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Perioperative Evaluation and Management of Patients with Cirrhosis: Risk Assessment, Surgical Outcomes, and Future Directions

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Abstract

Background and aims: Patients with cirrhosis are at increased risk of perioperative morbidity and mortality. We provide a narrative review of the available data regarding perioperative morbidity and mortality, risk assessment, and management of patients with cirrhosis undergoing non-hepatic surgical procedures.

Methods: We conducted a comprehensive review of the literature from 1998–2018 and identified 87 studies reporting perioperative outcomes in patients with cirrhosis. We extracted elements of study design and perioperative mortality by surgical procedure, Child-Turcotte-Pugh (CTP) class

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and Model for End-stage Liver Disease (MELD) score reported in these 87 studies to support our narrative review.

Results: Overall, perioperative mortality is 2–10 times higher in patients with cirrhosis compared to patients without cirrhosis, depending on the severity of liver dysfunction. For elective procedures, patients with compensated cirrhosis (CTP Class A, or MELD <10) have minimal increase in operative mortality. CTP Class C patients (or MELD >15) are at high risk for mortality; liver transplantation or alternatives to surgery should be considered. Very little data exist to guide perioperative management of patients with cirrhosis, so most recommendations are based on case series and expert opinion. Existing risk calculators are inadequate.

Conclusions: Severity of liver dysfunction, medical comorbidities and the type and complexity of surgery, including whether it is elective versus emergent, are all determinants of perioperative mortality and morbidity in patients with cirrhosis. There are major limitations to the existing clinical research on risk assessment and perioperative management, which warrant further investigation.

Keywords

Surgery outcomes; liver cirrhosis; perioperative risk assessment; perioperative management

Introduction

Patients with cirrhosis are at increased risk of perioperative morbidity and mortality. The multiple adverse effects of hepatic dysfunction on anatomy, physiology, and metabolism in cirrhosis present unique perioperative challenges including the accurate assessment of perioperative risk, the impact of anesthesia, risks unique to each surgical procedure, and postoperative care. For elective procedures, careful preoperative evaluation is essential to ensure a proper risk benefit assessment for elective surgery and to guide optimization if surgery is elected as the best treatment option.

This review's purpose is to provide a narrative summary of the available data regarding perioperative morbidity and mortality in patients with cirrhosis undergoing non-hepatic surgical procedures. Surgical procedures involving the liver, such as hepatic resection, shunts for portal hypertension, and liver transplantation, require special consideration and are not the focus of this review. It is also intended to complement the recently published American Gastroenterological Association (AGA) Clinical Practice Update[1] by including more details on the pathophysiology of cirrhosis, discussing risk estimators, providing reference tables for clinicians and investigators, and identifying areas for future research.

Methods

We conducted a literature review from 1998–2018 to identify studies reporting perioperative outcomes in patients with cirrhosis by surgical procedure and cirrhosis severity. We identified 87 studies extracted elements of study design and reported perioperative outcomes by type of surgical procedure, Child-Turcotte-Pugh (CTP) class, or MELD score from each (Table 2). We did not conduct a systematic review and meta-analysis but instead synthesized the findings of these studies in a narrative review.

Preoperative evaluation and management

Perioperative mortality is 2–10 times higher in patients with cirrhosis compared to patients without cirrhosis[2–5]. The causes are multifactorial (Figure 1). Preoperative evaluation of cirrhotic patients should focus on identifying which factors are present and how to optimize them prior to the planned operation.

Preoperative Evaluation—Along with routine preoperative evaluation of cardiac risk, functional status, and comorbidities,[6] it is vital to assess the degree of liver dysfunction in patients with cirrhosis by determining the presence of portal hypertension, synthetic dysfunction, and current or prior decompensations (varices with or without hemorrhage, ascites, hepatic encephalopathy). The Child-Turcotte-Pugh (CTP) and Model of End Stage Liver Disease (MELD) scores quantify disease severity (Table 1). Patients with greater liver dysfunction are at higher risk of decompensation from the physiologic stress of surgery[2, 7], and portal hypertension is a risk factor for mortality[8, 9].

In addition to a physical exam to assess for clinical manifestations of portal hypertension (e.g. ascites, encephalopathy), clinicians may consider an esophagogastroduodenoscopy (EGD) to screen for varices and/or portal gastropathy and an ultrasound or CT scan to assess for ascites, splenomegaly, and portosystemic collaterals. For particularly high risk elective procedures, further testing may occasionally include measurement of the hepatic venous pressure gradient (HVPG)—the gold standard for portal pressure measurement, calculated as the difference between the wedged and free hepatic venous pressure[10]. This is an invasive procedure performed by interventional radiologists and is not available in all centers. Values ≥10 mmHg indicate clinically significant portal hypertension[11]. Elevated liver stiffness>20–25 kilopascal (kPa) estimated by transient elastography may be a surrogate, noninvasive marker for portal hypertension[11, 12]. Hepatopulmonary syndrome is rare, but because hypoxia is a key feature, pulse oximetry is a simple initial test. If hypoxia is discovered, contrast echocardiography (i.e. with agitated saline; “bubble study”) can be used to further evaluate it[13].

Preoperative management of cirrhosis-associated conditions

Portal Hypertension: Portal hypertension may increase the liver’s susceptibility to hemodynamic changes during surgery, which can cause hepatic ischemia and decompensation[14]. Portosystemic collaterals alter typical anatomy and may increase the risk of intraoperative bleeding. Before elective procedures, it is prudent to complete indicated screening for esophageal varices by upper endoscopy per current AASLD guidelines[11]. If there are no visible varices, endoscopy should be repeated every 2 years (or every 3 years, if the cause of the liver injury has ceased, e.g. viral elimination or alcohol abstinence). If there are small varices, endoscopy should be repeated every 1–2 years. For medium or large varices, a non-selective beta blocker (propranolol or nadolol) may decrease bleeding risk by lowering portal venous pressure[15, 16]. The beta blocker should be started at least several days before surgery to assess effectiveness and tolerability[15]. Carvedilol also decreases variceal bleeding risk; patients on carvedilol for cardiac indications do not need to change to a non-selective beta blocker. If varices are banded, this should be completed at least 2 weeks prior to surgery to allow any post-banding ulcers to heal[17]. Transjugular intrahepatic

portosystemic shunt (TIPS) can decrease perioperative GI bleeding for patients with severe portal hypertension[18, 19]. However, hepatic encephalopathy may worsen.

Ascites: The presence of ascites increases the risk of peritoneal infection, ascitic fluid leak from surgical sites, and wound dehiscence in abdominal surgery[20]. Optimal ascites control with nearly undetectable levels of intraabdominal free fluid is preferred prior to non-emergent surgery. The AGA Clinical Practice Update recommends that abdominal hernia surgery be avoided unless ascites is completely controlled medically, except in cases of incarceration or suspected strangulation[1]. Patients may require diuretics, salt and fluid restriction, and therapeutic paracentesis. Care must be taken to avoid hypovolemia and renal insufficiency when dosing diuretics or performing large-volume paracentesis.

Another option for patients with large-volume ascites is preoperative TIPS. When performed for ascites management by experienced interventionalists prior to non-elective procedures, TIPS is anecdotally associated with improved perioperative outcomes[21, 22]. Higher-quality data from a small case-control study do not support routine use of TIPS before non-emergent procedures[23]. However, it has been used as a bridge to surgery in select patients, with a systematic review reporting that preoperative TIPS allowed for abdominal surgery in 64 patients with portal hypertension[24, 25].

