Received: 5 December 2022 | Accepted: 17 January 2023
DOI: 10.1097/HC9.0000000000000086

REVIEW

OPEN

Assessing the risk of surgery in patients with cirrhosis

Melissa G. Kaltenbach[1] | **Nadim Mahmud**[1,2,3,4]

[1]Division of Gastroenterology and Hepatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[2]Department of Medicine, Corporal Michael J. Crescenz VA Medical Center, Philadelphia, Pennsylvania, USA

[3]Leonard David Institute of Health Economics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

[4]Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics, Epidemiology & Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Correspondence
Nadim Mahmud, 3400 Civic Center Boulevard, 4th Floor, South Pavilion, Philadelphia, PA 19104, USA.
Email: nadim@pennmedicine.upenn.edu

Abstract

Patients with cirrhosis have an increased perioperative risk relative to patients without cirrhosis. This is related to numerous cirrhosis-specific factors, including severity of liver disease, impaired synthetic function, sarcopenia and malnutrition, and portal hypertension, among others. Nonhepatic comorbidities and surgery-related factors further modify the surgical risk, adding to the complexity of the preoperative assessment. In this review, we discuss the pathophysiological contributors to surgical risk in cirrhosis, key elements of the preoperative risk assessment, and application of risk prediction tools including the Child-Turcotte-Pugh score, Model for End-Stage Liver Disease-Sodium, Mayo Risk Score, and the VOCAL-Penn Score. We also detail the limitations of current approaches to risk assessment and highlight areas for future research.

INTRODUCTION

It is estimated that 1 in 400 individuals in the US have cirrhosis,[1] and the burden of liver disease has been rising over time, largely related to the obesity epidemic and NAFLD.[2] With an aging population of patients with advanced liver disease, the volume of surgical procedures in patients with cirrhosis, such as major orthopedic or hernia repairs, has also increased over time.[3] Surgery is being performed more frequently in part due to the increased burden of liver disease and improved long-term survival of individuals with chronic liver disease, and therefore accurate preoperative risk stratification is especially salient in the current era of practice. In this brief review, we discuss the elements of cirrhosis that uniquely contribute to surgical risk, detail the preoperative assessment and risk assessment for patients with cirrhosis undergoing nonhepatic surgeries, and discuss the limitations and ongoing challenges with risk stratification.

BASIS OF INCREASED SURGICAL RISK IN CIRRHOSIS

Patients with cirrhosis have an approximately 3-fold increased perioperative mortality compared with patients without cirrhosis.[4–6] The risk of surgical complications leading to morbidity and mortality is tied to several key pathophysiological changes that are proportional to the severity of liver disease (Figure 1). First, sarcopenia with muscle loss is common in patients with cirrhosis due to a catabolic state where muscle protein breakdown exceeds the synthesis of new proteins due to impaired liver synthetic function.[7] Patients with cirrhosis also tend to have malnutrition

Abbreviations: ASA, American Society of Anesthesiologists; CTP, Child-Turcotte-Pugh; INR, international normalized ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; MRS, Mayo Risk Score; VPS, VOCAL-Penn Score.

related to poor nutritional intake and absorption, particularly in those with alcohol-associated liver disease. This results in nutritional deficiencies that impair wound healing, promote frailty, and lead to poor physical recovery in the postoperative period.

Second, portal hypertension increases the risk of multiple intraoperative and postoperative complications. Ascites may develop for a variety of reasons including intraoperative resuscitation efforts, holding of home diuretics, and cardiac effects of anesthesia; with cirrhosis, the liver is especially prone to ischemic injury from relative intraoperative hypotension and/or splanchnic bed manipulation, thus increasing the risk of postoperative decompensation.[8] Ascites may also result from iatrogenic injuries to lymphatics resulting in chylous ascites, seen more frequently in major abdominal procedures such as pancreatic surgeries.[9] With portal hypertension, the risk of intraoperative and postoperative bleeding is elevated due to increased hydrostatic pressure and expansion of portosystemic collaterals, which impact thoracic and intra-abdominal surgeries in particular as they may involve the splanchnic circulation. Variceal hemorrhage may also occur due to hemodynamic shifts that occur during surgery in patients with preexisting portal hypertension, in addition to increases in portal pressure from intraoperative or post-operative volume expansion.

Third, patients with cirrhosis exhibit deranged coagulation and fibrinolysis where they are both more likely to develop thromboembolisms as well as more likely to develop bleeding relative to the general population.[10] The balance between these tendencies can be difficult to predict and not well-reflected by standard coagulation testing. If bleeding does occur, hemostasis may be more difficult given the baseline thrombocytopenia in the setting of splenic sequestration and relative thrombopoietin deficiency, synthetic deficiencies in clotting factors, and low fibrinogen due to decreased fibrin polymerization, reduced fibrinogen synthesis, and hyperfibrinolysis related to excess availability of tissue plasminogen activator and reduced fibrinolysis inhibitors.[11,12] Finally, cirrhosis renders patients more susceptible to infections due to immune dysregulation of the inflammatory response.[13]

As noted, surgical complications such as infection and bleeding are more common and more severe in the presence of chronic liver disease.[14] Septic shock, bleeding, and respiratory failure are the most common causes of attributable mortality after surgery and can all be impacted by the presence of advanced liver disease.[15] However, in addition to serious surgical complications such as wound infection, hemorrhage, or pulmonary embolism, surgery itself may precipitate acute deterioration in liver function leading to hepatic decompensation such as hepatic encephalopathy, ascites, or variceal bleeding through a variety of mechanisms.[14] Hemodynamic instability in the perioperative period can cause hepatic ischemia and worsen liver function in patients with underlying liver disease, especially in those with pre-existing portal hypertension. This phenomenon may precipitate any of the aforementioned hepatic decompensation including ascites or variceal bleeding. HE may also occur due to postoperative infection, acute kidney injury, bleeding, or medication-related factors including the effects of intraoperative anesthesia, withholding of lactulose for postoperative ileus, and/or the use of postoperative analgesics.[16]

PREOPERATIVE RISK ASSESSMENT

Preoperative risk stratification for cirrhotic patients can be difficult owing to the large number of variables in cirrhosis that may potentially contribute to surgical risk as stated above, in addition to other surgery-specific and patient factors that modify risk. However, with regard to cirrhosis-specific factors, there are several clinical factors that should be examined in the preoperative setting.

