Underlying liver disease has effects on the risk of morbidity and mortality after surgery. The magnitude of the risk depends on several factors, including the etiology and severity of liver disease, the surgical procedure, and the type of anesthesia used. In patients with cirrhosis, nontransplant surgery can lead to worsening of underlying liver disease or even liver failure. The reasons for this are unclear but may reflect circulatory changes brought on by surgery or anesthesia, resulting in impaired hepatic vascular flow.

The number of patients with advanced liver disease is on the increase, and so the number of patients with liver disease who will require surgery will likely increase. It is not uncommon for patients with liver disease to undergo surgical interventions other than liver transplant. Up to 10% of patients with advanced liver disease require a surgical procedure in the final 2 years of their life.1

Identification of the surgical risk is important in every patient; however, the risk assessment in patients with liver disease is imperative and can be lifesaving. Gastroenterologists and hepatologists are frequently asked to evaluate patients with liver disease and determine their risk of undergoing surgical procedures and to help make recommendations that may optimize outcomes.

PREOPERATIVE SCREENING FOR LIVER DISEASE

The primary goal of preoperative screening is to determine the presence of preexisting liver disease using the least invasive means possible.

The value of a thorough history and physical examination cannot be overestimated. It is crucial in providing clues as to whether a patient has liver disease or is at an increased risk of having liver disease. All patients should be questioned regarding prior...
remote blood transfusions, tattoos, illicit drug use, alcohol intake, sexual history, personal history of jaundice, and family history of liver disease. A complete review of medications, including over-the-counter analgesics and complementary or alternative medications should also be sought. Complaints of excessive fatigue, pruritus, and easy bruisability may be indicators of underlying liver dysfunction. Physical examination can identify signs that are consistent with chronic underlying liver disease, such as the presence of jaundice, palmar erythema, spider telangiectasia, parotid gland enlargement, Dupuytren contracture, hepatosplenomegaly, ascites, dilated abdominal veins, lower extremity edema, gynecomastia, testicular atrophy, temporal wasting, or loss of muscle mass.

Patients who are deemed healthy without clinical suspicion for underlying liver disease generally do not require laboratory testing of liver function. A study from 1976, in which 7620 subjects undergoing elective surgery were screened with blood work, revealed that only 11 had abnormal liver tests. Although this study preceded the current epidemics in viral hepatitis and fatty liver disease, it supports the notion that routine screening without clinical suspicion of underlying liver disease is of low yield and would likely not improve outcomes.

If the liver function tests are found to be abnormal, then it is prudent to defer elective surgery until a more thorough investigation can be performed to determine the nature, chronicity, and severity of the biochemical abnormalities. For those patients who are asymptomatic with only mild elevations in aminotransferases and normal total bilirubin concentration, cancellation of surgery is rarely required. If, however, patients are found to have elevated aminotransferase levels greater than 3 times the upper limits of normal or abnormalities in parameters of synthetic function (namely bilirubin and prothrombin time), further investigation is warranted. The incidence of underlying cirrhosis in patients with abnormal liver function tests has been reported to be anywhere from 6% to 34%. Further investigation in this subgroup of patients should proceed along standard pathways for the workup of chronic liver disease. Investigations should include viral hepatitis serology for hepatitis B and C, specific tests for metabolic liver disease, such as iron studies for hemochromatosis, ceruloplasmin level for Wilson disease, α1-antitrypsin level and phenotyping, serum markers for autoimmune liver disease, and imaging, such as a right upper quadrant ultrasound with Doppler to evaluate the hepatic parenchyma, biliary system, and flow within the portal venous vasculature, and CT or MRI scan for evidence of cirrhosis or portal hypertension (Fig. 1).

Once it has been determined that a patient has liver disease, the next step is estimating the risk of surgery. Patients with liver disease are at a greater risk for surgical and anesthetic complications than those without liver disease. The degree of risk associated with the surgery and postoperative outcomes is largely dependent on 3 factors: the etiology and severity of the liver disease, the specific surgery planned, and the type of anesthesia (Fig. 2).

