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Assessing surgical risk in patients with liver disease

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Literature review current through: **Sep 2023.** This topic last updated: **Dec 06, 2022.**

INTRODUCTION

Patients with liver disease who require surgery are at greater risk for surgical and anesthesiarelated complications than those with a healthy liver [1-7]. The magnitude of the risk depends upon the type of liver disease and its severity, the surgical procedure, and the type of anesthesia [6].

The assessment of surgical risk in patients with liver disease will be reviewed here. Patients with liver disease may have concomitant disorders (such as cardiovascular disease) that influence surgical outcomes; these issues are discussed separately. (See "Preoperative medical evaluation of the healthy adult patient" and "Evaluation of cardiac risk prior to noncardiac surgery".)

SCREENING FOR LIVER DISEASE BEFORE SURGERY

Patients undergoing surgery should undergo a history and physical examination to exclude findings of or risk factors for liver disease. This may include asking about prior blood transfusions, tattoos, illicit drug use, history of multiple sex partners and/or sexually transmitted infections, a family history of jaundice or liver disease, a history of jaundice or fever following anesthesia, alcohol use (current, prior and quantity), and a review of current medications. Clinical features suggestive of liver disease (such as fatigue, pruritus, increased abdominal girth, jaundice, palmar erythema, spider telangiectasias, splenomegaly, and gynecomastia and testicular atrophy in males) should be evaluated. We do not routinely check a liver biochemical profile in healthy individuals because most patients found to have abnormal liver biochemical tests do not have advanced liver disease. (See "Preoperative medical evaluation of the healthy adult patient".)

However, emerging data suggest that biochemical markers of liver fibrosis may be associated with risk of surgical mortality [8-10]. In a cohort study including 19,861 individuals without known liver disease who had preoperative laboratory testing, 1995 patients (10 percent) had a FIB-4 score \geq 2.67, which was defined as the threshold for advanced fibrosis [8]. Compared with FIB-4 score <2.67, a FIB-4 score \geq 2.67 was associated with increased risk of intraoperative mortality (odds ratio [OR] 3.63, 95% CI 1.25-10.58), mortality during hospitalization (OR 3.14, 95% CI 2.37-4.16), and 30-day mortality (OR 2.46, 95% CI 1.95-3.10). While biochemical markers of liver disease may have a future role for assessing surgical risk, additional studies are needed to confirm these findings.

The FIB-4 score (also referred to as the FIB-4 index) consists of age, aminotransferase levels, and platelet count, and use of FIB-4 and other serologic markers is discussed in more detail separately. (See "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations", section on 'Serologic tests'.)

EFFECTS OF ANESTHESIA AND SURGERY ON THE LIVER

The effects of anesthesia and surgery on the liver depend upon the type of anesthesia used, the specific surgical procedures, and the severity of liver disease. In addition, perioperative events, such as hypotension, sepsis, or the administration of hepatotoxic drugs, can compound injury to the liver occurring during the procedure. (See "Anesthesia for the patient with liver disease".)

ESTIMATING SURGICAL RISK

Assessment of surgical risk in patients with liver disease includes an appraisal of the severity of liver disease, the urgency of surgery (and alternatives to surgery), and coexisting medical illness. Surgical risk assessment is less relevant if immediate surgery is required to prevent death. On the other hand, the vast majority of decisions are made in the setting of semi-urgent or elective procedures for which there is time for risk assessment, optimization of the patient's medical status, consideration of alternative approaches, and the possibility of liver transplantation (ie, elective surgery may be deferred until after transplantation) [6,11].

The majority of studies examining the risk of surgery in patients with liver disease have focused on patients with cirrhosis, for which a number of risk factors have been identified (table 1)

[12-25]. Much less information has been published on the risk of surgery in patients with less advanced forms of liver disease. The available evidence is derived mostly from small retrospective studies and clinical experience. Furthermore, many of the studies were published prior to the availability of a number of serologic tests for specific types of liver disease and modern hepatobiliary imaging. Thus, there is relatively little information on the risk of surgery in patients with some specific types of liver disease.

Patients in whom surgery is contraindicated — A number of settings have been identified that are associated with unacceptable surgical mortality. As a result, these conditions are usually considered to be contraindications to elective surgery (table 2).

Acute hepatitis or acute liver failure — Acute hepatitis is a contraindication to elective surgery. This recommendation is based upon older studies, in which operative mortality rates of 10 to 13 percent were reported among icteric patients who underwent laparotomy as part of a diagnostic evaluation that ultimately led to a diagnosis of acute viral hepatitis [26].

Similarly, patients with acute liver failure are gravely ill and are unlikely to withstand surgery other than liver transplantation. (See "Acute liver failure in adults: Etiology, clinical manifestations, and diagnosis".)

