment of perioperative risk will not be covered in this brief, general review.

PREOPERATIVE MANAGEMENT OF COMPLICATIONS OF LIVER DISEASE

Before surgery, particular attention should be paid to the management of coagulation status, renal function, fluid and electrolyte changes, specific complications of end-stage disease such as encephalopathy and ascites, and nutrition.

Coagulation Status

Preoperative correction of coagulopathy is essential, even in urgent surgical situations. Coagulopathy in patients with chronic liver disease may be due to vitamin K deficiency secondary to poor nutrition or malabsorption due to cholestasis. This can be adequately corrected by a single dose of vitamin K₁, 10 mg intramuscularly. Coagulopathy may also be due to impaired hepatic synthetic function, which will not be corrected by vitamin K administration, and may require the use of fresh frozen plasma, given as needed. Because determination of the precise cause of coagulopathy may be difficult in some patients with advanced liver disease, both vitamin K and fresh frozen plasma may be given together. Some patients may not respond, and if the prothrombin time does not correct, additional measures such as cryoprecipitate (10 U intravenously, administered preoperatively) may be used. Cryoprecipitate contains large amounts of fibrinogen and von Willebrand factor. 1-Deamino-8-D-arginine vasopressin (DDAVP), 0.3 µg/kg intravenously, also causes the release of large amounts of endogenous von Willebrand factor. Plasma exchange has been used for refractory coagulopathy. Prophylactic platelet transfusions may be considered for thrombocytopenia (platelet count, $<20 \times 10^9/L$).

Renal and Electrolyte Abnormalities

Prevention of renal dysfunction is particularly important in the presence of jaundice. Anemia should be corrected preoperatively. Careful attention to volume status is critical. Nephrotoxic agents such as aminoglycosides or nonsteroidal anti-inflammatory drugs should be avoided. Urine output can be maintained by using a mannitol infusion for 1 to 2 hours preoperatively, then continued postoperatively (5% solution) to maintain a urine output of 60 mL/min. The use of lactulose to reduce endotoxemia has been advocated and may be useful in preserving renal function. Low-dose dopamine has been used to improve renal perfusion and dilate the splanchnic bed. Patients with cirrhosis often have hypokalemia and alkalosis, and these conditions should be corrected preoperatively to minimize the risk of cardiac arrhythmias and to diminish encephalopathy.

Ascites

The presence of ascites may influence respiratory mechanics and increase the risk of abdominal wound dehiscence. Thus, ascites should be controlled preoperatively. Large-volume paracentesis can be performed safely. Paracentesis fluid should be evaluated for the presence of spontaneous bacterial peritonitis by an analysis of the neutrophil count. If spontaneous bacterial peritonitis is present, appropriate therapy should be initiated. Dietary sodium restriction is necessary. Reaccumulation of ascites is common with administration of intravenous fluids. Careful attention is essential to avoid excessive use of intravenous saline solutions and medications containing sodium, and the use of albumin or blood products, fresh frozen plasma, or albumin for volume replacement should be considered to minimize reaccumulation of ascites. Diuretic therapy is the mainstay for the management of ascites, but electrolyte levels and renal function should be closely monitored. If hyponatremia occurs, fluid restriction may be necessary.

Encephalopathy

Patients with decompensated liver disease have a high risk of perioperative mortality, and surgery should be deferred, if possible, until the patient's condition is stabilized. Nonoperative or less invasive management should be considered in such circumstances. Encephalopathy can be treated with lactulose, 30 mL orally every 6 hours, titrated to 2 or 3 soft bowel movements daily. Protein restriction has also been recommended for patients who respond poorly, but excessive restriction of protein can actually contribute to malnutrition and may be undesirable preoperatively. Encephalopathy may be worsened or precipitated by the use of sedatives, and thus premedication should be avoided.

Table 2. Postoperative Liver Dysfunction in Patients With No Known Preexisting Liver Disease

Hepatocellular	Drugs (including anesthetics) Ischemia, including shock, hypotension, iatrogenic injury Viral hepatitis
Cholestatic	Drugs (antibiotics, antiemetics) Sepsis Bile duct injury Cholelithiasis or pancreatitis Cholecystitis (calculous or acalculous) Benign, multifactorial
Mixed	Drugs Multifactorial

Nutrition

Malnutrition is common in patients with chronic liver disease, and it may increase the risk of perioperative complications.¹⁸ Patients with alcoholic hepatitis have poor nutritional intake, and the short-term outcome may be improved with the use of supplemental enteral nutrition. Enteral nutrition may be helpful in improving the patient's Child class and in reducing mortality in those with cirrhosis and malnutrition. Enteral feeding is preferable to total parenteral nutrition if oral feeding can be tolerated. Because patients are often malnourished, protein restriction is not advised unless encephalopathy is present.

POSTOPERATIVE HEPATIC DYSFUNCTION

Close postoperative monitoring is essential for the patient with liver disease, particularly the maintenance of fluid balance and nutrition, as well as the identification and correction of electrolyte abnormalities, coagulopathy, encephalopathy, and infection. Medications often used postoperatively, such as nonsteroidal anti-inflammatory drugs and narcotic analgesics, should be used with caution in the patient with preexisting liver disease. The patient with alcoholic liver disease who may be more prone to acetaminophen-induced toxicity should be monitored closely. Liver dysfunction is common after surgery and anesthesia and can range from mild enzyme elevations to fulminant hepatic failure. Indeed, abnormalities of liver test results are frequently noted postoperatively and may

reflect changes related to the surgery itself or the anesthetic agents used.¹⁹ Although hyperbilirubinemia is common, especially in cirrhotic patients (up to 20%), jaundice is infrequent (<1%), and its presence should prompt a thorough evaluation for the cause.^{20,21}