Severity of liver disease and portal hypertension

Severity of liver disease is the most important factor in predicting postoperative outcomes. Given the exceptional

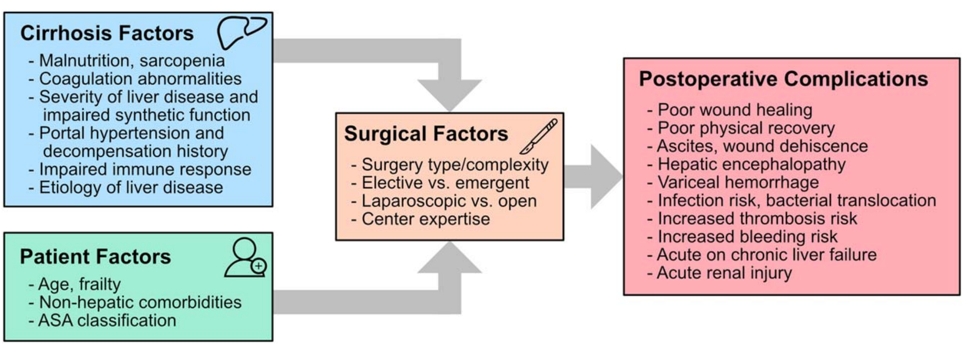

FIGURE 1 Conceptual model for increased perioperative risk in patients with cirrhosis. Abbreviation: ASA, American Society of Anesthesiologists.

high mortality rates, surgery should generally not be undertaken in patients with acute liver failure, severe acute hepatitis, or alcohol-associated hepatitis,[17] with the notable exception of liver transplantation where indicated. As liver disease progresses, hemodynamic changes characterized by splanchnic vasodilation, increased cardiac output, and decreased systemic vascular resistance occur that can impair organ perfusion during surgery. Higher Child-Turcotte-Pugh (CTP) and the Model for End-Stage Liver Disease-Sodium (MELD-Na) scores have been shown to be associated with worsening postoperative mortality.[18] Both scoring systems take into account basic laboratory values to stratify liver disease severity. Therefore, all patients should receive testing with complete blood count, comprehensive metabolic panel, and coagulation profile as part of the preoperative evaluation. A detailed history and physical examination should be performed to determine the presence of cirrhosis decompensation, including hepatic encephalopathy, ascites, and history of variceal bleeding. If a patient has not previously had abdominal imaging, an abdominal ultrasound or cross-sectional abdominal imaging may help to classify the degree of ascites, splenomegaly, or presence/absence of varices. Imaging will also serve as screening for HCC (if the patient is not already up to date) and may identify PVT, which may potentially modify surgical planning and prognostic discussions. If the surgery is elective, the patient should be up to date with variceal screening through esophagogastroduodenoscopy (if indicated) and appropriate management in accordance with the American Association for the Study of Liver Diseases guidance is recommended (eg, band ligation or initiation of nonselective beta blocker medication if medium or large varices identified). If band ligation is performed, it is advisable to allow 14 days to ensure healing of postbanding ulcers.[19,20]

Etiology of liver disease has also been found to predict postoperative mortality with NAFLD exerting a protective effect and viral etiology associated with increased mortality risk.[21] As compared with other etiologies of liver disease, alcohol-associated cirrhosis may favorably impact postoperative outcomes, potentially owing to the partial reversibility of liver injury with abstinence.[22] Hepatitis C has also been shown to have worse operative morbidity and mortality as compared with hepatitis B when undergoing hepatic resection for HCC.[23] Therefore, if not already completed, a comprehensive evaluation to determine the etiology of liver disease should be performed, including testing for hepatitis B and hepatitis C infection.

Consideration of surgical factors

Regarding surgery-specific factors, surgical procedure type categorized as abdominal wall, major vascular, laparoscopic abdominal, open abdominal, chest/cardiac, or major orthopedic was found to significantly impact postoperative mortality risk, with open abdominal surgeries associated with the highest mortality, followed by chest/cardiac surgeries (Figure 2A).[4,21] It is well-established that, when feasible, a laparoscopic approach to abdominal surgery confers a lower risk of perioperative morbidity and postoperative mortality as compared with an open approach.[24–27] Emergency status of surgery has also been found to be associated with more than double the mortality rate compared with elective surgeries.[28–30] A study evaluating the CTP and MELD score prediction of postoperative mortality found that patients undergoing emergency surgery had significantly higher mortality at 1 and 3 months after surgery.[18] Finally, center surgical volume has been

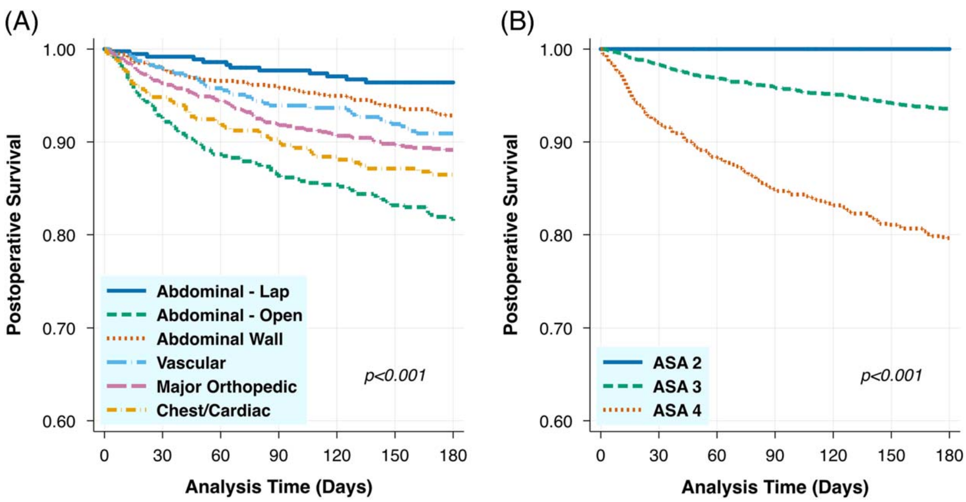

FIGURE 2 Association between surgery type (A) and ASA classification (B) and postoperative survival in patients with cirrhosis. Abbreviation: ASA, American Society of Anesthesiologists. Adapted from Mahmud et al[21] with permission.