Encephalopathy: Encephalopathy should be controlled and ideally reversed prior to non-emergent surgery using lactulose and/or rifaximin. Serum ammonia level correlates poorly with presence of hepatic encephalopathy thus should not be used for diagnosis or titrating treatment[26]. Lactulose 30–45 mL three to four times per day is generally required to achieve 2–4 soft stools per day and should be continued perioperatively. Rifaximin 550 mg twice daily can be added if lactulose is insufficient. If a patient is encephalopathic and unable to take food by mouth postoperatively, lactulose enemas of 300 mL lactulose in 1000 mL water can be given up to every two hours.

Coagulopathy: Cirrhosis causes alterations in prothrombotic and anticoagulant processes following even minor procedures. Cirrhotic patients have higher rates of hemorrhage and hematomas after minor invasive procedures[27]. Traditional laboratory tests for coagulopathy are difficult to interpret amidst liver dysfunction[28]. Platelet count and international normalized ratio (INR) may not correlate with post-procedural bleeding complications[29]. Bleeding time is multifactorial and should not be used for preoperative assessment[30]. Thromboelastography is an alternate option for coagulation testing, but the results may be difficult for clinicians unfamiliar with the test to interpret.

There is an uncertain role for vitamin K, fresh frozen plasma (FFP), factor VIIA, and cryoprecipitate to treat coagulopathy preoperatively in cirrhotic patients. Vitamin K 10 mg per day for three days prior to surgical procedures is sometimes recommended, though Vitamin K use in cirrhotic patients lacks high-quality data[31], and retrospective data suggests it does not reduce bleeding events[32]. FFP may transiently normalize laboratory values[33], but this may not be beneficial—the additional volume can increase bleeding by raising intravascular venous pressure[34]. There are scant data regarding the efficacy of cryoprecipitate and factor VIIA in cirrhotic patients[33], and randomized control trials do not

support factor VIIA for treatment of massive bleeding in a general population[35]. While there is insufficient data on pre-surgical correction of coagulopathy using pharmaceuticals or blood products, AASLD recommends consideration of their use as part of a rescue strategy for post-procedure bleeding[36], and experts generally recommend administration of cryoprecipitate for fibrinogen levels below 100 mg/dL.

Thrombocytopenia: A goal of >50,000 platelets/mm^3 is often used for average risk procedures[37], and experts recommend transfusion to reach this threshold. However, increasing data suggest that transfusing to a threshold may lead to unnecessary administration of blood products without decreasing hemorrhage or other adverse events during or after the procedure[33]. Perioperative transfusion may increase intravascular pressure, worsening the complications from portal hypertension. Platelet stimulating agents may increase the platelet count but should be used with caution, as they also may increase the risk of thrombotic events[33].

Immunologic deficiencies and inflammatory dysregulation: Patients with cirrhosis exhibit both immunologic deficiencies and an exaggerated inflammatory response[38, 39]. Cirrhosis leads to decreased synthesis of important proteins needed for innate immune response, cytopenia, and impaired cellular responses[39]. There is also increased systemic inflammation secondary to translocation of bacteria and bacterial products because of gut barrier dysfunction and dysbiosis[40, 41]. This disordered inflammatory balance may be responsible for the increased risk of decompensation following surgery. Currently, there are no validated prognostic markers of immune function or inflammation in patients with cirrhosis. We recommend that patients already on chronic antibiotics (such as for spontaneous bacterial peritonitis (SBP) prophylaxis), have those continued perioperatively, but there is insufficient data to recommend any additional prophylactic antibiotics beyond those routinely used intraoperatively.

Malnutrition and sarcopenia: Cirrhotic patients face multiple nutritional issues, including malnutrition, micronutrient deficiencies, and sarcopenia. Among cirrhotic patients, the prevalence of malnutrition is estimated at 80%[42], and the prevalence of sarcopenia ranges from 25–70%[43]. Nutrition can be assessed through the Royal Free Hospital-Subjective Global Assessment, which includes BMI, mid-arm muscle circumference, and dietary intake[42]. Sarcopenia can be detected through imaging, bioimpedance, or anthropometry[44]. Patients with cirrhosis can be sarcopenic even with a normal or elevated body mass index (BMI)[44]. Clinically, sarcopenia is associated with 3-times higher mortality among cirrhotic patients[43]. In surgery, sarcopenia is associated with delayed wound healing and poor surgical outcomes[45]. Patients should be encouraged to maintain their weight and eat a diet abundant in macro- and micronutrients[42]. In some patients, this may require consulting a nutritionist. Nutritional support for at-risk patients is associated with improved surgical outcomes[46].

Viral hepatitis B and C treatment: There is little data regarding the effect of antiviral treatments on non-hepatic surgical outcomes in patients with cirrhosis and concomitant hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. However, antiviral HBV treatment improves liver function, coagulopathy, and mortality in patients at risk of HBV

reactivation following surgery for hepatocellular carcinoma[47, 48]. HBV treatment should be initiated for patients with active disease and considered for patients with latent infection at high risk for reactivation (e.g. older patients, patients with immunosuppressive conditions or on immunosuppressive medications)[49]. HCV treatment can improve liver function, even in patients with advanced cirrhosis, and may reduce the frequency of decompensations[50]. Therefore, if the surgery is elective, it may be beneficial to delay until after HCV eradication, which is achieved in ~95% of patients with current antiviral regimens.

Alcohol cessation: Acute alcoholic hepatitis is a strict contraindication to surgery because of the high risk of postoperative hepatic failure and death[51, 52]. However, for patients with cirrhosis who regularly use alcohol, there is little data to guide recommendations. Among US Veterans screened for alcohol misuse in the year prior to surgery using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), those with scores ≥5 (out of 12) had significantly more postoperative complications, compared to patients with lower scores[53]. Complication rates ranged from 5.6% in those with AUDIT-C scores 1–4, to 14.0% in those with scores 11–12. The authors concluded that patients with scores ≥5 should be counseled that their alcohol use increases their risk for serious perioperative complications and encouraged to abstain preoperatively. A similar study showed an association between AUDIT-C scores and complications in male veterans undergoing total joint arthroplasty[54]. Only one small randomized trial has studied preoperative alcohol cessation, but it excluded patients with cirrhosis[55]. It showed that abstinence for one month prior to colorectal surgery was associated with a lower risk of complications (31% v 74%).

Altered medication metabolism: Loss of hepatocytes, shunting of blood through portosystemic collaterals, decreased production of medication-binding proteins, altered volume of distribution, and renal dysfunction are among the many factors that modify drug metabolism in cirrhosis[56]. This complicates both procedural anesthesia and postoperative pain management[57]. The degree of metabolic impairment is correlated with severity of hepatic dysfunction. Hepatic elimination tests of sorbitol, erythromycin, midazolam, and other substances to quantify metabolic impairment exist but are not widely used in clinical practice and therefore are not recommended for empiric dose adjustment calculations of medications[56].

Predictors of perioperative mortality in patients with cirrhosis

As shown in Table 2, the severity of liver dysfunction, estimated by CTP or MELD score, strongly modifies postoperative mortality, as does surgery type and urgency. Additionally, comorbidities that impact mortality in non-cirrhotic patients, such as diabetes, congestive heart failure, and advanced age, are also important in patients with cirrhosis. Therefore, to adequately estimate postoperative mortality, we need models that incorporate cirrhosis-related, surgery-related and comorbidity-related predictors (Figure 2). Such models do not currently exist. Most risk prediction for cirrhotic patients relies on clinically selected factors or limited models.