NATURE OF THE UNDERLYING LIVER DISEASE

Because of the high perioperative morbidity and mortality, acute hepatitis is regarded as a contraindication to elective surgery (Box 1). This recommendation is largely based upon older literature, in which patients with icteric hepatitis had a 10% to 13% mortality following laparotomy. The increased risk is likely the result of acute hepatocellular injury, inflammation, and associated hepatic dysfunction. If the degree of liver injury is severe, consideration should be given to delay even urgent surgery. Most cases of acute hepatitis are self-limited and so surgery should be postponed

Malik & Ahmad
until the patient’s clinical, biochemical, and histological parameters return to normal. Improvement in the underlying condition, whether it is viral, toxic, drug induced, thrombotic, or hypoxic, will likely reduce postoperative risk.

The specific case of acute alcoholic hepatitis deserves special mention. The presentation of acute alcoholic hepatitis (jaundice, right upper quadrant pain, elevated liver function tests, and leukocytosis) can many times mimic an acute biliary process, and lead to misdiagnosis and subsequent “therapeutic misadventures,” namely, cholecystectomy or endoscopic retrograde cholangiopancreatography, with devastating postoperative results. All elective surgeries should be delayed in patients with acute alcoholic hepatitis until clinical and laboratory parameters return to normal.

Patients with mild chronic hepatitis without evidence of portal hypertension and well-preserved hepatic function generally tolerate surgery well. However, when the disease is considered active, evidenced by clinical, biochemical, and histological measures, surgical risk increases. When a patient with chronic hepatitis has evidence of clinical decompensation (impaired hepatic synthesis, altered excretion, portal hypertension), the perioperative risk is higher. It is unclear whether interventions aimed at improving active disease in these patients will help to improve outcomes after surgery.

Patients with well-compensated cirrhosis, but significant portal hypertension, may still be at increased risk of postoperative decompensation, particularly if the surgery involves the liver, such as resection of a tumor. Limited data suggest that correction of the portal pressure by transjugular intrahepatic portosystemic shunt (TIPS) may reduce this risk in patients undergoing abdominal surgery.

With the epidemic rise in the metabolic syndrome, more patients are presenting for surgery with nonalcoholic fatty liver disease (NAFLD). In one study, which included patients with alcoholic and nonalcoholic steatohepatitis with moderate steatosis

![Algorithm for preoperative assessment in patients with suspected liver disease.](image-url)
(defined by >30% fat on liver biopsy) undergoing major hepatic resection, there was a trend towards increased morbidity and mortality following major hepatic resection. These patients tended to be obese (mean body mass index >30 kg/m²) with elevated total bilirubin levels (mean 2.2 mg/dL), indicating a degree of hepatic dysfunction. How much the steatosis alone contributed to the increased risk is unclear.

NAFLD is a common finding in patients undergoing bariatric surgery and typically improves after significant weight loss. Occasionally cirrhosis is found at the time of surgery, and increased perioperative mortality has been observed in this situation, leading some surgeons to abort gastric bypass if frank cirrhosis is noted.

**Box 1**

**High-risk patients with liver disease for any type of surgery**

- Child’s C
- MELD score greater than 15
- Acute liver failure
- Acute alcoholic hepatitis
- High serum bilirubin (>11 mg/dL)

**Fig. 2.** Algorithm for preoperative assessment in patients with known liver disease.
Obstructive jaundice has been shown to markedly increase perioperative mortality. Studies have suggested that patients with obstructive jaundice and risk factors including total bilirubin level greater than 11 mg/dL, presence of malignancy, serum creatinine 1.4 mg/dL or more, blood urea nitrogen concentration greater than 10 mg/dL, albumin concentration less than 3 g/dL, initial hematocrit less than 30%, aspartate aminotransferase greater than 90 IU/L, and age more than 65 years, portend worse outcome following surgery. Efforts to improve the jaundice either with endoscopic or percutaneous biliary drainage do not appear to improve mortality. This suggests that severe underlying disease (cirrhosis or malignancy) is present in most patients, and relieving the jaundice does not change the natural history of the disease process.

**CIRRHOSIS AND PREDICTIVE MODELS**

Of patients with liver disease, the outcomes of those with cirrhosis have been studied most extensively. Once a patient has developed cirrhosis, grading the severity of the liver disease is of crucial importance in determining their perioperative risk.