associated with improved postoperative outcomes in cirrhosis, highlighting the importance of surgical, anesthesia, and perioperative management expertise in these complex patients.[31]

Nonhepatic comorbidities

Finally, preoperative evaluation should also include an assessment of other nonhepatic comorbidities such as cardiovascular disease. This is particularly salient as there is an increasing prevalence of NASH in the US and worldwide.[2,32] NASH has been associated with an increased risk of heart failure, stroke, coronary artery disease, and arrhythmia and is the leading cause of death in this population.[33] A preoperative electrocardiogram should be performed in all patients, and in patients with concern for systolic, diastolic, or valvular dysfunction, a brain natriuretic peptide and transthoracic echocardiogram should also be performed. Increasing age as well as the American Society of Anesthesiologists (ASA) physical status classification are also known to predict increased postoperative mortality in patients with cirrhosis[21,22]; the latter should be assessed in all patients. The ASA classification, which is commonly used to predict surgical mortality in the general population,[34] ranges from 1 (healthy patient) to 6 (declared brain dead) and provides a global assessment of a patient's comorbid preoperative state. In patients with cirrhosis the ASA score is most often a 3 (severe systemic disease, ie, many patients with compensated cirrhosis) or 4 (severe systemic disease that is a constant threat to life, ie, decompensated cirrhosis), but may arguably be as low as 2 (mild systemic disease) in patients with well-compensated cirrhosis without ongoing liver injury or significant nonhepatic comorbidities.

RISK STRATIFICATION TOOLS

Surgical risk calculators have become increasingly popular tools to stratify patients based on their preoperative surgical risk. These risk calculators (Table 1) have the added benefit of using easily obtainable patient information such as laboratory values and demographic factors to determine surgical risk and help providers and patients make informed, personalized decisions about surgery.

CTP and MELD-Na scores

The CTP and MELD-Na scores are used universally in clinical practice to stratify liver disease severity. Although they are commonly used, they do not include any surgery-specific risks. CTP score uses 5 parameters including 3 laboratory values [international normalized ratio (INR), albumin, and bilirubin] and 2 subjective categories (ascites and hepatic encephalopathy) with scores ranging from 5 to 15 and classifying patients into CTP class A, B, or C. Previous studies have shown perioperative mortality rates of 10% for CTP A, 30% for CTP B, and 80% for CTP C patients after undergoing abdominal surgery.[35]

The MELD-Na score is used to prioritize patients on the liver transplant list and is used as a more objective measurement as compared with CTP. The MELD-Na is comprised only of 4 laboratory values (sodium, creatinine, bilirubin, and INR) with a score >26 corresponding to a $>90\%$ postoperative mortality rate in 1 study of diverse surgery types.[18] In this retrospective cohort study of 195 patients with cirrhosis undergoing emergent and elective surgeries, CTP and MELD-Na were found to perform similarly, with fair discrimination for a composite outcome of postoperative mortality or hepatic decompensation ($AUC = 0.755$ for MELD vs. $AUC = 0.696$ for CTP, $P = 0.3$).[18]

Mayo Risk Score (MRS)

The first dedicated surgical risk prediction model validated in patients with cirrhosis was the MRS.[22] Predictors in this score include the ASA physical status classification (dichotomized as 3 for compensated or 4 for decompensated cirrhosis), INR, total bilirubin, creatinine, age, and etiology of liver disease. The study found that the relative risk of 30- and 90-day mortality increased by 14% with each 1-point increase in the MELD score. When externally validated in a Korean cohort, the MRS was found to have good overall performance but overestimated the predicted 1-year mortality rate after surgery (22.6% predicted vs. 8.9% observed; $p < 0.01$) suggesting good discrimination but inadequate calibration.[36] Overestimates of surgical risk can result in undue denial of surgery for patients with otherwise acceptable risk profiles. MRS also is only designed to take into account orthopedic, cardiovascular, and major abdominal surgeries and does not provide any risk stratification based on the type of surgery despite evidence that the type of surgery is a major predictor of surgical risk.[4] Finally, given that the MRS was published in 2007, there has been a strong argument for updated risk prediction tools that reflect the modern era of practice.[37] This is especially important given the major advances in surgical and perioperative care, including expansion of endovascular surgeries, minimally invasive techniques, and robotic surgeries, among other advances, which have fundamentally change patient selection for both laparoscopic and open surgical approaches. Indeed, recent literature has demonstrated declining calibration of the MRS over time, with progressive overestimation of cirrhosis surgical risk (Figure 3).

TABLE 1 Inputs required to compute risk prediction models for cirrhosis surgical risk

VOCAL-Penn	Mayo risk	CTP	MELD-Na
Age	Age	Total bilirubin	Total bilirubin
Albumin	Total bilirubin	International normalized ratio	Creatinine
Total bilirubin	Creatinine	Ascites (absent, slight, moderate)	International normalized ratio
Platelet count	International normalized ratio	HE (absent, grade 1/2, grade 3/4)	Sodium
Body mass index	Alcohol-associated/cholestatic versus viral/other liver disease		
NAFLD	American Society of Anesthesiology physical status classification		
American Society of Anesthesiology physical status classification			
Emergency indication			
Surgery type			

Abbreviations: CTP, Child-Turcotte-Pugh; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; MELD-Na, MELD-sodium.

VOCAL-Penn Score (VPS)

The VPS was recently developed as an updated prediction model that could account for the type of surgery and improve model performance as compared with previous models.[21] Initially derived in a large cohort of patients in the Veterans Health Administration, the VPS includes the following predictors: age, preoperative albumin, platelet count, bilirubin, and surgery category such as laparoscopic abdominal versus open abdominal surgery, elective versus emergency indication, fatty liver disease, ASA classification, and obesity. The VPS online calculator can be found at http://www.vocalpennscore.com.

