

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Perioperative Risk in Patients With Cirrhosis



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G&H Why do patients with cirrhosis have an increased risk of perioperative morbidity and mortality?

KJ Patients with cirrhosis typically have hepatocellular dysfunction and portal hypertension, which increase the incidence of many different perioperative complications, including bleeding, infection, impaired wound healing, renal insufficiency, thrombosis, liver failure, and death. Hepatocellular dysfunction in cirrhosis leads to protein synthetic dysfunction and alterations in medication metabolism, and also contributes to malnutrition, which can harm wound healing and the ability to fight infections.

Clinically significant portal hypertension may be an even more important mechanism. Various factors around the time of surgery such as anesthesia-induced hypotension and positive pressure ventilation are thought to further decrease hepatic blood flow, leading to hepatic ischemia and decompensation. Especially during abdominal surgery, the pneumoperitoneum that is needed for laparoscopy and the traction on abdominal viscera may also decrease hepatic perfusion. Portal hypertension also predisposes patients to other complications such as hepatic encephalopathy, which can lead to aspiration risk and falls.

G&H How may perioperative mortality differ depending on the urgency and type of surgery in patients with cirrhosis?

KJ Emergent surgery is associated with a much higher risk of mortality than nonemergent surgery in patients who have cirrhosis. A study that my colleagues and I conducted of more than 8000 patients with cirrhosis

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undergoing nonhepatic abdominal surgery at Veterans Health Administration (VHA) medical centers found that the risk of dying within 30 days after surgery was almost 6 times higher for emergent surgery compared with nonemergent surgery. In this study, the 30-day risk of mortality was 17.2% for patients undergoing emergent surgery vs 2.1% after nonemergent surgery.

This study also illustrated the wide range of risk within the category of abdominal surgery. For example, 30-day mortality was less than 1% for nonemergent inguinal hernia repair, but was 7% for nonemergent colorectal resection. When performed in emergency situations, those procedures were associated with much higher mortality: 8% after emergent hernia repair and 35% after emergent colorectal resection.

Broadly speaking, in terms of anatomic or surgical specialty categories, perioperative risk for patients with cirrhosis is highest for open abdominal surgery, followed by chest or cardiac surgery, major orthopedic surgery, vascular surgery, abdominal wall surgery, and, finally, laparoscopic abdominal surgery. This order is based on data from the VOCAL-Penn study, which was also carried out in the national VHA population. This list also illustrates a potential problem inherent to the use of observational

studies to make risk estimates: patient selection. Perioperative risk appears much lower for laparoscopic abdominal surgery compared with open abdominal surgery. Is laparoscopic abdominal surgery drastically safer than open abdominal surgery, or is it a matter of patient selection, where sicker patients undergo open surgery and less-sick patients undergo laparoscopic surgery? Patient selection likely explains at least some of the observed difference in risk between open and laparoscopic surgery.

G&H Could you compare the use of different perioperative risk calculators for cirrhotic patients?

KJ In preoperative clinic, the surgical risk calculator that I use most, overall, is the American College of Surgeons National Surgery Quality Improvement Program (ACS NSQIP) Surgical Risk Calculator. However, it does not include any cirrhosis-specific variables other than recent ascites.

The Child-Turcotte-Pugh (CTP) score and Model for End-Stage Liver Disease (MELD) score are useful measures of severity of cirrhosis, which is an important variable in surgical risk. However, because these measures do not take into account the type or urgency of surgery, I do not consider them very useful for quantifying perioperative risk, at least not on their own. The CTP score was developed in 1964 and is used to categorize the severity of cirrhosis into class A, B, or C. Although the CTP class correlates with perioperative risk, each of these categories is very broad, encompassing a wide range of risk, especially CTP classes B and C. The CTP-based estimates of perioperative mortality that are still often quoted are based on data from the 1980s and 1990s: 10% for CTP class A, 30% for CTP class B, and 76% to 82% for CTP class C. However, perioperative mortality has improved since then, and as mentioned, the CTP score does not take into account the urgency of surgery, and it does not make sense to lump together all surgery types, from carpal tunnel to esophageal resection.

The MELD score is also associated with postoperative mortality and in 2007 was incorporated into the Mayo Risk Score, which uses age, American Society of Anesthesiologists (ASA) class, and etiology of cirrhosis. When I first started doing preoperative medicine evaluations a decade ago, I was excited to use this calculator since it was an improvement over the CTP score, but then I realized it did not take into account the type of surgery, because it was underpowered to do so, nor the urgency of surgery. Additionally, Mahmud and colleagues have demonstrated that the predictive accuracy of the Mayo Risk Score for postoperative mortality has decreased since its development, showing a trend of overestimating

postoperative risk in cirrhosis. Their VOCAL-Penn score is a large improvement, in my opinion. It was derived in 2020 from a large national cohort of patients within the VHA. It incorporates age, ASA score, serum albumin, total bilirubin, platelet count, body mass index, whether nonalcoholic fatty liver disease (now known as metabolic

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dysfunction-associated steatotic liver disease) is the etiology, emergency indication, and the 6 anatomic categories of surgery mentioned previously (open or laparoscopic abdominal surgery, abdominal wall surgery, cardiothoracic surgery, vascular surgery, and major orthopedic surgery).

Accuracy (based on area under the receiver operating characteristic curve) for the VOCAL-Penn score was superior to the MELD score, CTP score, and Mayo Risk Score in predicting mortality up to 30, 90, and 180 days postoperatively in their study. The VOCAL-Penn score was later externally validated in nonveteran populations and has also demonstrated good prediction of cirrhosis decompensation risk at 90 days. Given its superior performance, this score has become an important tool for estimation of surgical risk in this population and I think allows consideration of surgery in certain patients who previously would have been deemed too high risk based on older models. I use the VOCAL-Penn score often. One major limitation, however, is that not all types of surgery fall into the 6 surgical categories included in the score. For example, urologic, neurosurgical, and otolaryngology procedures are not included, and the categories that are included are still quite broad.