Alcohol-associated hepatitis — Elective surgery is contraindicated in patients with histologic evidence of alcohol-associated hepatitis. In the past, mortality rates as high as 55 to 100 percent were observed in such patients undergoing open liver biopsy [27], portosystemic shunt surgery [28-30], or exploratory laparotomy [31]. (See "Clinical manifestations and diagnosis of alcohol-associated fatty liver disease and cirrhosis".)

However, it is possible that advances in surgical technique and postoperative care may have improved the outcome in such patients compared with the above studies, some of which were conducted between the 1960s and 1980s. This was illustrated in a report from 1984, in which operative liver biopsy findings were reviewed in 164 patients with alcohol-related cirrhosis and bleeding varices who underwent emergency portacaval shunt surgery [32]. Of these patients, 49 (30 percent) had histologic evidence of alcohol-associated hepatitis but had survival rates similar to those without alcohol-associated hepatitis. These results have not been duplicated.

We recommend that elective surgery should be delayed for at least 12 weeks or that a repeat liver biopsy should be considered to confirm resolution of alcohol-associated hepatitis. The severity of underlying liver disease should be reassessed prior to making a final recommendation. **Severe chronic hepatitis** — Surgical risk in patients with chronic hepatitis correlates with the clinical, biochemical, and histologic severity of disease. Patients with symptomatic and histologically severe chronic hepatitis have increased surgical risk, particularly in those with impaired hepatic synthetic or excretory function, portal hypertension, or bridging or multilobular necrosis on liver biopsy [33,34].

Patients at variable increased risk — The risk of surgery in patients with cirrhosis depends upon the severity of disease, the clinical setting, and type of surgical procedure. For over 30 years, the principal predictor of operative risk in patients with cirrhosis was the Child-Turcotte-Pugh score or Child-Pugh (CP) class (table 3), but additional studies suggest that the Model for End-stage Liver Disease (MELD) score, Mayo risk score, and other alternative risk models may be superior [25,35]. Liver stiffness measurement by elastography to predict postoperative outcomes is under study [36].

Child-Pugh classification — A number of retrospective studies have demonstrated that perioperative mortality and morbidity in patients with cirrhosis correlate well with the Child-Turcotte [37] and the CP (table 3) [24,38] classifications of cirrhosis (see "Cirrhosis in adults: Overview of complications, general management, and prognosis", section on 'Predictive models'):

- In one study, perioperative mortality rates of 10, 31, and 76 percent were observed in 100 patients with predominantly alcohol-associated cirrhosis undergoing abdominal surgery who were CP class A, B, and C, respectively [23]. On multivariate analysis, the CP classification was the best predictor of surgical mortality and morbidity.
- Nearly identical results were observed in a similarly designed study of 92 patients with cirrhosis (approximately 50 percent alcohol-associated) undergoing abdominal surgery (mortality rates of 10, 30, and 82 percent in patients with CP class A, B, and C, respectively)
 [39].
- A subsequent study published, however, showed lower mortality rates of 2, 12, and 12 percent for patients CP class A, B, and C cirrhosis, respectively, undergoing abdominal surgery. However, many of the patients underwent laparoscopic surgery [40].
- A study of 138 patients undergoing intra-abdominal or abdominal wall surgery showed rates of 10, 17, and 63 percent, respectively [41].

Mortality rates declined in the 2000s, presumably because of improvements in the overall care of critically ill patients [41].

In a retrospective study of 261 patients (45 with cirrhosis and 216 matched controls without cirrhosis) undergoing cardiac surgery, patients with a CP score of less than 8 had a higher survival rate at 90 days compared with patients whose score was 8 or greater (95 versus 30 percent) [42]. In addition, patients with a CP score of less than 8 had survival rates similar to those of control patients without cirrhosis (95 versus 97 percent).

Patients with CP class A cirrhosis and portal hypertension are at increased risk of postoperative ascites, jaundice, and encephalopathy [43]. Limited observations suggest that postoperative morbidity may be reduced by preoperative placement of a transjugular intrahepatic portosystemic shunt [44].

Measures of hepatic function and the APACHE score — A number of measures of hepatic function have been proposed as predictors of perioperative morbidity and mortality in patients with cirrhosis. Examples include quantitative assessment of liver function with dynamic tests such as galactose elimination capacity, aminopyrine breath testing, indocyanine green clearance, and the rate of metabolism of lidocaine to monoethylglycinexylidide (see "Tests of the liver's biosynthetic capacity (eg, albumin, coagulation factors, prothrombin time)"). However, none has been shown convincingly to provide additional prognostic information compared with the CP classification, and, as a result, they are not used widely [45].