The VPS demonstrated superior discrimination to MELD, MELD-Na, CTP, and MRS at 30, 90, and 180 postoperative days in a Veterans Health Administration internal validation, and was subsequently externally validated in 2 non-Veterans Health Administration independent health systems.[38] In contrast to other risk stratification models, the VPS has been expanded to predict 90-day postoperative hepatic decompensation.[39] In addition, while the focus of this review is on nonhepatic surgeries, we point out that the VPS has also been externally validated as a predictor of postoperative mortality after liver resection, in both patients with and without cirrhosis.[40] In this validation study, the VPS performance was superior to MELD-Na, MRS, and the albumin-bilirubin score.

An important limitation of all dedicated surgical risk score is that they were derived from retrospective cohorts of patients who underwent surgery and were therefore judged to be surgical candidates. This can account for why more patients were low MELD and CTP A in the cohorts from which these risk stratification tools were designed. There are also other additional factors that providers may factor into their assessment such as frailty and sarcopenia that are difficult to accurately categorize using large database studies and are therefore not accounted for in these risk models.[41] These risk models are not meant to be used as a substitute for clinical judgment and should instead be used as a tool to be used to help patients and providers in shared decision-making. Given these limitations, if projected risk for an elective surgery is $>15\%$ at 90 days, it is generally recommended that a liver transplant evaluation be performed before surgery to determine if that patient is a candidate. A transplant evaluation will ensure that the patient is evaluated by medical and surgical liver specialists before surgery and may result in listing for transplant as a rescue if the patient decompensates after surgery.

PREOPERATIVE OPTIMIZATION

There are several measures that should be taken to optimize all patients with cirrhosis before surgery. Common pathology such as sarcopenia, hemostatic factors, and hepatic decompensation should be assessed and intervened upon before surgery.

Malnutrition and frailty

Malnutrition as seen with hypoalbuminemia and muscle wasting should be identified and mitigated through optimizing the patient's nutritional status. Careful nutritional assessment should be done by a skilled dietitian when possible and a diet high in protein should be emphasized. Risk of sarcopenia should be assumed to be high if the patient's body mass index is <18.5 kg/m^2.[42] Patients should be recommended to take in at least 30–35 kcal/kg calories per day with 1.25–1.5 g/kg per day of protein as calculated based on ideal body weight.[43] Given the longest intermeal duration is at night, strategies to shorten nocturnal fasting with an evening snack have been shown to improve patient quality of life and total body protein status.[44] Individuals with alcohol-associated liver disease should also be considered for thiamine and folic acid supplementation, and sustained sobriety should be supported. Physical prehabilitation, or physical therapy before undergoing surgery, may reduce frailty and improve conditioning before elective surgery, which may translate to improved postoperative recovery.[45] Although there are scant literature addressing this subject in nontransplant surgery in patients with cirrhosis, physical prehabilitation programs have been successfully shown to reduce hospital length of stay and decrease cost of care in a broad cohort of patients including those with cirrhosis.[46]

Hemostasis considerations

Many patients with chronic liver disease will be found to have anemia, thrombocytopenia, and coagulation abnormalities at baseline. There is no specific platelet cutoff where procedural bleeding risk is reliably increased and an individualized approach regarding correction of thrombocytopenia before surgery should be used.[47] Cirrhosis contributes to a wide variety of changes in hemostasis that may simultaneously promote bleeding and clotting. Thus, traditional tests of coagulation such as INR that measures only a limited portion of the hemostatic system provide inherently unreliable information about a given patient's propensity for these events, and there is no evidence that targeting a specific INR goal reliably reduces perioperative bleeding in patients not on vitamin K antagonists.[47] More comprehensive hemostasis tests that evaluate both coagulation and fibrinolysis, such as thromboelastography or rotational thromboelastometry, have been shown to reduce utilization of blood products without an increase in bleeding or complications in patients with cirrhosis undergoing nonsurgical procedures.[48] However, further research is needed to determine the role of these tests in the perioperative setting before they can be routinely recommended in clinical practice.[49] Thrombopoietin receptor agonists, such as avatrombopag and eltrombopag, increase native production of platelets and have been shown to reduce the need for platelet transfusions during or after invasive procedures.[50] These agents may be considered in thrombocytopenic patients undergoing high-risk elective surgery as it takes ~10 days for the effect to be realized; however, caution should be exercised given that these medications are associated with an increased risk of thrombosis including PVT. If fibrinogen is <100 mg/dL before surgery, low-volume cryoprecipitate should be administered. Finally, given that INR is not necessarily reflective of bleeding tendency in cirrhosis due to the imbalance of coagulation factors, there is limited utility in correcting INR with fresh frozen plasma in the absence of active bleeding, and transfusion carries the risk of volume overload (which may theoretically increase the risk of variceal bleeding) and transfusion reaction.

Optimizations related to portal hypertension

Patients with clinical evidence of ascites should be optimized with diuretics, salt restriction, and therapeutic paracentesis as needed before surgery, and there should be a clear plan to adequately manage ascites after surgery. This is particularly important for abdominal surgeries and hernia repairs given that ascites can contribute to abdominal wound dehiscence and abdominal wall herniation.[51] Before surgery, patients with ascites should have their diuretics titrated and a diagnostic paracentesis should be performed to rule out spontaneous bacterial peritonitis. In patients with indications for spontaneous bacterial peritonitis prophylaxis, antibiotics should be continued through the perioperative period. TIPS has been evaluated as a tool for preoperative portal decompression, but to date there is insufficient evidence to support its routine use before abdominal or thoracic surgery.[51] No prospective studies have been performed to evaluate the utility of preoperative TIPS, and retrospective studies have not demonstrated a survival benefit or differences in severe postoperative complications with this practice.[52–54] Nonselective beta-blockers decrease portal hypertension by counteracting splanchnic vasodilation and compensatory increases in cardiac output. In general, patients with indications to take nonselective beta-blockers such as those with medium or large varices or prior variceal bleeding should be started on or maintained on therapy; however, they should not be used in patients with refractory ascites or high CTP scores as they may reduce hemodynamic reserve and increase mortality in this setting.[55,56]

