REVIEW

CME CREDIT

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Assessing the risk of surgery in patients with liver disease

ABSTRACT

Recent studies have defined objective criteria for determining whether surgery is safe for patients with liver disease. Using these criteria, we may extend the benefit of surgery to more patients with liver disease without increasing the risk.

KEY POINTS

Patients with liver disease are at higher risk of death and hepatic decompensation if they undergo surgery than people without liver disease.

Liver disease is often undiagnosed before surgery unless it is specifically looked for.

Liver disease does not exclude surgery; certain types of surgery can be undertaken safely if patients are chosen carefully.

A recent study has suggested a Child-Pugh score of 8 and a Model for End-Stage Liver Disease (MELD) score of 14 as the cutoff values above which surgery poses too much risk for patients with cirrhosis.

Surgery is usually not advisable in patients with acute hepatitis, but it appears safe in mild chronic hepatitis.

BECAUSE LIVER DISEASE is common, many patients undergoing surgery have it. Patients with liver disease face a higher risk of surgical complications, including death from surgery and anesthesia, but the level of risk is hard to assess because all liver disease is not the same, and neither is all surgery.

Uncertainty has led some physicians to be reluctant to send any patient with liver disease to surgery, and others to take unjustified risks. Although risk assessment has often been based on anecdote, a number of studies can provide guidance in this respect. The goal is to avoid surgery in patients at high risk without denying the benefits of surgery to those at reasonable risk.

This review provides the clinician an up-to-date guide to risk assessment for anesthesia and surgery in patients with liver disease.

TWO CLINICAL SCORES FOR ASSESSING LIVER DISEASE

Nearly all candidates for surgery receive a panel of blood tests that includes markers of liver disease such as the serum concentrations of bilirubin, aminotransferases, alkaline phosphatase, and albumin. We have reviewed in detail how to interpret these values, singly and in clusters, in another article.[1]

Although these individual variables (and others, such as a low platelet count and variceal bleeding) are still valid and important, composite measures have been developed specifically to predict whether patients with advanced liver disease will survive surgery. Two scoring systems are in widespread use; the internist should be familiar with both of them as a means of stratifying risk for surgery.

TABLE 1

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The Child-Pugh and MELD scores are useful in stratifying the risk of surgery

The Child-Pugh score

The grandfather of composite scores,[2] the Child-Pugh score was originally designed to estimate the chances of survival after portosystemic shunt surgery, but over the years it also proved useful in patients with cirrhosis, and until recently it was used to prioritize patients for liver transplantation.

The Child-Pugh score is based on two clinical and three laboratory variables—ascites, hepatic encephalopathy, the serum bilirubin concentration, the serum albumin concentration, and the international normalized ratio (INR). Points are assigned for each of these (the more points the worse), and the total is ranked in three classes: A (best), B (intermediate), and C (worst) (TABLE 1).

The Model for End-Stage Liver Disease (MELD) score

The Model for End-Stage Liver Disease (MELD) scoring system was developed from univariate and multivariate analyses of clinical and laboratory variables. Originally designed to predict survival after placement of a transjugular intrahepatic portosystemic shunt to control bleeding varices,[3] the MELD score has also been shown to predict short-term survival in patients with cirrhosis more reliably than the Child-Pugh system. Accordingly, it has now been adopted for prioritizing patients for liver transplantation.

The MELD score is calculated from the serum concentrations of bilirubin and creati-