The Acute Physiology, Age, and Chronic Health Evaluation System (APACHE III) score can predict survival in patients with cirrhosis who are admitted to an intensive care unit [46]. However, it has not been studied specifically in patients with cirrhosis undergoing surgery. (See "Predictive scoring systems in the intensive care unit".)

MELD score and Mayo risk score — The MELD score is a statistical model predicting survival in patients with cirrhosis (calculator 1 and calculator 2). It was developed to predict mortality after placement of a transjugular intrahepatic portosystemic shunt (TIPS) and has been evaluated principally for selecting patients for liver transplantation. Use of this model for predicting surgical risk in the nontransplant setting has been promising and thus has supplanted the CP classification as the principal method for determining surgical risk [47-52]. The Mayo risk score includes the MELD score plus the American Society of Anesthesiologists (ASA) class and age. The following summarizes representative studies. (See "Model for Endstage Liver Disease (MELD)".)

• The Mayo risk score predicted mortality in a study of 772 patients with cirrhosis who underwent major digestive, orthopedic, or cardiovascular surgery [47]. The score was the best predictor of 30- and 90-day mortality. Mortality at 30 days ranged from 6 percent (MELD score, <8) to more than 50 percent (MELD score, >20) and correlated linearly with the MELD score.

- Another study compared the MELD score with the CP class in 40 patients with cirrhosis who required either elective or emergency surgery with general anesthesia [49].
 Emergency surgery was associated with significantly higher one- and three-month mortality rates. There was good correlation between the CP class and the MELD scores in predicting mortality, especially in the emergency surgery group.
- In other reports in selected settings, a MELD score ≥8 was useful for predicting morbidity in 33 patients undergoing cholecystectomy [50]; a MELD score >14 was a better predictor of poor outcomes than the CP class in a series of 53 cirrhotic patients undergoing abdominal surgery [51]; a MELD score ≥15 with an albumin ≤2.5 mg/dL predicted significantly increased mortality in a series of 100 patients undergoing abdominal surgery (60 versus 14 percent) [40]; and a MELD score ≥11 predicted a high risk for postoperative liver failure in 154 patients with cirrhosis undergoing partial hepatectomy for hepatocellular carcinoma [52].

It has been suggested that patients with a MELD score below 10 can undergo elective surgery, those with a MELD score of 10 to 15 may undergo elective surgery with caution, and those with a MELD score >15 should not undergo elective surgery [11,53]. An online calculator is available (calculator 3 and calculator 4) to estimate 7-day, 30-day, 90-day, 1-year, and 5-year mortality rates after surgery based on the patient's age, ASA class, international normalized ratio (INR), serum bilirubin, and serum creatinine (Mayo risk score). The model is based on the original MELD score, not the one currently being used for organ transplantation (MELD-Na), for which thresholds for preoperative risk assessment have not been established [54]. Since the first report of the Mayo risk score in 2007, however, its accuracy in predicting surgical mortality risk has been reported to have declined because of improved surgical outcomes [25,47].

VOCAL-Penn score — For patients with cirrhosis who undergo surgery, the Veterans Outcomes and Costs Associated with Liver Disease (VOCAL)-Penn score can be used to stratify patients according to risk of mortality at 30, 90, and 180 days postoperatively [25]. This risk calculator was derived from a large cohort of patients with primarily CP class A cirrhosis and a MELD score \leq 9 who underwent various surgical procedures (abdominal, vascular, abdominal wall, cardiac, and orthopedic surgery but not hepatic surgery). In addition to the type and urgency of surgery, the VOCAL-Penn score includes other clinical variables: age, albumin, platelet count, total bilirubin, presence of fatty liver disease, ASA class, and body mass index (BMI). Interestingly, a BMI \geq 30 kg/m² was found to be protective against postoperative mortality, as has been reported in other settings [55]. **Obstructive jaundice** — Patients with obstructive jaundice are at increased risk for several perioperative complications including infections (which result in part from bacterial colonization of the biliary tree, impaired Kupffer cell function, defective neutrophil function, and a high rate of endotoxemia), stress ulceration, disseminated intravascular coagulation, wound dehiscence, and renal failure [56-59]. Perioperative mortality ranged from 8 to 28 percent in several reports from the 1980s and 1990s [60-62]. As an example, an overall mortality rate of 9 percent was found in a large retrospective study that included 373 patients undergoing surgery for obstructive jaundice [61]. Multivariate analysis identified three predictors of postoperative mortality:

- An initial hematocrit value <30 percent
- An initial serum bilirubin level >11 mg/dL (200 micromoles/L)
- A malignant cause of obstruction (eg, pancreatic carcinoma or cholangiocarcinoma)

When all three factors were present, mortality approached 60 percent; when none was present, mortality was only 5 percent. Several other preoperative predictors of poor surgical outcome have been observed in other studies, including azotemia, hypoalbuminemia, and cholangitis (table 1) [60-65]. The presence of portal hypertension can also be presumed to increase the surgical risk.