Two scoring systems, the Model for End-Stage Liver Disease (MELD) (Box 2) and the Child-Turcotte-Pugh (CTP) classification (Table 1) have been adapted and evaluated to help clinicians determine perioperative morbidity and mortality in patients with cirrhosis undergoing surgical procedures.

The CTP was originally formulated by Child and Turcotte in 1964 to help predict mortality following portocaval shunt surgery. This was modified a decade later by Pugh and colleagues, who replaced nutritional status with prothrombin time and devised a scoring system for patients undergoing esophageal transections for bleeding varices.

The CTP score was the first-used predictor of surgical risk in patients with liver disease. Although the scoring system has never been prospectively validated, it is regarded to be an accurate predictor and is still widely used today to predict perioperative morbidity and mortality for elective and emergency surgeries in patients with cirrhosis.

The commonly quoted percentages linking perioperative mortality and CTP class are based largely upon two retrospective studies of patients with cirrhosis. Garrison and colleagues studied 100 patients with cirrhosis who underwent abdominal surgery. Thirty patients died and major complications occurred in another 30 patients. Fifty-two variables were analyzed and in multivariate analysis, the CTP classification was the best predictor of morbidity and mortality with CTP class A, B, and C.
corresponding to postoperative mortality of 10%, 31%, and 76% (Table 2). In another study involving 92 cirrhotic patients, Mansour and colleagues commented that the most accurate predictor of outcomes in patients with cirrhosis was Child’s class with mortality percentages nearly identical to those quoted by Garrison and colleagues with CTP A, B, and C corresponding to 10%, 30%, and 82%. In a larger review, spanning nearly 10 years, it was determined that cirrhotic patients undergoing any surgical procedure under anesthesia had perioperative mortality rates of 11.6% and complication rates of 30.1%. Mortality and complication rates correlated directly with the Child score.

One of the drawbacks of the CTP classification is its partly subjective nature. Parameters such as grades of encephalopathy and degree of ascites are left to the discrepancy of the clinician. The need for a more accurate model to assess patients with liver disease was highlighted by Malinchoc and colleagues to predict outcome following TIPS. In this landmark study, the investigators formulated the MELD scoring system to help predict short-term mortality in patients with cirrhosis undergoing TIPS. The MELD score incorporates three biochemical measurements into a complex logarithmic formula—the total bilirubin concentration, serum creatinine, and the international normalized ratio (INR). Patient scores range from 6 to 40, with 6 reflecting “early” disease and 40 “severe” disease. In 2002, the MELD score was adopted by the United Network for Organ Sharing as a means of more fairly allocating donor organs to ensure priority to the “sickest” recipients.

<table>
<thead>
<tr>
<th>Clinical Trait</th>
<th>1 Point</th>
<th>2 Points</th>
<th>3 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Present</td>
<td>Moderate/severe</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1–2</td>
<td>Grade 3–4</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt;2</td>
<td>2–3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt;3.5</td>
<td>2.8–3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7–2.3</td>
<td>&gt;2.3</td>
</tr>
</tbody>
</table>

The CTP score uses 5 variables and assigns point values according to severity. The composite score is between 5 (well compensated disease) and 15 (severe decompensation).

Child’s A 5–6 points.
Child’s B 7–9 points.
Child’s C 10–15 points.

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>CTP/MELD Score</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal</td>
<td>A</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>30–31</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>76–82</td>
</tr>
<tr>
<td>Cardiac</td>
<td>A</td>
<td>0–11</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>18–50</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>67–100</td>
</tr>
<tr>
<td>Abdominal/cardiac/orthopedic</td>
<td>&lt;8</td>
<td>5.7</td>
</tr>
<tr>
<td>(30-d mortality)</td>
<td>&gt;20</td>
<td>&gt;50</td>
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</table>
The MELD score has been validated in a number of prospective studies as a prognostic score in determining mortality in patients with cirrhosis, acute variceal bleeding, acute alcoholic hepatitis, and acute liver failure.\(^{31-36}\) The MELD score has also been examined as a prognostic tool in determining mortality following surgery.