CTP Score—Quantification of cirrhosis severity to predict surgical outcome was described by Child and Turcotte in the 1960s and modified in 1973 by Pugh[58, 59]. CTP score

categorizes patients as Class A, B or C based on the presence and severity of encephalopathy and/or ascites, plus serum albumin, bilirubin and PT-INR. For many non-hepatic abdominal surgeries, patients with CTP Class A cirrhosis have a mortality rate of <5–10%; Class B 10–40%; and Class C 20–100% (Table 3).

MELD—The MELD score was developed to predict mortality in patients undergoing TIPS[60] and is most commonly used to prioritize patients for liver transplant, but it is also predicts perioperative mortality[1, 61–64]. It is calculated using only laboratory tests (bilirubin, PT-INR, and creatinine). Higher MELD scores correlate with worse outcomes (Table 3)[61–64]. The recent AGA Clinical Practice Update presents evidence on a range of the proposed cut-points for MELD score by surgical type. The heterogeneity between studies and surgeries limits the ability to propose a single threshold value for what constitutes a “high-risk” preoperative MELD score. The risk of postoperative mortality and MELD score are linearly correlated, especially for values of 8 and above[61, 63, 65]. For cardiovascular surgery, research has shown that CTP score may be a better outcome predictor than MELD[66, 67]. Reasons for this discrepancy are unclear.

Mayo model—A calculator Mayo Clinic researchers developed uses age, American Society of Anesthesiologists (ASA) classification, and MELD score to predict postoperative mortality in patients with cirrhosis[61]. It is based on a retrospective study of 772 patients undergoing abdominal, cardiovascular or orthopedic surgeries conducted in 1980–1990 and 1994–2004. Limitations of the study include the exclusion of common low risk surgeries (appendectomy, herniorrhaphy, laparoscopic cholecystectomy) and inability of the calculator to provide estimates stratified by procedure types and urgency. Surgery type and emergent status were not statistically significant in their multivariable model, but this may be due to an insufficient sample size or inclusion of ASA score in the model while excluding ASA class 5 patients, all of whom underwent emergency surgery.

Adequate Operative Treatment for Liver Cirrhosis (ADOPT-LC) Score—Sato, *et al.* studied 2197 cirrhotic patients in Japan undergoing major surgery (abdominal, breast, musculoskeletal, cardiovascular, and urologic)[68]. For patients undergoing elective surgery, age, CTP class, Charlson Comorbidity Index (CCI), and duration of anesthesia predicted in-hospital mortality. Their ADOPT-LC score is based on this model. Limitations include the need to enter 18 clinical data points from past medical history, and the need to estimate duration of anesthesia, although anesthesia time ranges are broad (< 3, 3–7, and >7 hours).

Limitations for these calculators include lack of external validation, limited numbers, and insufficient detail to estimate procedure-specific risks. A common surgical risk estimator for non-cirrhotic patients, the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) score, does not distinguish between cirrhotic and non-cirrhotic patients, also limiting its use in this population. Cardiac risk calculators such as the Revised Cardiac Risk Index (RCRI) and Gupta perioperative cardiac risk score are similarly inadequate.

Surgery-specific perioperative morbidity and mortality in patients with cirrhosis

Type and complexity of surgery affect perioperative mortality and morbidity in patients with cirrhosis (Table 2). Among gastrointestinal surgeries, the highest postoperative mortality is after colorectal resection (13%–26%), esophagectomy (11%–25%) and pancreaticoduoenectomy (11.9%–17%). The lowest postoperative mortality is after laparoscopic cholecystectomy and elective uncomplicated hernia repair (0% in most studies). High mortality was reported after coronary artery bypass graft and valvular heart surgery, whereas low mortality was reported after elective hip and knee replacements. Patients with CTP class C disease or high MELD score had very high mortality across all surgical procedures.

Common abdominal surgical procedures—Umbilical and inguinal hernia repairs and cholecystectomies are more common in patients with cirrhosis. When performed in an *elective* setting in patients with a MELD score <15 or CTP class A or B, perioperative mortality is low and not significantly increased compared to non-cirrhotic patients[69]. For these three procedures, cirrhosis is not a contraindication when well-compensated. Even for patients with some high-risk features, such as ascites, elective surgery after medical optimization may still be reasonable.

Emergent versus elective surgery—Although many studies group elective and emergent procedures, urgency is a strong predictor of worse outcomes[7]. Patients undergoing emergent surgery have a 4 to >10 times higher rate of postoperative mortality[7, 8, 68–73]. Emergent colorectal surgery is associated with 20–35% postoperative mortality[8, 71], emergent cholecystectomy with 20% postoperative mortality[74], and emergent hernia repair with 10–22% postoperative mortality[70, 75, 76]. Emergent surgery is also associated with a higher rate of postoperative complications, with rates of major complications 5–7 times higher than for elective procedures[70, 72, 77]. Therefore, in stable and well-compensated patients, it may be appropriate to consider elective surgery to reduce the likelihood of requiring an emergent surgery in the future, although this has not been prospectively studied. For example, elective umbilical hernia repair might prevent future presentation with incarceration, which could require emergency surgery. If a procedure for a cirrhotic patient is potentially life-saving and must be conducted emergently, it is imperative to properly inform the patients about the risks. Consideration in these cases should also be given to less-invasive alternatives, which may include ongoing medical therapy, delay of procedure to allow for optimization, interventional radiology, or palliative care.

Trauma—Trauma is associated with high mortality for cirrhotic patients, with an adjusted likelihood of mortality exceeding five times that of non-cirrhotic patients[78, 79]. Furthermore, cirrhotic patients who undergo emergent laparotomy have 2–7 times higher rates of mortality when compared to matched non-cirrhotic patients also undergoing emergent laparotomy[78–80], and cirrhotic patients are more likely to suffer postoperative ARDS, coagulopathy, and sepsis[78, 80]. Cirrhotic patients requiring emergent laparotomy with temporary abdominal closure fare particularly poorly when compared to non-cirrhotic controls[80]. They have higher rates of mortality (67% vs 21% in controls), coagulopathy, pressor requirements, and multiorgan failure.

Intraoperative care

Cardiovascular assessment and intraoperative monitoring—Cirrhosis is characterized by a hyperdynamic state with low systemic vascular resistance, tachycardia, and elevated cardiac output analogous to sepsis[81]. Therefore, invasive blood pressure monitoring with an intra-arterial catheter is often employed perioperatively, particularly for patients with advanced cirrhosis. Unfortunately, the central venous catheter does not accurately measure blood volume or fluid responsiveness[82], however it may be useful for administration of drugs such as vasopressors. For high-risk operations, transesophageal echocardiography offers another way to monitor cardiac status intraoperatively. Although it is possible for the probe to cause rupture of esophageal varices, the reported incidence in liver transplant operations is relatively low (<1%)[83, 84].

Anesthetic technique and medications—To avoid further liver damage, the overarching intraoperative goals are to maintain hepatic blood flow and oxygen supply and to minimize exposure to hepatotoxic medications. There is limited evidence to guide decisions regarding the use of neuraxial anesthesia (spinal or epidural), general anesthesia or modified anesthesia care (MAC). Because of concerns for spinal epidural hematoma in the setting of coagulopathy or thrombocytopenia, general anesthesia is used more often than neuraxial anesthesia for major surgery[85]. However, uniformly accepted thresholds to safely perform neuraxial anesthesia are not known, and there are few studies reporting its use in cirrhotic patients[76].

For induction of anesthesia, a variety of agents such as propofol, etomidate, and ketamine are available. Propofol may be preferred because of its rapid redistribution[86]. Longer half-life and increased levels of unbound (i.e., free) drug lead to increased sedative effect and duration of circulating benzodiazepines; this in turn may precipitate encephalopathy. Shorter-acting agents, such as midazolam, are preferred at reduced dosages and with careful monitoring.