Surgery-specific considerations

There are several additional specific surgical situations that should be considered. For patients undergoing elective cholecystectomy, surgery should be delayed until after liver transplant evaluation given the risk of bile duct injury, which may make transplant potentially more difficult. If cholecystectomy is emergent, the patient should ideally be transferred to a transplant center for further consideration.[57] If the patient is CTP class C or has refractory ascites, it is not advisable to proceed with surgery and nonsurgical options such as endoscopic transpapillary gallbladder drainage can be considered. Patients requiring cardiopulmonary bypass for intrathoracic procedures are at high risk for bleeding given the need for intraoperative anticoagulation and hyperfibrinolysis that occurs. These procedures should only be performed at an experienced center with expertise in perioperative management of patients with cirrhosis and are historically contraindicated in patients with CTP >7 or MELD >13.5 and a less invasive approach is preferred.[58]

Cirrhosis increases the risk of traumatic and nontraumatic orthopedic injuries as it predisposes patients to low bone density, sarcopenia, and frailty. However, orthopedic surgeries in patients with cirrhosis have been found to be associated with a higher postoperative mortality and length of stay compared with patients without cirrhosis.[59] Prehabilitation and careful preoperative optimization are thus important in this scenario. In addition, as patients may be immobilized after selected orthopedic surgeries, postoperative prophylaxis against venous thromboembolism should be utilized in patients with cirrhosis given a predisposition to a potential thrombophilic state.[60] Note that pharmacologic venous thromboembolism prophylaxis should be used with caution in patients with profound thrombocytopenia.[61]

Ventral and inguinal hernias frequently occur in patients with cirrhosis and ascites due to increased intra-abdominal pressure and are common indications for surgery in this population. If hernia repair is performed, postoperative ascites may result in wound dehiscence and recurrent hernia, in addition to increasing the risk of infection and ascitic fluid leak.[28] Thus, it is critical that ascites be well-managed before hernia repair whenever possible; this may be addressed through medical management such as diuretics and salt restriction, or potentially through preoperative TIPS in eligible patients.[62] The timing of hernia repair may also present a clinical conundrum, as historically the surgical risks in cirrhosis were perceived to outweigh the benefits in elective scenarios. A recent randomized control trial evaluated outcomes of elective repair versus conservative treatment for patients with cirrhosis and umbilical hernias. While there were no significant differences in patient morbidity, likely related to small sample size, patients with conservative management had higher numerical rates of complications (77.8%) as compared with those who underwent elective repair (50.0%).[63] Several risk factors for adverse outcomes after hernia repair have been identified in retrospective studies such as a MELD >15, hypoalbuminemia, anemia, and preoperative small bowel obstruction.[28,64] These studies suggest that elective hernia repair is safe in selected patients with cirrhosis, although ongoing studies are needed to identify patients most likely to benefit from a surgical approach.

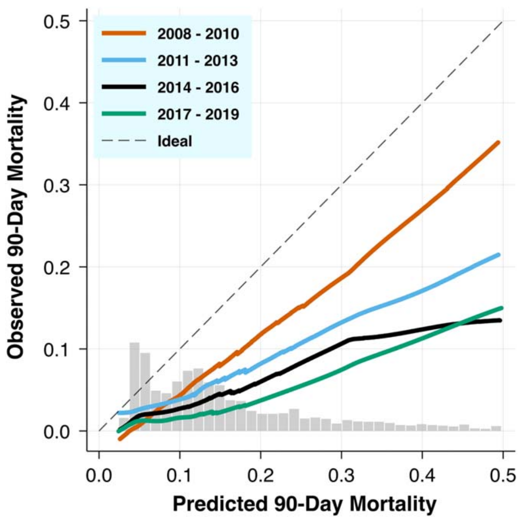

FIGURE 3 Declining calibration of the Mayo Risk Score over time for 90-day postoperative mortality. With each successive 3-year period since the publication of the Mayo Risk Score, the model has experienced degrading calibration such that the risk score progressively overestimates the true risk of postoperative mortality. This may be related to improvements in surgical technique, perioperative management, and the advent of more minimally invasive surgical techniques over time. Adapted from Mahmud et al,[21] with permission.

Finally, given the increasing burden of NASH in the general population, many patients with cirrhosis may also be candidates for bariatric surgery with sleeve gastrectomy at the time of liver transplant consideration.[65] For individuals with compensated cirrhosis and no significant portal hypertension, bariatric surgery is a viable weight loss option and is associated with a decreased risk of liver adverse outcomes.[66] There are small studies that have reported feasibility in performing bariatric surgery in patients with clinically significant portal hypertension, but this should be restricted to highly experienced centers with expertise in managing hepatic complications.[67]

LIMITATIONS TO EXISTING APPROACHES OF RISK ASSESSMENT

There are currently limited data to help contextualize the risk of surgery against nonoperative options for patients with cirrhosis. The risks of not proceeding with surgery are impacted not only by the severity of liver disease but by the indication for surgery itself. These scenarios have not been well studied making truly informed decisions to proceed or not to proceed with surgery challenging. This is because estimation scores, such as MRS or VOCAL-Penn, were derived only from cohorts of patients who underwent surgical treatment. Given the likely historic overestimation of surgical risk in many patients with cirrhosis, there are limited data available on patients with more advanced liver disease undergoing surgery with which to inform risk projections.

Decision analysis studies may help to address this gap on a surgery-by-surgery basis if short-term mortality can be estimated in patients with an indication for surgery but who did not receive it. As an example, a recently published study used Markov cohort analysis as applied to the patients with cirrhosis and a symptomatic abdominal hernia. The decision analytic model identified a MELD-Na score of 21.3 as a threshold below which elective surgical hernia repair is favored over nonoperative management using quality-adjusted life years as the outcome.[68] This result implies that the currently perceived thresholds for acceptable surgical risk are excessively high when hernia repair is considered. This is consistent with findings of other studies,[69] especially when an alternative nonoperative scenario may lead to hernia incarceration or rupture that necessitates surgery under higher-risk emergent settings. Similar risk aversion is likely to be present in many other surgeries in patients with cirrhosis, though this will need to be demonstrated in future literature.