One of the first studies to evaluate MELD score and postoperative outcomes involved 33 patients with cirrhosis undergoing laparoscopic cholecystectomy.\(^{37}\) Two patients died in the study group versus none in noncirrhotic controls. The authors concluded that a MELD score of 8 or more identified patients at risk for postoperative morbidity following cholecystectomy. Several studies have since evaluated the usefulness of the MELD score in predicting perioperative morbidity and mortality.\(^{38-41}\) These studies involved elective and emergent surgeries including abdominal, cardiac, and hepatic resection and orthopedic procedures. The type of surgery performed plays a large role in determining outcome, and so it is difficult to apply such studies to individual patients. A recent large study of almost 800 cirrhotic patients undergoing major digestive, orthopedic, or cardiac surgery demonstrated that the MELD score correlated with short-term and long-term mortality extending out to 20 years. For each point increase in the MELD score above 8, there was a 14% increase in 30- and 90-day mortality.\(^{42}\) Overall, the MELD score correlates well with postoperative mortality and in some cases is superior to CTP class.

It has been recommended that patients with MELD scores below 10 can undergo elective surgery, whereas caution needs to be taken for patients with MELD scores between 10 and 15. For patients with MELD scores above 15, elective surgery should be avoided. It is most prudent in this group of patients to consider evaluation for liver transplant listing, in case the patient should decompensate post procedure.\(^{43}\)

**TYPE OF SURGERY**

Studies have shown that patients with cirrhosis who undergo any type of emergency surgery (especially abdominal) have a higher mortality than patients with normal liver function (Box 3).

Emergency surgeries obviously do not permit for delays in the decision to intervene. Emergent surgeries, as the name implies, are life-threatening and many times must be undertaken irrespective of the patient’s comorbidities. Patients with cirrhosis who require emergent surgical procedures have extremely high mortality rates. One study in which 14 patients with cirrhosis underwent emergent surgical procedures under general anesthesia showed a 1- and 3-month mortality of 19% and 44%, respectively.

<table>
<thead>
<tr>
<th>Box 3</th>
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<tbody>
<tr>
<td><strong>High-risk surgery in patients with liver disease</strong></td>
</tr>
<tr>
<td>Abdominal surgery</td>
</tr>
<tr>
<td>Cholecystectomy</td>
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<tr>
<td>Colectomy</td>
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<tr>
<td>Gastric surgery</td>
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<tr>
<td>Liver resection</td>
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<tr>
<td>Cardiac surgery</td>
</tr>
<tr>
<td>Emergent surgery (any type)</td>
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<tr>
<td>Surgery with high anticipated blood loss</td>
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which was significantly higher than that in cirrhotic patients undergoing elective surgical procedures.39

Abdominal surgical procedures, including cholecystectomy, gastric bypass, biliary procedures, ulcer surgery, and colonic resection, result in an increased morbidity and mortality in patients with cirrhosis. In a 2007 study by Teh and colleagues,42 586 cirrhotic patients underwent major digestive system surgery including esophageal, gastric, intestinal, hepatic, and splenic procedures. The type of procedure did not affect the outcome, but older age and higher MELD score predicted an increased risk of short-term and long-term mortality, with a median survival of almost 5 years for a MELD score of less than 8, but only 14-day median survival if the MELD score was greater than 26.

Three small studies15,44,45 have evaluated the role of preoperative TIPS insertion in patients with cirrhosis and portal hypertension undergoing extrahepatic abdominal operations. Although the premise of reducing portal hypertension before a major abdominal operation makes sense, the results were mixed, and so no recommendations can be made in support of preoperative TIPS placement.

Cardiac surgery involving cardiopulmonary bypass also carries an increased perioperative risk in patients with cirrhosis. One of the largest studies reviewed 44 cirrhotic patients undergoing either cardiac bypass grafting, valve replacement, or pericardectomy.38 Twelve patients developed hepatic decompensation and 7 patients died. The authors concluded that cardiac surgery could be conducted safely if the CTP score was 7 or less. Two additional studies46,47 confirmed the results of the aforementioned study and support the findings that Child’s class is an accurate predictor of hepatic decompensation and mortality following cardiac surgery. Mortality tends to be related to gastrointestinal complications, hemorrhage, and sepsis, as opposed to cardiac failure. Thus, whenever possible, major cardiac operations should be avoided in patients with cirrhosis and the least invasive means of treating coronary disease should be sought.48