Volatile (i.e., inhaled) anesthetic agents include halothane, isoflurane, sevoflurane and desflurane. Because of adverse liver effects, occasionally severe, halothane is not used in the United States or Europe but remains a common agent in other countries due to its low cost[87]. Two forms of halothane hepatotoxicity are recognized: 1) a relatively common (20–30% of patients), self-limited transaminitis without or with only mild symptoms and 2) “halothane hepatitis” which is rarer, immunologically mediated, and causes severe hepatitis which may progress to acute liver failure. The newer agents undergo less hepatic metabolism, thereby decreasing the likelihood of hepatotoxicity, and have less effect on hepatic blood flow, making them safer in patients with cirrhosis[88]. For neuromuscular blockade, atracurium and cisatracurium do not require hepatic metabolism and are the preferred agents[85, 88].

Postoperative management

Encephalopathy—For patients at increased risk of encephalopathy due to severity of cirrhosis or history of encephalopathy, bowel movements should be monitored, and lactulose administered, if needed, aiming for 2–4 per day as discussed above. Dietary protein intake should not be restricted[14]. If encephalopathy occurs, it should be managed with lactulose or

polyethylene glycol 3350-Electrolyte Solution, and possibly rifaximin. If a patient is unable to swallow, a nasogastric tube may facilitate dosing, or enemas can be used. Triggers of encephalopathy, including GI bleeding, infection, central nervous system depressing medications, electrolyte disturbances, hypoxia, constipation, and renal insufficiency should be considered.

Volume status—Renal function should be monitored daily. For patients on chronic diuretics, these can be restarted after surgery if the patient is stable, can take oral medications, and has preserved renal function. Judicious fluid and electrolyte management is also essential to avoid accumulation of ascites or edema while maintaining adequate intravascular volume to perfuse the kidneys. In patients with gastroesophageal varices, fluid overload or over-transfusion should be specifically avoided because of increased risk of bleeding[34]. Patients with abdominal incisions may require therapeutic paracentesis or placement of an intra-abdominal drain to allow for controlled drainage of ascites and reduce strain on the wound[21, 89].

Postoperative SBP—Patients on prophylactic antibiotics for SBP should continue them postoperatively. Current guidelines do not cover the evaluation of postoperative SBP in individuals who have undergone intraabdominal surgery. Cell-count-based thresholds for diagnosis may be confounded by postoperative inflammatory changes[90]. However, it is important to have a high index of suspicion. Patients suspected to have SBP-related symptoms (fever, encephalopathy, worsening abdominal pain) should receive empiric antibiotics until cultures and sensitivities allow for narrowing or stopping antimicrobial therapy. SBP treatment should not preclude further evaluation of other potential postoperative complications, including hepatic decompensation, clot, wound infection, and others.

Pain management—Analgesia is notoriously challenging in patients with cirrhosis[57]. Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided because of the risk of gastrointestinal bleeding and renal toxicity. In patients not using alcohol, acetaminophen may be safely used at total daily dose <2 grams per day. Opioids may be used with caution. Decreased clearance and increased bioavailability results in drug accumulation with deleterious effects. In general, reduced dosages of opioids and increased dosing intervals is recommended[57, 91]. Meperidine should be avoided in patients with liver disease because its metabolite can cause central nervous system toxicity[57]. With appropriate reduction of dose and frequency, fentanyl and hydromorphone are better choices due to the absence of toxic metabolites.

Venous thromboembolism (VTE) prophylaxis—Cirrhotic patients are at risk of VTE postoperatively, especially after orthopedic surgery or if immobilized[92]. Importantly, the presence of coagulation abnormalities in the INR or platelet count do not protect patients[93]. There is limited data on the safety and efficacy of pharmacologic VTE prophylaxis in cirrhotic patients. Evidence suggests it may be safe in patients without profound thrombocytopenia (<15,000–50,000)[94, 95], but current guidelines do not provide definite guidance regarding prophylaxis of cirrhotic patients[96].

Rescue transplantation—For patients who are potential transplant candidates and require a prior non-urgent operation, it is reasonable to complete a transplant work up prior to surgery to expedite listing for an organ in case of post-operative hepatic failure. Published cohort data on postoperative rescue transplantation is largely from post-hepatectomy acute liver failure. In these cases, transplantation offers a highly morbid but life-saving treatment for an otherwise fatal condition[97, 98]. Case reports suggest that this also holds true for patients who receive rescue transplantation following non-hepatic procedures[21]. For liver transplant candidates with an estimated wait time of 3 months or less, elective procedures should be postponed if MELD>20, and if MELD is 12–19, a full transplant work up should be completed prior to surgery[61]. For potential transplant candidates, the general surgery team is advised to discuss surgical plans with the transplant team beforehand. This may allow for simultaneous procedures (e.g. cholecystectomy at the time of transplant) and avoidance of procedures that might complicate transplant surgery, such as the placement of mesh for hernia repair that would interfere with the field for transplant exposure.

Limitations of current research

The major limitations of the currently available research highlighted in Table 4 are that sample sizes in many studies have been small, data are often from single-center retrospective chart review, control groups are infrequently available, and some data are relatively old. Because of limited numbers of cases for certain types of surgical procedures and the even lower frequency of their use in cirrhotic patients, studies have often been retrospective over a relatively long time period. For earlier time periods, those surgeries may not reflect current best practices or technologies. These limitations raise issues of selection bias, confounding, and generalizability and highlight the need for prospective, randomized, and multi-center studies.

Conclusions

The severity and sequelae of cirrhosis, the type and complexity of surgery, and the urgency of an operation all affect perioperative morbidity and mortality. Patients with compensated cirrhosis (CTP Class A, or MELD<10) and few comorbidities generally tolerate surgery well. Risks and benefits of elective surgery should be weighed for CTP Class B patients (MELD 11–15); preoperative optimization and perioperative monitoring are essential for this moderate-risk group. CTP Class C patients (MELD>15) are at high risk for mortality; liver transplantation or alternatives to surgery should be considered. There are major limitations to the existing clinical research on risk assessment and perioperative management, which warrant further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ACS NSQIP	American College of Surgeons National Surgical Quality Improvement Program
ADOPT-LC	Adequate Operative Treatment for Liver Cirrhosis
AGA	American Gastroenterological Association
AKI	acute kidney injury
aPTT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
ASA	American Society of Anesthesiologists
ATN	acute tubular necrosis
AUDIT-C	Alcohol Use Disorders Identification Test-Consumption
BMI	body mass index
CTP	Child-Turcotte-Pugh
EGD	esophagogastroduodenoscopy
GI	gastrointestinal
HBV	hepatitis B virus
HCV	hepatitis C virus
HVPG	hepatic venous pressure gradient
INR	international normalized ratio
kPa	kilopascal
MELD	Model of End-Stage Liver Disease
NSAID	Non-steroidal anti-inflammatory drug
PT	prothrombin time
RCRI	Revised Cardiac Risk Index
TIPS	transjugular intrahepatic portosystemic shunt
VTE	venous thromboembolism