A number of interventions have been attempted to reduce morbidity and mortality in these patients:

- Perioperative administration of broad-spectrum intravenous antibiotics reduces the frequency of postoperative infections but does not influence mortality [66].
- External biliary drainage via a transhepatic approach has not been proven to improve morbidity or mortality in controlled studies [67-70]. In one report, it increased overall and infectious postoperative complication rates when used before resection for hilar cholangiocarcinoma [71].
- Endoscopic biliary drainage has the advantage of restoring enterohepatic circulation of bile acids while avoiding the complications of percutaneous puncture. However, as for external biliary drainage, it also has not been shown to improve surgical mortality in patients with a malignant cause of biliary obstruction [72,73], although preoperative biliary drainage has been recommended in patients undergoing extended hepatic resection [74] or with cholangitis or pruritus when surgery is delayed [75]. In patients with cholangitis and choledocholithiasis, broad-spectrum intravenous antibiotics and endoscopic drainage have been associated with lower mortality and morbidity rates compared with surgical decompression [76-78]. Although endoscopic sphincterotomy is

associated with an increased rate of complications in patients with cirrhosis [79,80], morbidity and mortality rates are low, even in patients with CP class C cirrhosis, when biliary decompression can be achieved [81]. Morbidity rates have been reported to correlate with the MELD score [82]. (See "Endoscopic management of bile duct stones".)

 A major cause of morbidity in patients with obstructive jaundice is postoperative renal failure, which is usually due to acute tubular necrosis; the average frequency was approximately 8 percent in several reports [58,83,84]. The high incidence may be related to the absorption of endotoxin from the gut [85]. In normal subjects, endotoxin absorption is limited by the detergent effect of bile salts on the lipopolysaccharide endotoxin molecule; this protection is lost with obstructive jaundice, since bile salt secretion is minimal. As a result, patients may develop exaggerated renal vasoconstriction. (See "Pathogenesis and etiology of ischemic acute tubular necrosis".)

Limited evidence suggests that the administration of bile salts or lactulose to patients with obstructive jaundice can prevent both the endotoxemia and the exaggerated renal vasoconstriction [66,85-87]. In one report, for example, 102 patients with obstructive jaundice who had a serum bilirubin concentration >5.8 mg/dL (100 micromoles/liter) were randomly assigned to receive lactulose, sodium deoxycholate (a bile salt), or no specific treatment prior to surgery [86]. Postoperative deterioration in renal function in patients with normal preoperative function was significantly more common in patients who had received no specific treatment.

Another approach that has been attempted to reduce the incidence of renal failure is the postoperative administration of mannitol [66,88]. Despite its theoretical benefit, maintenance of intravascular volume and the avoidance of nephrotoxic drugs such as aminoglycosides are probably more critical elements in management [89-91].

Prophylactic oral antibiotics, such as rifaximin, have also been proposed as a means to reduce adverse effects of endotoxemia, but a benefit has not yet been demonstrated. Furthermore, it is possible that oral antibiotics could increase endotoxemia because they may lead to increased release of endotoxin caused by destruction gram-negative organisms. On the other hand, intravenous broad-spectrum antibiotics should generally be given perioperatively to reduce the incidence of postoperative infection, although a benefit on mortality has not been demonstrated [66].

Whether patients with cholestatic liver disease (such as primary biliary cholangitis and primary sclerosing cholangitis) also have an increased risk of acute tubular necrosis following surgery has not been well studied. An interesting clinical observation is that patients with primary biliary cholangitis appear to be at decreased risk for developing hepatorenal syndrome after surgery

compared with patients with other forms of liver disease [92]. A possible explanation is the natriuretic and renal vasodilator actions of retained bile salts.

Cardiac surgery — Cardiac surgery is associated with increased mortality in patients with cirrhosis compared with other surgical procedures [93,94]. The need for cardiac surgery in patients with cirrhosis has increased, because nonalcoholic steatohepatitis (NASH), in association with the metabolic syndrome, has become a common cause of cirrhosis. (See "Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults", section on 'Epidemiology'.)

A number of studies of patients undergoing cardiac surgery have found that CP class identifies patients at highest risk [48,95-97]. In an analysis of nine studies involving 210 patients with cirrhosis who underwent various cardiac procedures, the overall mortality was 17 percent. The mortality rates per CP class A, B, and C were 5 percent, 35 percent, and 70 percent, respectively [98]. The MELD score may also be useful in this regard. Because many patients with cardiac disease are anticoagulated, a modification of the MELD score that excludes the INR (MELD XI) is often used in this group of patients [99]. In general, a CP score >7 or a MELD score ≥13.5 is considered a contraindication to cardiac surgery [48].