TABLE 2

Reported surgery risk in patients with liver disease

LIVER DISEASE	TYPE OF SURGERY	MORTALITY	PROGNOSTIC FACTORS
Cirrhosis	Nonlaparoscopic biliary surgery	20%[4]	Ascites, prothrombin time, albumin
	Peptic ulcer surgery	54%[5]	Prothrombin time, systolic blood pressure, hemoglobin
	Umbilical herniorrhaphy	13%[6]	Urgent surgery
	Colectomy	24%[7]	Hepatic encephalopathy, ascites, albumin, hemoglobin
	Abdominal surgery for trauma	47%[8]	
	Emergency abdominal surgery	57%[10]	Child-Pugh class, urgent surgery
	Laparoscopic cholecystectomy	0.9%[14], 6%[15]	
	Emergency cardiac surgery	80%[16]	Child-Pugh class
	Elective cardiac surgery	3%–46%[18]	Child-Pugh score
	Knee replacement	0%[19]	
	Transurethral resection of the prostate	6.7%[20]	
Chronic hepatitis	Various types	0%[21]	
Hepatitis C	Laparoscopic cholecystectomy	0%[22]	
Acute hepatitis	Exploratory laparotomy	100%[23]	
Obstructive jaundice	Abdominal surgery	5%–60%[24]	Hemoglobin, bilirubin, malignancy

ADAPTED FROM RIZVON MK, CHOU CL. SURGERY IN THE PATIENT WITH LIVER DISEASE. MED CLIN NORTH AM 2003; 87:211–227.

nine and the INR. The formula is rather complicated (TABLE 1), but calculators are available online (**www.unos.org/resources/meldPeldCalculator.asp**) and in software such as Epocrates for personal digital assistant devices.

RISK OF SURGERY IN CIRRHOSIS

Abdominal surgery. Most of the data on the risk of surgery in patients with cirrhosis come from studies of abdominal surgery (TABLE 2). The risk appears to be much higher with "open" abdominal surgery than with laparoscopic surgery. Reported mortality rates range from 20% to 54% for various types of open abdominal surgery,[4–9] and multiple factors have been found to be associated with mortality. Emergent surgery has a worse prognosis, with mortality rates around 50%.[10]

Although the data vary considerably because not all cirrhosis is the same, most of the studies found that the mortality rate was higher in patients with one or more of the following: elevated bilirubin, prolonged prothrombin time, ascites, decreased albumin, encephalopathy, portal hypertension, and emergent surgery. The first five of these factors are the components of the Child-Pugh score, and the Child-Pugh class was useful in stratifying the risk of death: patients in class A (5 or 6 points) had mortality rates of about 10%, those in class B (7–9 points) had mortality rates of around 30%, and those in class C (> 9 points) had mortality rates above 70% in two studies.[10,11] The Child-

Pugh score, therefore, emerged as a broadly accepted criterion for predicting the risk posed by abdominal surgery in patients with cirrhosis.

The MELD score was also evaluated for predicting survival after nontransplant surgery in patients with cirrhosis in a recent large retrospective analysis,[12] published as yet only in abstract form. The investigators did not offer any cutoff MELD score for avoiding surgery, but in patients with MELD scores lower than 10, the survival rate was 99% at 7 days, 96% at 30 days, and 92% at 90 days—numbers that were deemed acceptable. Survival rates were significantly lower with MELD scores of 10 or more.

Another recent retrospective analysis[13] suggested that a MELD score of 14 or more and a hemoglobin concentration of less than 10 g/dL predicts a poor outcome of abdominal surgery in patients with cirrhosis.

Laparoscopic cholecystectomy carries a low mortality rate. No deaths were reported in several series of cirrhotic patients undergoing laparoscopic cholecystectomy. Yeh et al,[14] in one of the largest retrospective analyses, reported that, out of 226 patients with cirrhosis (Child-Pugh class A or B) who underwent laparoscopic cholecystectomy, only two died—0.88%. Though low, this figure was still significantly higher than in noncirrhotic controls (0.01%).

In a recent study of patients undergoing laparoscopic cholecystectomy, 2 (6%) of 33 patients with cirrhosis had died at 90 days, compared with none of 31 matched controls. The rate of morbidity was 33% vs 17%.[15] The study also found that a preoperative MELD score of 8 or more had 91% sensitivity and 77% specificity in predicting 90-day morbidity and suggested this as the cutoff mark for clearing patients with cirrhosis for laparoscopic cholecystectomy.