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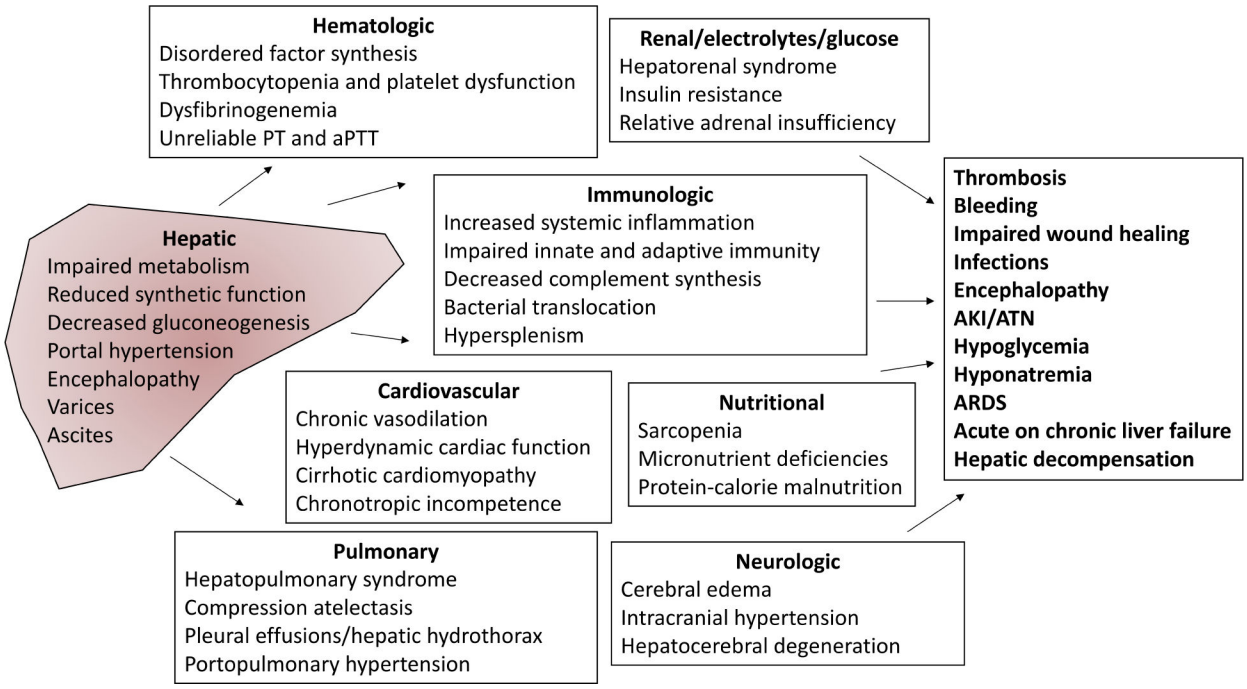

Figure 1.

Metabolic, anatomic, and physiologic changes in cirrhosis and potential surgical consequences. Abbreviations: aPTT=activated partial thromboplastin time, AKI=acute kidney injury, ARDS=acute respiratory distress syndrome, ATN=acute tubular necrosis, PT=prothrombin time.

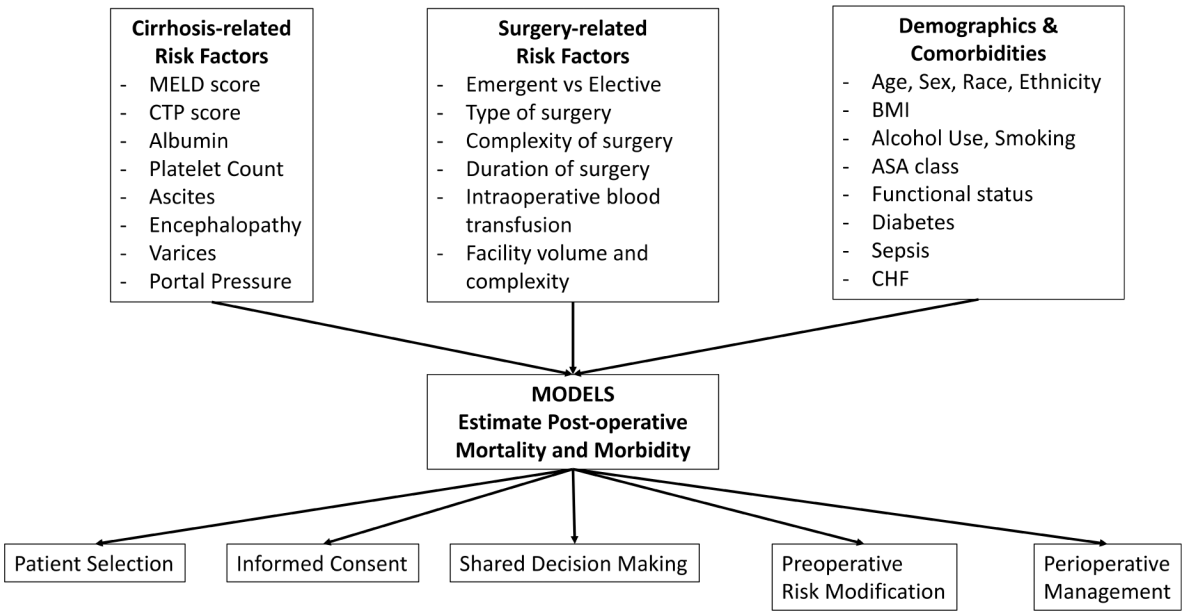

Figure 2.

Postoperative mortality in patients with cirrhosis depends on cirrhosis-related, surgery-related and comorbidity-related factors. These factors need to be combined in multivariable models to enable accurate estimates of postoperative mortality in individual patients undergoing a specific surgery – but such models have not yet been developed. Accurate estimates of postoperative mortality can be used to optimize patient selection and perioperative care.

TABLE 1.

Preoperative evaluation of patients with cirrhosis

	All patients with cirrhosis	**In selected cases:**
Clinical evaluation	Determine whether the cirrhosis is compensated or decompensated by taking a detailed history, including history of ascites, varices, hepatic encephalopathy, GI bleeding. Review medications, alcohol use (screen using the AUDIT-C), and previous surgeries including complications. Physical exam, including pulse oximetry, jaundice, sarcopenia, ascites, caput medusa, edema, mental status, asterixis	If edema is present, evaluate jugular venous pressure and consider BNP to help evaluate whether CHF is also present. If evidence of malnutrition or sarcopenia, consider nutrition consult for optimization.
Laboratory studies	Hemoglobin, white cell count, platelets, PT/INR. Serum creatinine, electrolytes, calcium, phosphate, AST, ALT, alkaline phosphatase, bilirubin, albumin	If cause of cirrhosis is unknown: HBV and HCV screening, iron studies, consider further testing for autoimmune hepatitis, etc.
Imaging studies		Screen for HCC, if past due, using US or CT. When unclear whether portal hypertension is present, consider imaging, transient elastography, and possibly portal venous pressure measurement if this will alter surgical plan
Additional testing		EGD if past due for variceal screening. TTE if systolic, diastolic or valvular dysfunction is suspected.
Risk assessment	Assign ASA classification Calculation of MELD, CTP scores	Consider using the Mayo Surgical Risk Calculator
Facility capabilities		If high MELD, determine whether patient should undergo procedure at a facility with greater experience, dedicated hepatologists, and capability for rescue transplantation if needed

Abbreviations: ALT=alanine aminotransferase, ASA=American Society of Anesthesiologists, AST=aspartate aminotransferase, BNP=B-type natriuretic peptide, CHF=congestive heart failure, CT=computed tomography, CTP=Child-Turcotte-Pugh, EGD=esophagogastroduodenoscopy, GI=gastrointestinal, HBV=hepatitis B virus, HCC=hepatocellular carcinoma, HCV=hepatitis C virus, INR=international normalized ratio, MELD=Model for End-Stage Liver Disease, PT=prothrombin time, TTE=transthoracic echocardiogram, US=ultrasound.

Table 2.

Published studies reporting postoperative mortality in patients with cirrhosis, according to type of surgery and severity of liver dysfunction.