A number of risk factors for hepatic decompensation following cardiac surgery have been identified, including the total time of cardiopulmonary bypass, use of nonpulsatile as opposed to pulsatile cardiopulmonary bypass, and need for perioperative pressor support [100]. Cardiopulmonary bypass can exacerbate underlying coagulopathy by inducing platelet dysfunction, fibrinolysis, and hypocalcemia [101]. The need for anticoagulation during and after the procedure poses an added challenge.

Thus, the least invasive options, such as angioplasty, valvuloplasty, or minimally invasive revascularization techniques, should be considered in patients with advanced cirrhosis who require invasive intervention for cardiac disease [102,103]. (See "Off-pump and minimally invasive direct coronary artery bypass graft surgery: Clinical use".)

Cardiac surgery followed by liver transplantation has been performed in rare instances [100,104,105]. Even more rarely, liver transplantation has been undertaken before cardiac surgery in patients with left ventricular dysfunction [101]. This approach is hazardous because of the risk of hemodynamic instability resulting from reduced venous return and reperfusion of the graft during liver transplantation [100].

Hepatic resection — Patients with cirrhosis undergoing resection for hepatocellular carcinoma or other liver tumors are at increased risk for hepatic decompensation compared with those undergoing other types of operations [106]. In addition to having severe underlying

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disease, a significant portion of functional hepatocellular mass may be removed in a setting in which patients already have severely compromised hepatic reserve. In a patient with cirrhosis, a 40 percent remnant is generally considered the lower limit needed for safe resection, compared with 20 percent in a noncirrhotic liver [107]. In the past, cirrhosis was considered to be a contraindication to resection of hepatic tumors, since mortality rates exceeded 50 percent.

The perioperative mortality rate for hepatic resection has decreased to 3 to 16 percent, although postoperative morbidity rates are still as high as 60 percent [108-118]. In the National Surgical Quality Improvement Program database, mortality rates were 8.3 percent for major hepatectomy and 3.4 percent for minor hepatectomy [117]. The improvement in outcomes has been attributed to better patient selection (including earlier detection of tumors), meticulous preoperative preparation, intensive intra- and postoperative monitoring, and improved surgical techniques. Postresectional liver failure is defined as an INR >1.7 (prothrombin time index <50 percent) and serum bilirubin greater than 2.9 mg/dL (50 micromol/L), the so-called 50-50 criteria, and is associated with a mortality rate of about 60 percent compared with 1.2 percent when the criteria are not met [119]. Clinically significant portal hypertension (ie, associated with gastroesophageal varices or a platelet count less than 100,000/mL with splenomegaly) has been shown to be associated with clinical decompensation after surgery and three- and five-year mortality [120]. The use of liver stiffness measurement (eq, by ultrasound-based elastography) to guide decisions regarding hepatic surgical resection has been suggested, but optimal cutoff values have not been validated [121]. Options for treating hepatocellular carcinoma, including surgical resection, are discussed elsewhere. (See "Surgical management of potentially resectable hepatocellular carcinoma".)

Several systems for risk stratification of patients undergoing hepatic resection have been proposed, although none has been validated extensively. A database study of 587 patients who underwent hepatic resection concluded that the Child-Turcotte-Pugh score and ASA score were better predictors of morbidity and mortality than the MELD score [122]. The ASA score was the only significant predictor of 30-day mortality (area under the receiver operating curve [ROC] of 0.63), while the ASA score and Charlson Index of Comorbidity were the only significant predictors of morbidity (ROC of 0.56 and 0.40, respectively). However, the low ROC areas indicate that none of these models was an accurate predictor of outcomes. Another study has shown that a MELD score of 9 or more was associated with a higher perioperative mortality rate (29 percent) than a lower score (0 percent) [123]. Moderate to severe hepatic steatosis (>30 percent of liver volume) is a risk factor for postoperative complications after major hepatectomy [124]. The Albumin-Bilirubin score (ALBI), based on the serum albumin level and serum total bilirubin level, has been shown to predict post-hepatectomy liver failure and mortality [125,126].

Trauma — Trauma patients found to have cirrhosis at laparotomy are at increased risk for morbidity and mortality. In one study, the overall mortality rate was 45 percent, significantly higher than that of a matched control population (24 percent) [127]. Mortality and morbidity rates were increased even for patients considered to have relatively minor trauma. The authors recommended that trauma patients found to have cirrhosis at laparotomy be admitted to the intensive care unit for close monitoring and aggressive management irrespective of the severity of their injuries.