Cardiac surgery. Data on cardiac surgery in patients with cirrhosis are meager. In small retrospective studies, the results were good in patients in Child-Pugh class A, but more than 50% of patients in class B died.[16,17] The largest reported series (also retrospective) of patients with cirrhosis undergoing open heart surgery consisted of 44 patients from the Cleveland Clinic over a 10-year period. The mortality rate was 3% in patients in Child-Pugh class A and 46% in class B or C.[18] Hepatic decompensation (development of ascites, encephalopathy, or variceal hemorrhage) occurred in 9.6% of the patients in class A and 69% in class B. A Child-Pugh score greater than 7 and a MELD score greater than 13 were suggested as the cutoff points for avoiding surgery. These scoring systems were similar in their ability to predict short-term hepatic decompensation, but Child-Pugh scores higher than 7 had a somewhat higher positive predictive value for mortality: 67% vs 56%, with a larger area under the receiver operating characteristic curve.

Other types of surgery have few reports to document their outcomes in patients with cirrhosis. A recent analysis of total knee arthroplasty found that the rate of complications (local as well as systemic, including but not limited to hepatic decompensation) was significantly higher, at 44% in patients with cirrhosis vs 6% in a control group.[19] Previous hepatic decompensation and variceal bleeding were found to be independent predictors of complications. Accordingly, it was concluded that only Child-Pugh class A patients could undergo such surgery safely.

In a series of men undergoing transurethral prostatectomy, the mortality rate was 6.7%.[20]

Surgical mortality in cirrhotic patients in 2 studies, by Child-Pugh class:
Class A 10%
Class B 30%
Class C > 70%

RISK OF SURGERY IN HEPATITIS

In chronic hepatitis, the risk of surgery has not been reported widely. Runyon[21] reported that surgery was safely performed in 20 such patients. Similarly, there were no deaths or complications reported in patients with chronic hepatitis C undergoing laparoscopic cholecystectomy.[22] It appears reasonable to believe that surgery is safe for patients with mild chronic hepatitis.

In acute hepatitis, most of the reports are old, from the time when laparotomy was done to differentiate between medical and surgical causes of jaundice, and mortality rates of up to 100% were reported in acute viral as well as acute alcoholic hepatitis.[23] Unless it is a life-saving measure, surgery should not be considered in acute hepatitis of any cause.

RISK OF SURGERY IN OBSTRUCTIVE JAUNDICE

In a retrospective analysis of 373 patients with obstructive jaundice,[24] risk factors for perioperative death included a low hematocrit (< 30%), an elevated serum bilirubin (> 11 mg/dL), and a malignant cause of biliary obstruction. The mortality rate was 60% when all three were present vs only 5% when none were present.

There is some evidence that postoperative renal failure may occur in those with very high serum bilirubin levels. The mechanism is unclear.

Hypoalbuminemia, azotemia, and cholangitis are also thought to increase the risk of death. None of these necessarily indicates the severity of parenchymal liver disease; they may reflect only the degree of biliary obstruction and the duration of illness. However, long-standing biliary obstruction can lead to biliary cirrhosis, which may then influence the outcome of surgery irrespective of these factors. The mortality rate in patients with secondary biliary cirrhosis was 13% within 30 days of surgery.[9] Given that obstructive jaundice is a collective term encompassing a variety of conditions, the perioperative mortality rate varies significantly.

Obstructive jaundice can be treated without surgery in most cases

Modern management of obstructive jaundice obviates the need for direct surgical intervention in most cases. The bile duct can usually be unblocked by endoscopic placement of internal stents or by radiographic placement of external stents or drains. Lactulose and ursodeoxycholic acid (to reduce endotoxemia) and antibiotics (to treat infection) have been shown to reduce perioperative mortality in patients with benign conditions such as choledocholithiasis and cholangitis, but not in malignant biliary obstruction.[25]

RISK IN RESECTION OF HEPATOMA

A special group are patients with cirrhosis undergoing hepatic resection, most commonly for hepatocellular carcinoma. Now that the MELD scoring system has been adopted and patients with high scores are being carefully monitored for hepatocellular carcinoma, this disease is being detected earlier and is being treated by liver transplantation.