Although preexisting liver disease predisposes to postoperative morbidity, postoperative liver dysfunction may occur for various reasons in the patient with no known preexisting liver disease (Table 2). On the basis of the pattern of liver enzyme abnormalities, postoperative hepatic dysfunction may be separated into 3 groups: hepatocellular, cholestatic, and mixed. Hepatocellular dysfunction may be due to drugs, including anesthetic agents, ischemia, shock, iatrogenic injury, or viral hepatitis. Known causes of predominantly cholestatic dysfunction include sepsis, drugs, prolonged blood transfusions, biliary tract injury, total parenteral nutrition, cholelithiasis, or cholelithiasis. In the presence of a cholestatic pattern, an evaluation for extrahepatic biliary obstruction is warranted. Cholangiography may be necessary if there is a strong clinical suspicion of biliary obstruction, even if abnormalities are not noted on computed tomography or ultrasonography. However, postoperative jaundice is often multifactorial (Table 3), and identifying a precise cause is often difficult. Furthermore, postoperative liver disease may be a manifestation of unrecognized preoperative disease. Nevertheless, most cases of postoperative jaundice for which no obvious cause is identified (so-called benign postoperative jaundice) eventually resolve spontaneously, and thus only supportive management is needed. A predominantly unconjugated hyperbilirubinemia may reflect hemolysis (due to multiple transfusions or resolving hematomas); thus, the presence of reticulocytosis, decreased haptoglobin, or anemia should be sought.

SUMMARY

Optimal perioperative care of the patient with liver disease necessitates an understanding of basic hepatic pathophysiological perturbations. Multiple factors contribute to the increased mortality observed in patients with liver disease. The risks are greater with increased impairment of hepatic function. Clearly, a need exists for a more rigorous, current analysis and evaluation of risk factors in various liver conditions. Reduction of mortality in patients with liver disease undergoing surgery will depend on close attention to coagulation, intravascular volume, renal function, electrolyte levels, cardiovascular status, and nutrition.

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Table 3. Factors Contributing to Postoperative Jaundice

Reduction in hepatic blood flow (anesthetics)
Increased pigment load
Multiple blood transfusions
Resolving hematoma
Hypotension
Sepsis, endotoxemia

REFERENCES

1. Jackson FC, Christophersen EB, Peternel WW, Kirimli B. Preoperative management of patients with liver disease. *Surg Clin North Am.* 1968;48:907-930.
2. Schemel WH. Unexpected hepatic dysfunction found by multiple laboratory screening. *Anesth Analg.* 1976;55:810-812.
3. Kowalski HJ, Abelmann WH. The cardiac output at rest in Laennec's cirrhosis. *J Clin Invest.* 1953;32:1025-1033.
4. Gelman S, Fowler KC, Smith LR. Liver circulation and function during isoflurane and halothane anesthesia. *Anesthesiology.* 1984; 61:726-730.
5. Krowka MJ, Cortese DA. Pulmonary aspects of liver disease and liver transplantation. *Clin Chest Med.* 1989;10:593-616.
6. Runyon BA. Surgical procedures are well tolerated by patients with asymptomatic chronic hepatitis. *J Clin Gastroenterol.* 1986;8:542-544.
7. Zacks SL, Sandler RS, Rutledge R, Brown RS Jr. Liver disease markedly increases the risk of perioperative death in cholecystectomy patients [abstract]. *Hepatology.* 1997;26(program issue):179A.
8. Harville DD, Summerskill WHJ. Surgery in acute hepatitis: causes and effects. *JAMA.* 1963;184:257-261.
9. Hardy KJ, Hughes ESR. Laparotomy in viral hepatitis. *Med J Aust.* 1968;1:710-712.
10. Greenwood SM, Leffler CT, Minkowitz S. The increased mortality rate of open liver biopsy in alcoholic hepatitis. *Surg Gynecol Obstet.* 1972;134:600-604.
11. Powell-Jackson P, Greenway B, Williams R. Adverse effects of exploratory laparotomy in patients with unsuspected liver disease. *Br J Surg.* 1982;69:449-451.
12. Aranha GV, Sontag SJ, Greenlee HB. Cholecystectomy in cirrhotic patients: a formidable operation. *Am J Surg.* 1982;143:55-60.
13. Sirinek KR, Burk RR, Brown M, Levine BA. Improving survival in patients with cirrhosis undergoing major abdominal operations. *Arch Surg.* 1987;122:271-273.
14. Gill RA, Goodman MW, Golfus GR, Onstad GR, Bubrick MP. Aminopyrine breath test predicts surgical risk for patients with liver disease. *Ann Surg.* 1983;198:701-704.
15. Child CG III, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg.* 1964;1:1-85.
16. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg.* 1973;60:646-649.
17. Garrison RN, Cryer HM, Howard DA, Polk HC Jr. Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. *Ann Surg.* 1984;199:648-655.
18. DiCecco SR, Wieners EJ, Wiesner RH, Southorn PA, Plevak DJ, Krom RAF. Assessment of nutritional status of patients with end-stage liver disease undergoing liver transplantation. *Mayo Clin Proc.* 1989;64:95-102.
19. Boyer TD. Preoperative and postoperative hepatic dysfunction. In: Zakim D, Boyer TD, eds. *Hepatology: A Textbook of Liver Disease.* Vol 2. 3rd ed. Philadelphia, Pa: WB Saunders Co; 1996:1912-1917.
20. Evans C, Evans M, Pollock AV. The incidence and causes of postoperative jaundice: a prospective study. *Br J Anaesth.* 1974; 46:520-525.
21. Clarke RS, Doggart JR, Lavery T. Changes in liver function after different types of surgery. *Br J Anaesth.* 1976;48:119-128.