An additional important limitation to existing preoperative decision-making approaches is a paucity of data on the patient perspective. Risk prediction tools have been provider-facing and overwhelmingly focused on predicting mortality as a key outcome. While this is an essential outcome, it is likely that patients value myriad other factors beyond mortality when faced with a decision about major surgery. Qualitative and mixed-method studies may help to identify patient-important attributes, as well as thresholds above or below which patients alter decisions regarding surgery. This is an important area of future research that may shift surgical risk counseling from a paternalistic framework to one of shared decision-making.

Finally, it cannot be overstated that risk prediction models are merely a tool to evaluate patient risk informed by available clinical and surgical characteristics and should not replace clinical judgment. Risk models should also be limited to patients who could plausibly be surgical candidates and cannot yet be generalized to patients who clearly have unacceptable surgical risk. They additionally do not account for hospital factors such as center/surgeon/anesthesia experience and access to subspecialty care, which can have a significant impact on patient outcomes. Thus, the preoperative evaluation of a patient with cirrhosis remains a complex challenge that, while to some degree, has been simplified by risk prediction tools, nonetheless requires the engagement of thoughtful clinicians.

CONCLUSIONS

Cirrhosis uniquely contributes to an increased risk of postoperative complications including infections, bleeding, and/or incident hepatic decompensation that may drive mortality. Severity of liver disease is the most important factor in predicting postoperative outcomes, therefore a detailed history, physical examination, and review of laboratory and imaging data should be performed in the preoperative setting to determine the presence of portal hypertension and hepatic decompensation. Preoperative optimization should be performed whenever feasible and may include addressing common pathology such as sarcopenia/malnutrition, hemostatic abnormalities, optimization of hepatic decompensation, and consideration of surgery-specific factors. Surgical risk prediction tools such as the CTP Score, MELD-Na scores, MRS, and the VOCAL-Penn Score are powerful tools to help risk stratify patients based on preoperative factors; however, they should be used as an adjunct alongside good clinical judgment. In the future, decision analysis studies may be helpful to better delineate scenarios in which the benefits of surgery outweigh the risks for patients with cirrhosis with varying predisposition to operative risk.

FUNDING INFORMATION

Nadim Mahmud is supported by the National Institute of Diabetes and Digestive and Kidney Diseases (K08-DK124577). He has also received investigator-initiated funding from Grifols, which is unrelated to this work.

CONFLICTS OF INTEREST

The authors have no conflicts to report.

ORCID

Melissa G. Kaltenbach https://orcid.org/0000–0003–0124–6670
Nadim Mahmud https://orcid.org/0000–0003–1889–3954

REFERENCES

1. Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the United States: a population-based study. J Clin Gastroenterol. 2015;49:690–.
2. Kabbany MN, Selvakumar PKC, Watt K, Lopez R, Akras Za, Zein N, et al. Prevalence of nonalcoholic steatohepatitis-associated cirrhosis in the United States: an analysis of national health and nutrition examination survey data. Am J Gastroenterol. 2017;112:581–7.
3. Tessiatore KM, Mahmud N. Trends in surgical volume and in-hospital mortality among United States cirrhosis hospitalizations. Ann Gastroenterol. 2021;34:85–92.
4. Mahmud N, Fricker Z, Serper M, Kaplan DE, Rothstein KD, Goldberg DS. In-hospital mortality varies by procedure type among cirrhosis surgery admissions. Liver Int. 2019;39:1394–9.
5. Nguyen GC, Correia AJ, Thuluvath PJ. The impact of cirrhosis and portal hypertension on mortality following colorectal surgery: a nationwide, population-based study. Dis Colon Rectum. 2009;52:1367–74.
6. Carbonell AM, Wolfe LG, DeMaria EJ. Poor outcomes in cirrhosis-associated hernia repair: a nationwide cohort study of 32,033 patients. Hernia. 2005;9:353–7.
7. Tandon P, Montano-Loza AJ, Lai JC, Dasarathy S, Merli M. Sarcopenia and frailty in decompensated cirrhosis. J Hepatol. 2021;75(suppl 1):S147–62.
8. Ziser A, Plevak DJ, Wiesner RH, Rakela J, Offord KP, Brown DL. Morbidity and mortality in cirrhotic patients undergoing anesthesia and surgery. J Am Soc Anesthesiol. 1999;90:42–53.
9. Weniger M, D'Haese JG, Angele MK, Kleespies A, Werner J, Hartwig W. Treatment options for chylous ascites after major abdominal surgery: a systematic review. Am J Surg. 2016;211:206–13.
10. Forkin KT, Colquhoun DA, Nemergut EC, Huffmyer JL. The coagulation profile of end-stage liver disease and considerations for intraoperative management. Anesth Analg. 2018;126:46–61.
11. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med. 2011;365:147–56.
12. Islam R, Kundu S, Jha SB, Rivera AP, Monar GVF, Islam H, et al. Cirrhosis and coagulopathy: mechanisms of hemostasis changes in liver failure and their management. Cureus. 2022;14:e23785.
13. Clària J, Stauber RE, Coenraad MJ, Moreau R, Jalan R, Pavesi M, et al. Systemic inflammation in decompensated cirrhosis:

characterization and role in acute-on-chronic liver failure. Hepatology. 2016;64:1249–64.
14. Mahmud N, Fricker Z, Lewis JD, Taddei TH, Goldberg DS, Kaplan DE, et al. Risk prediction models for postoperative decompensation and infection in patients with cirrhosis: a Veterans Affairs Cohort Study. Clin Gastroenterol Hepatol. 2021;20:e1121–34.
15. Freundlich RE, Maile MD, Sferra JJ, Jewell ES, Kheterpal S, Engoren M. Complications associated with mortality in the national surgical quality improvement program database. Anesth Analg. 2018;127:55–62.
16. Saleh ZM, Solano QP, Louissaint J, Jepsen P, Tapper EB. The incidence and outcome of postoperative hepatic encephalopathy in patients with cirrhosis. United European Gastroenterol J. 2021;9:672–80.
17. Friedman LS. The risk of surgery in patients with liver disease. Hepatology. 1999;29:1617–23.
18. Hoteit MA, Ghazale A-H, Bain A-J, Rosenberg E-S, Easley K-A, Anania F-A, et al. Model for end-stage liver disease score versus Child score in predicting the outcome of surgical procedures in patients with cirrhosis. World J Gastroenterol. 2008;14:1774–80.
19. Vanbiervliet G, Giudicelli-Bornard S, Piche T, Berthier F, Gelsi E, Filippi J, et al. Predictive factors of bleeding related to post-banding ulcer following endoscopic variceal ligation in cirrhotic patients: a case-control study. Aliment Pharmacol Ther. 2010;32: 225–32.
20. Dueñas E, Cachero A, Amador A, Rota R, Salord S, Gornals J, et al. Ulcer bleeding after band ligation of esophageal varices: risk factors and prognosis. Dig Liver Dis. 2020;52:79–83.
21. Mahmud N, Fricker Z, Hubbard RA, Ioannou GN, Lewis JD, Taddei TH, et al. Risk prediction models for post-operative mortality in patients with cirrhosis. Hepatology. 2021;73:204–18.
22. Teh SH, Nagorney DM, Stevens SR, Offord KP, Therneau TM, Plevak DJ, et al. Risk factors for mortality after surgery in patients with cirrhosis. Gastroenterology. 2007;132:1261–9.
23. Higashi H, Matsumata T, Adachi E, Taketomi A, Kashiwagi S, Sugimachi K. Influence of viral hepatitis status on operative morbidity and mortality in patients with primary hepatocellular carcinoma. Br J Surg. 1994;81:1342–5.
24. Pei KY, Asuzu DT, Davis KA. Laparoscopic colectomy reduces complications and hospital length of stay in colon cancer patients with liver disease and ascites. Surg Endosc. 2018;32:1286–92.
25. Del Olmo JA, Flor-Lorente B, Flor-Civera B, Rodriguez F, Serra MA, Escudero A, et al. Risk factors for nonhepatic surgery in patients with cirrhosis. World J Surg. 2003;27:647–52.
26. Cheng Y, Xiong X-Z, Wu S-J, Lin YX, Cheng NS. Laparoscopic vs. open cholecystectomy for cirrhotic patients: a systematic review and meta-analysis. Hepatogastroenterology. 2012;59: 1727–34.
27. Kazi A, Finco TB, Zakhary B, Firek M, Gerber A, Brenner M, et al. Acute colonic diverticulitis and cirrhosis: outcomes of laparoscopic colectomy compared with an open approach. J Am Coll Surg. 2020;230:1045–53.
28. Odom SR, Gupta A, Talmor D, Novack V, Sagy I, Evenson AR. Emergency hernia repair in cirrhotic patients with ascites. J Trauma Acute Care Surg. 2013;75:404–9.
29. Andraus W, Pinheiro RS, Lai Q, Haddad LBP, Nacif LS, D'Albuquerque LAC, et al. Abdominal wall hernia in cirrhotic patients: emergency surgery results in higher morbidity and mortality. BMC Surg. 2015;15:1–7.
30. Farnsworth N, Fagan SP, Berger DH, Awad SS. Child-Turcotte-Pugh versus MELD score as a predictor of outcome after elective and emergent surgery in cirrhotic patients. Am J Surg. 2004;188: 580–3.
31. Mosko JD, Nguyen GC. Increased perioperative mortality following bariatric surgery among patients with cirrhosis. Clin Gastroenterol Hepatol. 2011;9:897–901.
32. Beste LA, Leipertz SL, Green PK, Dominitz JA, Ross D, Ioannou GN. Trends in burden of cirrhosis and hepatocellular carcinoma by underlying liver disease in US veterans, 2001–2013. Gastroenterology. 2015;149:1471–82.e5.
33. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol. 2020;73:202–9.
34. Hackett NJ, De Oliveira GS, Jain UK, Kim JYS. ASA class is a reliable independent predictor of medical complications and mortality following surgery. Int J Surg. 2015;18:184–90.
35. Mansour A, Watson W, Shayani V, Pickleman J. Abdominal operations in patients with cirrhosis: still a major surgical challenge. Surgery. 1997;122:730–5; discussion 735–6.
36. Kim SY, Yim HJ, Park SM, Kim JH, Jung SW, Kim JH, et al. Validation of a Mayo post-operative mortality risk prediction model in Korean cirrhotic patients. Liver Int. 2011;31:222–8.
37. Wong NZ, Mahmud N. The imperative for an updated cirrhosis surgical risk score. Ann Hepatol. 2020;19:341–.
38. Mahmud N, Fricker Z, Panchal S, Lewis JD, Goldberg DS, Kaplan DE. External validation of the VOCAL-Penn cirrhosis surgical risk score in 2 large, independent health systems. Liver Transpl. 2021;27:961–70.
39. Mahmud N, Fricker Z, Lewis JD, Taddei TH, Goldberg DS, Kaplan DE. Risk prediction models for postoperative decompensation and infection in patients with cirrhosis: a Veterans Affairs Cohort Study. Clin Gastroenterol Hepatol. 2022;20: e1121–34.
40. Mahmud N, Panchal S, Turrentine FE, Kaplan DE, Zaydfudim VM. Performance of risk prediction models for post-operative mortality in patients undergoing liver resection. Am J Surg. 2022; 225:198–205.
41. Mahmud N, Kaplan DE, Taddei TH, Goldberg DS. Frailty is a risk factor for postoperative mortality in patients with cirrhosis undergoing diverse major surgeries. Liver Transpl. 2021;27: 699–710.
42. Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L, Plauth M, Parés A. EASL Clinical Practice Guidelines on nutrition in chronic liver disease. J hepatology. 2019;70(1):172–93.
43. Lai JC, Tandon P, Bernal W, Tapper EB, Ekong U, Dasarathy S, et al. Malnutrition, frailty, and sarcopenia in patients with cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74:1611–44.
44. Plank LD, Gane EJ, Peng S, Muthu C, Mathur S, Gillanders L, et al. Nocturnal nutritional supplementation improves total body protein status of patients with liver cirrhosis: a randomized 12-month trial. Hepatology. 2008;48:557–66.
45. Vinaixa C, Martínez Palli G, Milliken D, Sellers D, Dharancy S, Spiro M, et al. The role of prehabilitation on short-term outcomes after liver transplantation—a review of the literature and expert panel recommendations. Clin Transplant. 2022;36:e14686.
46. Englesbe MJ, Grenda DR, Sullivan JA, Derstine BA, Kenney BN, Sheetz KH, et al. The Michigan Surgical Home and Optimization Program is a scalable model to improve care and reduce costs. Surgery. 2017;161:1659–66.
47. Northup PG, Garcia-Pagan JC, Garcia-Tsao G, Intagliata NM, Superina RA, Roberts LN, et al. Vascular liver disorders, portal vein thrombosis, and procedural bleeding in patients with liver disease: 2020 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;73:366–413.
48. Shenoy A, Louissaint J, Shannon C, Tapper EB, Lok AS. Viscoelastic testing prior to non-surgical procedures reduces blood product use without increasing bleeding risk in cirrhosis. Dig Dis Sci. 2022;67:1–10.
49. Davis JPE, Northup PG, Caldwell SH, Intagliata NM. Viscoelastic testing in liver disease. Ann Hepatol. 2018;17:205–13.