Many factors that predict a better prognosis after liver resection have been identified: eg, Child-Pugh class A; smaller unifocal lesions (< 5 cm); recent surgery (after 1996); lack of active hepatitis or portal hypertension; normal bilirubin, aminotransferase, and lactate levels; low indocyanine green retention at 15 minutes (reflecting normal hepatic blood flow); a normal hippurate ratio; and larger residual liver volume after surgery.[26] The 30-day mortality rate after hepatoma resection ranges from 3% to 8%.[27,28] In a recent analysis of 82 patients, those with a MELD score of 9 or greater had a 30-day mortality rate of 29%, compared with 0% in those with a MELD score of 8 or less.[29]

ANESTHETIC CONSIDERATIONS

The risk of surgery cannot be separated from the risk of anesthesia.

Anesthesia can affect the liver by reducing its blood flow. In healthy volunteers, hepatic blood flow decreased by 35% to 42% in the first 30 minutes of induction of anesthesia.[30] Studies in animals have shown that under conditions of stress, hepatic blood flow increases to compensate for reduced portal blood flow.[31] Patients with liver disease, especially cirrhosis, cannot compensate for the reduced portal blood flow, which may cause hepatic dysfunction.[32]

The anesthetic agents halothane and enflurane reduce hepatic arterial blood flow. These effects are minimal with isoflurane, which consequently has become the choice in patients with liver disease.[33] In addition, isoflurane, desflurane, and sevoflurane undergo less hepatic metabolism: 0.2% for isoflurane, 2% to 4% for enflurane, and 20% for halothane.[34] Presumably, this leads to a lesser incidence of drug-induced hepatitis.

In addition, anesthetic agents, sedatives, and skeletal muscle relaxants can all have toxic adverse effects. The actions of neuromuscular blocking agents may be prolonged in patients with liver disease because of reduced pseudocholinesterase activity, decreased biliary excretion, and larger volume of distribution. Atracurium is not metabolized in the liver, so it has been recommended.[31]

Of the various narcotics and sedatives used in conjunction with anesthetics, fentanyl/sufentanil and oxazepam/lorazepam are recommended, as their actions are less likely to be prolonged in patients with liver disease.[35] In cardiac surgery in patients with cirrhosis, however, we found no association between the use of enflurane, isoflurane, fentanyl, sufentanil, midazolam, or morphine and hepatic decompensation or mortality.[18]

The type of anesthetic management—general anesthesia, regional anesthesia, or monitored anesthesia care—did not affect mortality in one of the largest reported series (733 patients).[9]

CONCLUSIONS

- Liver disease can be clinically silent. A high degree of suspicion is needed during the preoperative evaluation, and a detailed workup may be needed in patients with risk factors for liver disease, such as alcoholism, obesity, diabetes mellitus, drug abuse, blood transfusion, sexual promiscuity, or family history of liver disease. The presence of any abnormal liver test or otherwise unexplained reductions in hemoglobin, white blood cell count, or especially platelet count, should alert the clinician to the possibility of cirrhosis.
- In acute hepatitis, surgery appears unwise, especially if the acute liver disease is severe enough to cause jaundice. Surgery in noncirrhotic chronic liver disease appears relatively safe.
- Patients with cirrhosis whose Child-Pugh scores are less than 8 appear to be reasonable candidates for most types of surgery, including cardiothoracic surgery. In the MELD scoring system, the suggested cutoff value appears to be 14, though some studies suggest that lower values should be used.
- Biliary obstruction can usually be relieved without surgery, allowing the hepatic function to improve prior to needed surgery later.
- Emergency surgery carries higher risk in general, but it may not be avoidable in life-threatening situations (eg, dissecting aneurysm or bowel perforation).

Liver disease can be clinically silent

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