Abdominal surgery — In patients undergoing cholecystectomy, a laparoscopic approach is associated with lower mortality rates than an open approach [128-131] and can be performed in patients with CP class A and B cirrhosis and MELD scores up to 13 [130,131]. Percutaneous cholecystostomy is often precluded in patients with CP class C cirrhosis because of ascites and high rates of infection and procedural complications, but endoscopic transpapillary gallbladder drainage may be an option if expertise in the technique is available [132]. Endoscopic ultrasound-guided cholecystostomy may also be an option in some centers [133].

Colorectal surgery, primarily for diverticular disease and colorectal cancer, is associated with mortality rates as high as 26 percent in patients with cirrhosis [134,135]. Laparoscopic resection is associated with lower rates of mortality and complications compared with open resection [136]. Less invasive approaches such as stent placement to relieve obstruction should be considered when possible. On the other hand, elective umbilical hernia repair can be performed with excellent outcomes, even in patients with CP class C cirrhosis [137,138]. Surgery for umbilical hernia incarceration or rupture, however, is associated with higher mortality rates [139]. Except for umbilical hernia repair [139,140], the value of transjugular intrahepatic portosystemic shunt placement prior to abdominal surgery in patients with cirrhosis and ascites is uncertain [141].

Bariatric surgery — For patients with cirrhosis related to NASH or other causes who are evaluated for bariatric surgery, preoperative testing includes assessing for clinically significant portal hypertension with upper endoscopy to exclude esophageal varices or with cross sectional imaging to exclude venous abdominal collaterals [6,142]. In general, bariatric surgery, particularly sleeve gastrectomy, has been well tolerated in patients with compensated cirrhosis and without complications of portal hypertension when performed by an experienced surgeon at a high-volume bariatric center [143-147]. Bariatric surgery may reduce the risk of recurrent nonalcoholic fatty liver disease post-transplantation [148]. In rare instances, combined liver transplantation and bariatric surgery has been performed [149]. (See "Bariatric surgery for management of obesity: Indications and preoperative preparation" and 'Fatty liver and nonalcoholic steatohepatitis' below.) However, emerging endoscopic bariatric therapies are not used for patients with clinically significant portal hypertension [142].

Patients with minimally increased risk — Patients with mild to moderate chronic liver disease without cirrhosis usually tolerate surgery well. However, medical therapy should be optimized prior to surgery.

Mild chronic hepatitis — Asymptomatic patients with mild chronic hepatitis are at low risk for complications [150]. In one report, for example, no major complications were noted during 34 surgical procedures in 24 patients with mild to moderate chronic hepatitis [150]. Two patients developed sustained hyperbilirubinemia, both of whom had preoperative bilirubin levels of 2.5 mg/dL (35.91 micromoles/liter) or more.

Fatty liver and nonalcoholic steatohepatitis — Although the histologic appearance of nonalcoholic steatohepatitis (NASH) is similar to that of alcohol-associated hepatitis, patients with NASH do not appear to have excessive mortality following elective surgery. However, increased mortality following hepatic resection has been observed in those with moderate to severe steatosis (>30 percent of hepatocytes containing fat), and with metabolic syndrome [124,151-153].

NASH is common in patients with Class II obesity who undergo bariatric surgery. Cirrhosis, due presumably to NASH, has been found unexpectedly in up to 6 percent of such patients, in whom a perioperative mortality rate of 4 percent has been observed [22]. (See 'Bariatric surgery' above.)

It may be difficult to distinguish NASH from alcohol-associated hepatitis, since the histologic features can be identical and patients do not always admit to alcohol ingestion (see "Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults" and "Screening for unhealthy use of alcohol and other drugs in primary care"). Thus, recommending a period of abstinence from alcohol prior to surgery is advisable for all patients with the histologic appearance of steatohepatitis or those who are suspected of excessive alcohol consumption, since patients with alcohol use disorder are at increased risk for perioperative complications, such as alcohol withdrawal and hepatotoxicity with therapeutic doses of acetaminophen (often used for analgesia in the postoperative period) [154], even if they do not have liver disease. Furthermore, alcohol may potentiate the toxicity of halothane (which is no longer available in the United States) [155,156].

Autoimmune hepatitis — Elective surgery is usually well tolerated in patients with autoimmune hepatitis who have compensated liver disease. Perioperative "stress" doses of hydrocortisone should be given to patients taking prednisone.

Hemochromatosis — Patients with hemochromatosis should be evaluated for complications such as diabetes mellitus and cardiomyopathy, which could influence perioperative care (see "Clinical manifestations and diagnosis of hereditary hemochromatosis"). In the past, a relatively poor outcome of liver transplantation in these patients compared to those with other types of liver disease was attributed to underlying cardiomyopathy [157], but outcomes have improved with careful patient selection.