50. Terrault N, Chen YC, Izumi N, Kayali Z, Mitrut P, Tak WY, et al. Avatrombopag before procedures reduces need for platelet transfusion in patients with chronic liver disease and thrombocytopenia. Gastroenterology. 2018;155:705–18.
51. Bhangui P, Laurent A, Amathieu R, Azoulay D. Assessment of risk for non-hepatic surgery in cirrhotic patients. J Hepatol. 2012;57:874–4.
52. Tabchouri N, Barbier L, Menahem B, Perarnau JM, Muscari F, Fares N, et al. Original study: transjugular intrahepatic portosystemic shunt as a bridge to abdominal surgery in cirrhotic patients. J Gastrointest Surg. 2019;23:2383–90.
53. García-Pagán JC, Saffo S, Mandorfer M, Garcia-Tsao G. Where does TIPS fit in the management of patients with cirrhosis? JHEP Rep. 2020;2:100122.
54. Vinet E, Perreault P, Bouchard L, Bernard D, Wassef R, Richard C, et al. Transjugular intrahepatic portosystemic shunt before abdominal surgery in cirrhotic patients: a retrospective, comparative study. Can J Gastroenterol. 2006;20:401–4.
55. Serstė T, Francoz C, Durand F, Rautou PE, Melot C, Valla D, et al. Beta-blockers cause paracentesis-induced circulatory dysfunction in patients with cirrhosis and refractory ascites: a cross-over study. J Hepatol. 2011;55:794–9.
56. Serstė T, Melot C, Francoz C, Durand F, Rautou PE, Valla D, et al. Deleterious effects of beta-blockers on survival in patients with cirrhosis and refractory ascites. Hepatology. 2010;52:1017–22.
57. Sotiropoulos GC, Tsaparas P, Kykalos S, Machairas N, Molmenti EP, Paul A, et al. From laparoscopic cholecystectomy to liver transplantation: when the gallbladder becomes the pandora s box. Chirurgia (Bucur). 2016;111:450–4.
58. Lopez-Delgado JC, Esteve F, Javierre C, Ventura JL, Mañez R, Farrero E, et al. Influence of cirrhosis in cardiac surgery outcomes. World J Hepatol. 2015;7:753–60.
59. Parikh ND, Chang YH, Tapper EB, Mathur AK. Outcomes of patients with cirrhosis undergoing orthopedic procedures: an analysis of the nationwide inpatient sample. J Clin Gastroenterol. 2019;53:e356–61.
60. Senzolo M, Sartori MT, Lisman T. Should we give thromboprophylaxis to patients with liver cirrhosis and coagulopathy? HPB. 2009;11:459–64.
61. Intagliata NM, Henry ZH, Shah N, Lisman T, Caldwell SH, Northup PG. Prophylactic anticoagulation for venous thromboembolism in hospitalized cirrhosis patients is not associated with high rates of gastrointestinal bleeding. Liver International. 2014;34:26–32.
62. Fagan SP, Awad SS, Berger DH. Management of complicated umbilical hernias in patients with end-stage liver disease and refractory ascites. Surgery. 2004;135:679–82.
63. de Goede B, van Rooijen MMJ, van Kempen BJH, Polak WG, de Man RA, Taimr P, et al. Conservative treatment versus elective repair of umbilical hernia in patients with liver cirrhosis and ascites: results of a randomized controlled trial (CRUCIAL trial). Langenbecks Arch Surg. 2021;406:219–5.
64. Telem DA, Schiano T, Goldstone R, Han DK, Buch KE, Chin EH, et al. Factors that predict outcome of abdominal operations in patients with advanced cirrhosis. Clin Gastroenterol Hepatol. 2010;8:451–7; quiz e58.
65. Sharpton SR, Terrault NA, Tavakol MM, Posselt AM. Sleeve gastrectomy prior to liver transplantation is superior to medical weight loss in reducing posttransplant metabolic complications. Am J Transplant. 2021;21:3324–2.
66. Aminian A, Al-Kurd A, Wilson R, Bena J, Fayazzadeh H, Singh T, et al. Association of bariatric surgery with major adverse liver and cardiovascular outcomes in patients with biopsy-proven nonalcoholic steatohepatitis. JAMA. 2021;326:2031–42.
67. Pestana L, Swain J, Dierkhising R, Kendrick ML, Kamath PS, Watt KD. Bariatric surgery in patients with cirrhosis with and without portal hypertension: a single-center experience. Mayo Clin Proc. 2015;90:209–15.
68. Mahmud N, Goldberg DS, Abu-Gazala S, Lewis JD, Kaplan DE. Modeling optimal clinical thresholds for elective abdominal hernia repair in patients with cirrhosis. JAMA Netw Open. 2022;5: e2231601.
69. Johnson KM, Newman KL, Berry K, Itani K, Wu P, Kamath PS, et al. Risk factors for adverse outcomes in emergency versus nonemergency open umbilical hernia repair and opportunities for elective repair in a national cohort of patients with cirrhosis. Surgery. 2022;172:184–92.

How to cite this article: Kaltenbach MG, Mahmud N. Assessing the risk of surgery in patients with cirrhosis. Hepatol Commun. 2023;7:e0086. https://doi.org/10.1097/HC9.0000000000000086