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
Abdominal and gastroesophageal surgeries										
	Esophageal									
Wang 2017[99]	Esophagectomy	RC, single center	37	74, propensity matched	11%[a]	1%	3%	43%	N/A	N/A
Valmansoni 2017[100]	Esophagectomy	RC, single center	73	146, matched	15.1%[b]	8.9%	N/A	N/A	N/A	11.9% in MELD ≤9 28.6% in MELD >9
Sozzi 2017[101]	Minimally invasive esophagectomy	RC, single center	18	425, unmatched	16.7%[a]	3.3%	13%	33%	N/A	13% in MELD ≤9 67% in MELD >9
Lu 2005[102]	Esophagectomy	RC, single center	16	N/A	25%[a]	N/A	10%	50%	100%	N/A
	Gastric									
Alshahrani 2017[103]	Laparoscopic gastrectomy	RC, single center	27	N/A	0%[c]	N/A	N/A	N/A	N/A	N/A
	Open gastrectomy		48	N/A	2.1%[c]	N/A	N/A	N/A	N/A	N/A
Kim 2017[104]	Laparoscopic gastrectomy	RC, single center	36	N/A	2.8%[c]	N/A	0%	0%	100%	N/A
	Open gastrectomy		39	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Guo 2014[105]	Radical gastrectomy with D1 lymphadenectomy	RC, single center	24	N/A	4.2%[c]	N/A	0%	7.1%	N/A	N/A
	Radical gastrectomy with D2 lymphadenectomy		32	N/A	25%[c]	N/A	7%	41%	N/A	N/A
Jang 2008[106]	Radical gastrectomy	RC, single center	57	N/A	9%[c]	N/A	4.3%	27.2% (B and C)	See CTP B	N/A
Lee 2005[107]	Radical gastrectomy with D2 lymphadenectomy	RC, single center	94[h]	N/A	2.1%[c]	N/A	0%	16.7% (B and C)	See CTP B	N/A
	Bariatric									
Pestana 2015[108]	Roux-en-y or sleeve gastrectomy	RC, single center	14	N/A	0%[c]	N/A	0%	N/A	N/A	N/A

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
Woodford 2015[109]	Laparoscopic adjustable gastric banding	RC, single center	14	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Shimizu 2013[110]	Laparoscopic Roux-en-Y, sleeve gastrectomy, or gastric banding	RC, single center	23[h]	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Dallai 2004[111]	Laparoscopic Roux-en-Y	RC, single center	30	N/A	0%[c]	N/A	0%	N/A	N/A	N/A
Brolin 1998[112]	Bariatric surgery	RC, multi-center	125[h]	N/A	3.2%[d]	N/A	N/A	N/A	N/A	N/A
	Cholecystectomy									
Fei 2017[113]	Selective double disconnection combined cholecystolithotomy with Armilarisin A	RC, single center	29	N/A	0%[d]	N/A	N/A	N/A	N/A	N/A
	Selective double disconnection combined cholecystolithotomy without Armilarisin A		32	N/A	0%[d]	N/A	N/A	N/A	N/A	N/A
Stromberg 2015[114]	Laparoscopic or open cholecystectomy	RC, national database	77	61,711, unmatched	0%[d]	0.2%	N/A	N/A	N/A	N/A
Quillin 2013[115]	Laparoscopic cholecystectomy	RC, single center	94	N/A	4.3%[d]	N/A	3%	0%	100%	4% in MELD <10, 0% in MELD 10–15 13.3% in MELD>15
de Goede 2013[116] (metaanalysis)	Laparoscopic cholecystectomy	Meta-analysis	115	N/A	0%[c]	N/A	0%	0%	N/A	N/A
	Open cholecystectomy		119	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Laurence 2012[117] (metaanalysis)	Laparoscopic cholecystectomy	Meta-analysis	1756	N/A	0.74%[g]	N/A	0.1%	0.4%	21.1%	N/A
	Open cholecystectomy		249	N/A	2%[g]	N/A	N/A	N/A	N/A	N/A
Chmielecki 2012[118]	Laparoscopic cholecystectomy	RC, national database	2857	N/A	1.3%[a]	N/A	N/A	N/A	N/A	N/A
	Open cholecystectomy		383	N/A	8.3%[a]	N/A	N/A	N/A	N/A	N/A
Lledo 2011[119]	Laparoscopic cholecystectomy	RC, single center	43	460, unmatched	0%[c]	0%	0%	0%	0%	N/A
Bessa 2011[120]	Laparoscopic cholecystectomy with harmonic scalpel	RCT, single center	20	N/A	0%[c]	N/A	0%	0%	N/A	N/A

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
	Laparoscopic cholecystectomy with diathermy		20	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Nguyen 2011[121]	Laparoscopic cholecystectomy	RC, single center	68	N/A	0%[c]	N/A	0%	0%	0%	N/A
Hamad 2010[122]	Laparoscopic cholecystectomy	RC, single center	15	N/A	0%[c]	N/A	0%	0%	N/A	N/A
	Open cholecystectomy		15	N/A	0%[c]	N/A	0%	0%	N/A	N/A
El Nakeeb 2010[123]	Laparoscopic cholecystectomy with harmonic scalpel	RCT, single center	60	N/A	0%[c]	N/A	0%	0%	N/A	N/A
	Laparoscopic cholecystectomy with traditional method		60	N/A	0%[c]	N/A	0%	0%	N/A	N/A
Delis 2010[124]	Laparoscopic cholecystectomy	RC, single center	220	N/A	0%[c]	N/A	0%	0%	N/A	0% in MELD≤13 0% in MELD>13
El Awadi 2009[125]	Laparoscopic cholecystectomy	RCT, single center	55	N/A	0%[c]	N/A	0%	0%	N/A	N/A
	Open cholecystectomy		55	N/A	0%[c]	N/A	0%	0%	N/A	N/A
	Hernia Repair									
Chatzizacharias 2015[126]	Ruptured umbilical hernia	RC, single center	11	N/A	0%[c]	N/A	N/A	0%	0%	N/A
Andraus 2015[70]	Abdominal wall hernia	RC, single center	56	N/A	19.6%[d]	N/A	N/A	N/A	N/A	N/A
Hassan 2014[127]	Uncomplicated umbilical hernia	PC, single center	70	N/A	0%[e]	N/A	N/A	0%	0%	N/A
Gurita 2013[128]	Strangulated umbilical hernia	RC, single center	12	N/A	0%[g]	N/A	N/A	N/A	N/A	0%
Banu 2013[76]	Complicated umbilical hernia	RC, single center	22	N/A	22.7%[g]	N/A	0%	9%	100%	N/A
Oh 2011[69]	Inguinal hernia	PC, single center	129	N/A	1.6%[c]	N/A	0%	0%	11%	N/A
Eker 2011[129]	Elective umbilical hernia	PC, single center	30	N/A	0%[c]	N/A	0%	0%	0%	0%
Choi 2011[130]	Elective umbilical hernia	RC, single center	22	N/A	9%[c]	N/A	N/A	5.3%	30%	N/A