Patients sustaining trauma who are found to have cirrhosis at the time of laparotomy are at an increased risk of morbidity and mortality following surgery. In one study, 40 cirrhotic patients undergoing laparotomy following trauma had a significantly higher mortality of 45% versus 24% in matched noncirrhotic controls. The increased morbidity and mortality was even true in cirrhotic patients who suffered minor trauma.49

Surgical resection in patients with liver disease raises concerns about the adequacy of residual hepatic mass in patients who have compromised function to begin with. Most patients with hepatocellular carcinoma have significant underlying liver disease, and so it is not surprising therefore that such patients have high rates of postsurgical complications, hepatic decompensation, and death.50 Although cirrhosis is no longer considered a contraindication to hepatic resection, morbidity and mortality are still substantial, with mortality rates quoted as high as 16% and morbidity as high as 60%.51–57 The improvement in outcomes over the years is likely multifactorial, related to better patient selection, improved intra- and postoperative monitoring, and advancements in surgical techniques.58,59

**ANESTHESIA**

Liver disease can significantly impair the metabolism of anesthetics and certain medications used during surgery. Hepatic dysfunction can affect the distribution, metabolism, and excretion of drugs. Caution must be taken in deciding which drugs to use.
The clinician should also be mindful of the class of drugs, drug doses, and scheduling when confronting postoperative decompensation.

Of the volatile anesthetics, isoflurane is generally recommended as it undergoes the least amount of hepatic metabolism and does not affect hepatic blood flow.60 Halothane, in contrast, undergoes significant hepatic metabolism and reduces hepatic blood flow. Halothane is a known culprit of severe hepatic injury and has been reported to be the cause of acute liver failure.61,62 The incidence of acute liver failure is approximately 1 case in 6,000 to 35,000 patients after exposure.63 This concern has all but eliminated the use of halothane in the United States.

Hepatic dysfunction can result in a longer half-life of many drugs as a result of impairment of the cytochrome P450 enzymes. The perioperative use of certain narcotic opioids, such as morphine and oxycodone, should be avoided in patients with cirrhosis or significant hepatic impairment. The bioavailability of such drugs is markedly increased and their half-life prolonged.64 Fentanyl, however, does not seem to be affected by hepatic dysfunction.65

The metabolism of certain benzodiazepines such as diazepam and midazolam may be slowed in patients with cirrhosis and impaired liver function. Because of their ability to undergo conjugation without hepatic metabolism, benzodiazepines such as oxazepam and temazepam are not affected.66–68 The increased duration of action of benzodiazepines and narcotics in patients with cirrhosis and liver dysfunction can lead to prolonged depression of the central nervous system and may act as precipitants of hepatic encephalopathy.

Anesthesia can lead to changes in blood flow to the liver that can occur with general or regional anesthesia, meaning the risk of decompensation after surgery is not reduced even if local or spinal anesthesia is used.60,69 Advanced liver disease is typically associated with systemic and splanchnic vasodilation that leads to activation of the sympathetic nervous system in an attempt to maintain arterial perfusion.70 The normal cardiac inotropic and chronotropic response to stress may be decreased in cirrhotic patients,71 and the combination of a hyperdynamic circulation without compensatory mechanisms can lead to hepatic hypoperfusion during surgery. This can be exacerbated by the type of surgery (particularly laparotomy or cardiac surgery), hemorrhage, vasoactive medications, and even patient positioning.72

SUMMARY

Preexisting liver disease can lead to significant mortality after surgery. The severity of liver disease measured by the CTP score and the MELD score are relatively accurate predictors of outcome after surgery but are influenced by the type of surgery and the urgency. The algorithms shown in Figs. 1 and 2 summarize our recommendations using the available literature. In general, Child’s class A or MELD score less than 10 are at low risk for death after elective surgery; Child’s B or MELD 10 to 15 are at moderate risk, and surgery should be considered depending on the indication and urgency; Child’s C or MELD greater than 15 are at high risk, and surgery should be avoided or deferred until the clinical situation changes.

REFERENCES