Wilson disease — Patients with Wilson disease who have neuropsychiatric involvement may not be able to provide informed consent. Furthermore, surgery can precipitate or aggravate neurologic symptoms. D-penicillamine (a copper chelator commonly used for treatment), interferes with the crosslinking of collagen and may impair wound healing [158,159]. As a result, the dose should be decreased prior to surgery and during the first one to two postoperative weeks. (See "Wilson disease: Treatment and prognosis".)

OPTIMIZING MEDICAL THERAPY

In addition to assessing surgical risk, all patients with known liver disease should be assessed for the presence of jaundice, hemostatic defects, ascites, electrolyte abnormalities, renal dysfunction and encephalopathy, all of which may require specific treatment prior to surgery. A preoperative checklist has been proposed [160]. The basic principles involved in the evaluation of patients with specific forms of liver disease are discussed in detail separately. (See "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis".)

- **Hemostasis** Individuals with liver disease are thought to have a form of "rebalanced" hemostasis, in which multiple abnormalities that increase risks of hypo- and hypercoagulability may co-exist in an individual patient. The following interventions may be appropriate, as discussed in detail elsewhere. (See "Hemostatic abnormalities in patients with liver disease", section on 'Invasive procedures'.)
 - Global measures of clot formation, such as thromboelastography (TEG), are used in many centers for assessing hemostasis, although they lack validated target levels [161].
 Fibrinogen levels and platelet count are also useful, especially if a global test is unavailable. The prothrombin time (PT) correlates poorly with bleeding risk. Large or unexpected changes in the platelet count or coagulation tests (PT or activated partial thromboplastin time [aPTT]) typically require evaluation for a source, which may include infection, new medication(s), or portal vein thrombosis.

- Vitamin K may be given to patients with suspected vitamin K deficiency (as a result of poor nutritional status or cholestatic disease). However, plasma or cryoprecipitate should not be administered to "correct" an asymptomatic prolongation of the PT or INR. These interventions lack strong evidence for benefit and carry risks of transfusion reactions and volume overload.
- Severe thrombocytopenia (platelet count <50,000/microL) may be treated with a short course of a thrombopoietin receptor agonist (eg, avatrombopag) [162]. These drugs should be used with caution in patients with liver disease because of the risk of thrombotic events, including portal vein thrombosis. Moreover, administration for approximately 10 days is required to raise the platelet count.
- **Portal hypertension and varices** Patients with known esophageal varices should receive appropriate prophylactic treatment. (See "Primary prevention of bleeding from esophageal varices in patients with cirrhosis".)

Maintaining a low central venous pressure (<5 mmHg) may reduce the risk of variceal or other gastrointestinal bleeding [163,164]. Although surgery has not been associated with an increased risk of variceal bleeding, fluid overload should be avoided postoperatively.

Preoperative transjugular intrahepatic portosystemic shunts (TIPS) has been reported in patients with portal hypertension [141,165-167]; however, the benefit of this approach over standard care has not been well studied. (See "Overview of transjugular intrahepatic portosystemic shunts (TIPS)".)

- Ascites Ascites increases the risk of wound dehiscence and abdominal wall herniation, may increase postoperative mortality risk independent of the MELD score [168], and should be treated aggressively before surgery. This can be achieved safely with diuretics in patients who also have peripheral edema. In patients without edema or those in whom there is not enough time for a course of diuretic therapy, ascites can be drained completely during laparotomy. (See "Ascites in adults with cirrhosis: Initial therapy".)
- **Metabolic changes** Electrolyte abnormalities, particularly hypokalemia, and metabolic alkalosis, should be corrected to reduce the chance of cardiac arrhythmias and hepatic encephalopathy.

Renal function should be evaluated and optimized. For most patients, assessment of the blood urea nitrogen and creatinine is sufficient. However, these measures often overestimate renal function in patients with cirrhosis because of the reduction in urea and

creatinine synthesis. (See "Hepatorenal syndrome", section on 'Clinical presentation' and "Hepatorenal syndrome", section on 'Problems with estimating kidney function'.)

• **Nutrition** – Patients with cirrhosis are often malnourished and may have sarcopenia (loss of muscle mass), even in the presence of obesity [169]. Perioperative nutritional support can reduce the frequency of postoperative complications and short-term mortality; its benefit on long-term survival is uncertain [170-174]. A reasonable approach is to provide total calories equal to 1.3 times the estimated resting energy expenditure, or at least 35 kcal/kg, and 1.2 to 1.5 g/kg per day of protein [169]. Approximately 30 to 35 percent of total energy should be given as fat and the remainder (typically 50 to 55 percent) as carbohydrates. Supplementation of the fat-soluble vitamins A, D, E, and K may also be necessary [173].