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
	Emergent umbilical hernia		9	N/A	0%[c]	N/A	N/A	0%	0%	N/A
Gray 20 08[77]	Elective and emergent umbilical hernia	RC, national database	127	1294, unmatched	0.8%[d]	0.4%	N/A	N/A	N/A	N/A
Marsman 2007[131]	Elective umbilical hernia repair	RCT, single center	17	13, cirrhotic conservative management	0%[c]	15.4%	N/A	N/A	N/A	N/A
	Colorectal									
Pirolla 2017[132]	Stapled hemorrhoidopexy	RC, single center	10	12, unmatched	0%[g]	N/A	N/A	0%	N/A	N/A
Sabbagh 2016[133]	Colorectal resection	RC, single center	40	80, matched	22.5%[a]	1.30%	12%	40%	N/A	N/A
Nguyen 2009[8]	Colorectal surgery	RC, national database	4042	499,541, unmatched	18.9%[a]	N/A	N/A	N/A	N/A	N/A
Meunier 2008[71]	Colectomy, rectal resection, diverting ostomy, reconnection	RC, single center	41	N/A	26%[c]	N/A	24%	29%	20%	N/A
Huang 2007[134]	Stapled hemorrhoidopexy	RC, single center	8	N/A	0%[e]	N/A	0%	0%	N/A	N/A
Gervaz 2003[135]	Colorectal resection	RC, single center	72	N/A	13%[c]	N/A	6%	13%	28%	N/A
	Abdominal, other									
Loftus 2017[80]	Emergent laparotomy and temporary abdominal closure	RC, single center	15	216, unmatched	67%[a]	21%	N/A	N/A	N/A	N/A
Regimbeau 2015[136]	Pancreaticoduodenectomy	RC, 14 center	35	70, matched	17%[c]	5%	4%	55%	N/A	12.5% in MELD<20 67% in MELD≥20
Harrington 2013[73]	Non-hepatic abdominal surgery	RC, single center	120	N/A	7%[f]	N/A	7%	5%	20%	4.3% in MELD<10 7.5% in MELD 10–19 33.3% in MELD>19
El Nakeeb 2013[9]	Pancreaticoduodenectomy	RC, single center	67	375, unmatched	11.9%[a]	1.6%	9.50%	50%	N/A	N/A
Neeff 2011[74]	Hernia, PUD, colon, cholecystectomy	RC, single center	138	N/A	28%[c]	N/A	10%	17%	63%	9% in MELD<10 19% in MELD 10–15 54% in MELD >15

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
Warnick 2011[137]	Pancreatic resection	RC, single center	32	32, matched	9%[c]	0%[c]	3%	100%	N/A	N/A
Telem 2010[138]	Hernia, colon	RC, single center	100	N/A	7%[c]	N/A	2%	12%	12%	3% in MELD< 10, 8% in MELD 10–14, 29% in MELD 15–25, 0% in MELD>25
Costa 2009[139]	Hernia, liver, cholecystectomy	RC, single center	190	N/A	13%[c]	N/A	5%	14%	31%	N/A
Befeler 2005[140]	Open nonhepatic abdominal surgery	RC, single center	53	N/A	17%[a]	N/A	N/A	N/A	N/A	N/A
Cardiothoracic surgery										
	Cardiac									
Chou 2017[141]	CABG and/or valve surgery	RC, national database	1040	1040, matched	15.3%[a]	7.8%	N/A	N/A	N/A	N/A
Steffen 2017[142]	Aortic valve replacement	RC, national database	2769	2769, matched	16%[a]	5%	N/A	N/A	N/A	N/A
Hsieh 2015[143] (metaanalysis)	Cardiac surgery (excluding transplant)	Meta-analysis	939	N/A	--	N/A	8.9%[a]	31.4%	47.6%	6.1% in MELD<15 18.9% in MELD≥15
Lin 2014[144]	Cardiac surgery	RC, single center	55	N/A	16.4%[a]	N/A	17%	15%	20%	N/A
Morimoto 2013[145]	CABG, valve surgery, aortic surgery	RC, single center	32	N/A	16%[a]	N/A	7%	21%	0%	0% in MELD<10 7% in MELD 10–15 50% in MELD>15
Gopaldas 2013[146]	CABG on pump	RC, national database	4202	3,040,261, unmatched	10.7%[a]	2.5%	N/A	N/A	N/A	N/A
	CABG off pump		2246	3,040,261, unmatched	10.0%[a]	2.5%	N/A	N/A	N/A	N/A
Arif 2012[147]	CABG, valve surgery, transplant, VAD implant	RC, single center	109	N/A	26%[d]	N/A	20%	40%	33%	N/A
Vanhuyse 2012[148]	CABG, valve surgery, aortic surgery, ASD closure	RC, single center	34	N/A	26%[a]	N/A	18%	30%	100%	18.5% in MELD<15 57.1% in MELD≥15

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
Marui 2011[149]	CABG on pump	RC, national database	58	N/A	6.9%[a]	N/A	N/A	N/A	N/A	N/A
	CABG off pump		41	N/A	2.4%[a]	N/A	N/A	N/A	N/A	N/A
	PCI		233	N/A	0.4%[a]	N/A	N/A	N/A	N/A	N/A
Gundling 2010[150]	CABG, valve surgery, aortic surgery, tumor resection	RC, single center	47	47, matched	19.1%[d]	8.5%	6.1%	50%	N/A	N/A
Morisaki 2010[151]	CABG and/or valve surgery	RC, single center	42	N/A	9.5%[a]	N/A	0%	33%	N/A	N/A
Thielmann 2010[152]	CABG, valve surgery, aortic surgery, tumor resection	RC, single center	57	N/A	30%[d]	N/A	15%	50%	100%	9% in MELD < 13.5 56% in MELD≥13.5
Murashita 2009[153]	CABG and/or valve surgery	RC, single center	12	N/A	33%[c]	N/A	50%	17%	N/A	N/A
Fisoufi 2007[66]	CABG, valve surgery, pericardectomy, aortic surgery	RC, single center	27	N/A	26%[a]	N/A	11%	18%	67%	N/A
Lin 2005[154]	CABG and/or valve surgery	RC, single center	55	N/A	16.4%[a]	N/A	16.7%	16% (B and C)	See CTP B	N/A
Hayashida 2004[155]	CABG, valve surgery, aortic surgery	RC, single center	18	N/A	17%[c]	N/A	0%	28.6%	100%	N/A
Suman 2004[67]	CABG, valve surgery pericardiectomy	RC, single center	44	N/A	16%[b]	N/A	3%	41%	100%	N/A
Kaplan 2002[156]	CABG and/or valve surgery	RC, single center	10	N/A	30%[g]	N/A	0%	50%	N/A	N/A
Bizouam 1999[157]	CABG and/or valve surgery	**PC**, single center	12	N/A	8.3%[a]	N/A	20%	50%	N/A	N/A
Klemperer 1998[158]	CABG and/or valve surgery	RC, single center	13	N/A	31%[c]	N/A	0%	80%	N/A	N/A
	Other thoracic									
Iwata 2007[159]	Lung cancer surgery	RC, single center	33	N/A	6.5%[a]	N/A	N/A	N/A	N/A	N/A
Iwasaki 2006[160]	Lung cancer surgery	RC, single center	17	N/A	5.9%[a]	N/A	0%	7.8%	N/A	N/A
Orthopedic and trauma surgery										