Percutaneous endoscopic gastrostomy (PEG) is contraindicated in patients with ascites and should usually be avoided in patients with portal hypertension due to the possibility of lacerating an abdominal wall varix during PEG insertion. Nasoenteric tubes are not contraindicated in patients with nonbleeding esophageal varices.

Following surgery, patients with liver disease should be observed closely for hepatic decompensation, which often presents with worsening jaundice, encephalopathy, and ascites. The best biochemical measures of liver function are probably the PT/INR and serum bilirubin concentration. However, the serum bilirubin concentration can be expected to rise, particularly after complicated surgery, multiple blood transfusions, perioperative bleeding, hemodynamic instability, or systemic infection. Renal function, serum electrolytes, and glucose should also be monitored carefully.

 Venous thromboembolism prophylaxis – There are limited data on the safety of venous thromboembolism prophylaxis in patients with cirrhosis. It is thought to be safe in patients with nonsevere thrombocytopenia (platelets ≥50,000/microL) [7].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Cirrhosis".)

SUMMARY AND RECOMMENDATIONS

Considering the available data and clinical experience, assessing the risk of elective or semiurgent surgery in patients with liver disease includes:

- Optimizing medical therapy Medical therapy should be optimized in all patients with liver disease. This may include correcting electrolyte abnormalities, treating hepatic encephalopathy, and optimizing hemostasis. (See 'Optimizing medical therapy' above and "Hemostatic abnormalities in patients with liver disease", section on 'Invasive procedures'.)
- Anesthesia-related issues The effects of anesthesia and surgery on the liver depend upon the type of anesthesia used, the specific surgical procedures, and the severity of liver disease. In addition, perioperative events, such as hypotension, sepsis, or the administration of hepatotoxic drugs, can compound injury to the liver occurring during the procedure. (See "Anesthesia for the patient with liver disease".)
- Estimating surgical risk Operative mortality can be estimated based upon the Child-Pugh (CP) classification (table 3) and the Model for End-stage Liver Disease (MELD) score (calculator 3 and calculator 4) taking into consideration other factors such as the patient's age, ASA score, and additional comorbidities. (See 'Estimating surgical risk' above.)
 - Contraindications to elective surgery We recommend that elective or semi-urgent surgery **not** be performed in patients with acute hepatitis, acute liver failure, alcoholassociated hepatitis, severe chronic hepatitis, CP class C or MELD score >15 cirrhosis, severe coagulopathy, or severe extrahepatic manifestations of liver disease (such as hypoxia, cardiomyopathy, or acute renal failure) (**Grade 1B**). (See 'Patients in whom surgery is contraindicated' above.)
 - Patients at variable increased risk For other patients, the risk of surgery depends upon the severity of liver disease and the type of procedure (see 'Patients at variable increased risk' above):
 - Surgery is generally well tolerated in patients with cirrhosis and CP class A or MELD score <10 and those with chronic liver disease but without cirrhosis.
 - Surgery is generally permissible in patients with cirrhosis and CP class B or MELD score 10 to 15 (except those undergoing extensive hepatic resection or cardiac surgery) who have undergone thorough preoperative preparation.

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GRAPHICS

Risk factors for morbidity and mortality in patients with cirrhosis undergoing surgery

Type of surgery

Abdominal (especially cholecystectomy, gastric resection or colectomy)

Cardiac

Emergency

Hepatic resection

Patient characteristics

Anemia				
Ascites				
Child's class (C>B)				
Encephalopathy				
Hypoalbuminemia				
Нурохетіа				
Infection				
Jaundice				
Malnutrition				
Portal hypertension				
Prolonged prothrombin time (>2.5 seconds above control that does not correct with vitamin K)				

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Contraindications to elective surgery in patients with liver disease

Acute alcoholic hepatitis
Acute liver failure
Acute viral hepatitis
Child-Pugh class C cirrhosis
Severe chronic hepatitis
Severe coagulopathy (prolongation of the prothrombin time >3 seconds despite vitamin K administration; platelet count <50,000/mm ³)
Severe extrahepatic complications
Acute renal failure
Cardiomyopathy, heart failure
Нурохетіа

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Child-Pugh classification of severity of cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time (seconds over control) or	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

INR: international normalized ratio.

Graphic 78401 Version 15.0

Contributor Disclosures

Lawrence S Friedman, MD Other Financial Interest: Elsevier [Gastroenterology]; McGraw-Hill [Gastroenterology]; Wiley [Gastroenterology]. All of the relevant financial relationships listed have been mitigated. **Sanjiv Chopra, MD, MACP** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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