Study	Surgery type	Study design	Number of Patients (N)		Overall mortality		Mortality by CTP class			Mortality by MELD score
			Cirrhosis	No Cirrhosis (Controls)	Cirrhosis	No Cirrhosis (Controls)	CTP A	CTP B	CTP C	
	Orthopedic									
Tiberi 2014[161]	THA, TKA	RC, single center	115	115, matched	1%[b]	0%	N/A	N/A	N/A	10% in MELD<10 32% in MELD≥10
Bakaeen 2008[162]	Debridement or en block resection of infected sternoclavicular joint	RC, single center	5	N/A	40%[c]	N/A	N/A	50%	0%	N/A
Moon 2007[163]	THA	RC, single center	30	N/A	6.7%[d]	N/A	0%	0%	100%	N/A
Cohen 2005[72]	THA, TKA	RC, single center	29	93, unmatched	10.3%[c]	1.1%	4.76%	14.3%	100%	N/A
Shih 2004[164]	TKA	RC, single center	42	42, matched	0%[c]	0%	0%	0%	N/A	N/A
	Trauma									
Georgiou 20 09[78]	Emergent laparotomy	RC, single center	45	2039, unmatched	40%[g]	15%	N/A	N/A	N/A	N/A
Christmas 2005[165]	Emergent laparotomy	RC, single center	22	156, matched	33%[g]	1%	15%	37%	63%	N/A
Demetriades 20 04[79]	Emergent laparotomy	RC, single center	40	80, matched	45%[g]	24%	N/A	N/A	N/A	N/A
Other surgery										
	Neuroloaic									
Chen 2018[166]	Craniostomy for SDH	RC, national database	1233	2446, matched	8.7%[a]	3.1%	7.10%	11.2%	17.2%	N/A
Lin 2014[167]	Instrumented lumbar surgery	RC, single center	29	N/A	3.4%[a]	N/A	N/A	N/A	N/A	N/A
Chen 2012[168]	Brain procedures	RC, single center	121	N/A	24.3%[g]	N/A	5.30%	38%	63.2%	N/A
	Otolaryngology									
Kao 2010[169]	Surgical resection followed by free flap	RC, single center	62	N/A	12.9%[a]	N/A	4.80%	23.5%	66.7%	N/A
Cheng 2008[170]	Head and neck reconstruction	RC, single center	7	N/A	28.5%[d]	N/A	0%	33.3%	100%	N/A

Notes: references not cited in text available in supplement. Case series included as retrospective cohorts.

[a] inpatient mortality

[b] 90-day mortality

[c] postoperative mortality

[d] 30-day mortality

[e] procedure-related mortality

[f] 30-day mortality or liver transplant

[g] follow-up period for mortality not specified

[h] includes intraoperative diagnoses of cirrhosis

Abbreviations: N/A = No available data, ASD=atrial septal defect, CABG=coronary artery bypass graft, CTP=Child-Turcotte-Pugh, MELD=Model of End-Stage Liver Disease, PC=prospective cohort, PCI=percutaneous coronary intervention, PUD=peptic ulcer disease, RC=retrospective cohort, RCT=randomized controlled trial, SDH=subdural hematoma, THA=total hip arthroplasty, TKA=total knee arthroplasty, VAD=ventricular assist device.

Table 3.

Predictors of mortality and models estimating mortality in patients with cirrhosis undergoing surgery

Study	Surgery types included in model creation	Components	Outcomes
Models specific to patients with cirrhosis			
CTP	Multiple studies including a range of surgeries	Encephalopathy, ascites, bilirubin, albumin, PT or INR	In-hospital mortality
MELD	Multiple studies including a range of surgeries	Bilirubin, Creatinine, dialysis, INR	In-hospital and 30-day mortality, morbidity, liver transplant
Mayo Model[61]	Digestive n=586 Orthopedic n=107 Cardiovascular n=79 (Does not distinguish emergent vs. non-emergent)	Age, ASA, MELD *	7-day, 30-day, 90-day, 1-year and 5-year mortality
ADOPT-LC score[68]	Elective only GI n=1173 Breast n=151 Cardiovascular n=132 Urological n=132	Age, CTP class, CCI, duration of anesthesia	In-hospital mortality
Models not specific to patients with cirrhosis			
ACS NSQIP Surgical Risk Calculator (Universal)[171]	Nearly any type, over 3.8 million operations in dataset	Type of procedure, age, gender, functional status, emergency, ASA, steroid use, ascites, sepsis, ventilator, disseminated cancer, diabetes, HTN, CHF, dyspnea, smoker, severe COPD, dialysis, acute renal insufficiency, BMI	30-day: mortality, serious complication, any complication, pneumonia, cardiac complication (cardiac arrest or MI), surgical site infection, UTI, VTE, renal failure, readmission, return to OR, death, discharge to nursing or rehab facility. LOS
ASA[138]	Abdominal surgery	Presence and severity of systemic disease, need for operation	Mortality
RCRI[172]	Non-urgent major noncardiac surgery, n=4315	High risk surgery (intraabdominal, intrathoracic, or suprainguinal vascular), ischemic heart disease, CHF, Stroke/ TIA, preoperative insulin use, creatinine >2.0	MI, pulmonary edema, cardiac arrest, heart block
Gupta perioperative cardiac risk score[173]	All types (ACS NSQIP 2007 database, included over 200,000 surgical patients)	Age, functional status, ASA class, creatinine >1.5, type of surgery (organ system)	MI or cardiac arrest

Note: references not cited in text available in supplement.

* Online risk calculator also includes etiology of cirrhosis

Abbreviations: ADOPT-LC= Adequate Operative Treatment for Liver Cirrhosis, ACS NSQIP=American College of Surgeons National Surgical Quality Improvement Program, ASA=American Society of Anesthesiologists class, BMI=body mass index, CCI=Charlson Comorbidity Index, CHF=congestive heart failure, CPT=Current Procedural Technology, CTP=Child-Turcotte-Pugh, HTN=hypertension, GI=gastrointestinal, INR=international normalized ratio, LOS=length of stay, MELD=model of end-stage liver disease, MI=myocardial infarction, PT=prothrombin time, RCRI=Revised Cardiac Risk Index.

Table 4.

Research gaps and limitations in available evidence on surgical outcomes for patients with cirrhosis.

Gaps in existing research	
Data quality and study design	• Prospectively designed studies • Studies with control group • Randomized trials of surgical and medical management options • Large cohorts/multi-center data • Studies that distinguish emergent from elective surgeries • Stratification by MELD or CTP scores • Financial cost as an outcome
Epidemiology	• Frequency and types of surgery among cirrhotic patients nationally and internationally • Outcomes data stratified by specific surgical procedure • Outcomes data by level of experience of surgical center • Natural history of inguinal or umbilical hernias (proportion of patient with cirrhosis who need emergency surgery if not repaired electively, and outcome); randomized trial of surgery vs watchful waiting in these patients • Racial and socio-economic disparities in receipt of elective procedures
Preoperative evaluation and management	• Prospective validation of cirrhosis-specific risk calculators • Validation of other widely used risk calculators (e.g. ACS NSQIP) in patients with cirrhosis • Relative importance of comorbidities as risk factors • Importance of prior decompensations in predicting postoperative decompensation • Non-invasive preoperative screening for portal HTN by elastography • Randomized trial of TIPS prior to surgery if severe portal HTN • Benefits vs harms of non-selective beta blockers in patients with esophageal varices • Risks of elective surgery if encephalopathy cannot be completely corrected • Whether to transfuse platelets if <50,000 • Utility of thromboelastography • Platelet stimulating agents • Risks/benefits of replacing coagulation factors • Nutritional optimization • Urgent optimization
Intraoperative management	• Local blocks for anesthesia • Comparison of surgical techniques/approaches • Fluid management intraoperatively, including whether albumin vs crystalloid are preferred • Safety of intraoperative cardiopulmonary bypass
Postoperative management	• Decision to admit to ICU postoperatively • Choice of venous thromboembolism prophylaxis

Abbreviations: ACS NSQIP=American College of Surgeons National Surgical Quality Improvement Project, CTP=Child-Turcotte-Pugh, HTN=hypertension, ICU=intensive care unit, MELD=Model of End-Stage Liver Disease, TIPS=Transjugular intrahepatic portosystemic shunt