G&H What are the main limitations of existing approaches to risk assessment?

KJ One limitation is the lack of prospective data. Risk prediction models are based on observed outcomes of patients who ended up receiving surgery and not what are referred to as *all comers* (ie, patients who would like to be

considered for surgery). Therefore, the estimate of risk can be overly optimistic to an unclear extent, assuming that sicker patients were sometimes excluded from receiving surgery. Another limitation is that it is difficult to develop a calculator that includes a broad range of surgeries, each with its own level of risk. Lumping together surgeries by organ system is not optimal, as already discussed. Ideally, a clinician could enter any specific procedure type into a calculator, similar to the ACS NSQIP calculator.

Another challenge is how to balance the risk of surgery against its potential benefit, instead of only considering the risk side of the equation. For example, a common dilemma in patients with cirrhosis is whether to electively repair their umbilical hernias, which occur frequently in this patient population, especially in those with ascites (ie, advanced cirrhosis). Patients with umbilical hernias can present with life-threatening strangulation or with erosion through the skin, requiring emergent surgery. In a large study that my colleagues and I conducted, 30-day mortality after emergent umbilical hernia repair was 12.2%, compared with 1.2% in nonemergent settings (which is still a fairly high risk). The clinical question is, at what threshold would the benefit of repair (to improve symptoms and prevent emergent repair) outweigh the significant risk of elective repair? The risk-benefit balance of elective repair is not clear because of a lack of data on the number who would progress to an emergency situation over time.

G&H What are some examples of when surgery should be delayed in patients with cirrhosis?

KJ There are many examples, but uncontrolled hepatic encephalopathy is one reason to delay surgery, and another is uncontrolled ascites, especially before any abdominal or abdominal wall (hernia) surgery because pressure from ascites significantly impairs wound healing. Patients with a MELD score greater than 15 or CTP class C are at extremely high risk for complications and mortality, so surgery should be delayed until after a liver transplant workup has been completed, when possible. Although not based on strong data, surgery is often delayed in order to correct a platelet count below 50,000 platelets/ μ L (or below 100,000 platelets/ μ L for very high bleeding risk surgery).

Another reason to delay surgery is when patients have transaminase elevations that are higher than expected for cirrhosis, indicating ongoing inflammation from acute hepatitis, including alcohol-related hepatitis, which should be investigated prior to any nonemergent surgery. Acute hepatitis is considered a contraindication to nonemergent surgery. Transaminase levels 3 times

the upper limit of normal are generally considered high enough to raise this concern. Additionally, in my opinion, nonemergent surgery should be delayed if treatment for the underlying liver disease could help decrease risk. For example, in some patients with chronic alcohol-induced liver injury or chronic hepatitis C infection, treating their underlying disorder probably decreases their perioperative risk by decreasing inflammation and even portal hypertension.

If bariatric surgery is being considered, it is important to pause to look for signs of clinically significant portal hypertension, which would place the patient at higher risk. Guidelines suggest skipping surgery or at least performing it at a transplant center when patients have clinically significant portal hypertension. These are just a few examples of times I would delay surgery.

G&H How do you assess patients with cirrhosis preoperatively?

KJ I first identify comorbidities, including frailty and other nonhepatic deal-breakers such as unstable or severe cardiac or pulmonary conditions. I put those first on my checklist to think more broadly, beyond cirrhosis. If the patient still appears to be a surgical candidate, I screen for alcohol use disorder and rule out acute hepatitis (alcohol-related hepatitis, viral hepatitis, drug-induced liver injury, and so on) in patients with transaminases more than 3 times the upper limit of normal.

I then review evidence of cirrhosis based on history, physical examination, and laboratory findings; look at reports from prior imaging and endoscopies; and then think about whether the cause of the cirrhosis is known. I also assess the severity of cirrhosis. Is there a history of decompensation? If so, how well are complications being managed? Is the patient on diuretics, nonselective beta blockers, or lactulose and/or rifaximin for hepatic encephalopathy? If the patient's cirrhosis is still compensated, I look for clinical evidence of portal hypertension. I always review the platelet count and synthetic function, looking at the albumin and international normalized ratio (INR). I generally determine the patient's MELD score and/or CTP class. I consider whether esophageal variceal screening is indicated, and if so, whether it is up-to-date. I do the same for hepatocellular carcinoma screening because I consider the presence and treatment of this disease to take precedence over most elective surgeries.

In terms of risk prediction, I generally use the VOCAL-Penn score if the patient is undergoing surgery within one of the aforementioned 6 anatomic categories. In general, I consider a MELD score of less than 10 to indicate a fairly low risk for surgery, but there are exceptions; some patients who have a MELD score of less

than 10 have portal hypertension and even a history of decompensation.

I also think about optimization. There are many possibilities, so I will just mention a few; there are very little data to go on. I recommend referring to the 2019 American Gastroenterological Association Clinical Practice Update on this topic. Can the cause of the cirrhosis be treated quickly? For instance, I believe alcohol use disorder or hepatitis C treatment may help decrease inflammation and portal hypertension, as previously discussed. I have also seen improvement in platelet count with alcohol cessation because alcohol suppresses bone marrow activity and platelet production.

If applicable, I continue nonselective beta blockers perioperatively unless there is a contraindication such as hypotension or bradycardia. If esophageal variceal screening is indicated but past due, I consider whether there is time for the patient to undergo upper endoscopy. If the surgery is time sensitive, I consider starting the patient on a selective beta blocker (or switching any current selective beta blocker to a nonselective one) as long as there are at least several weeks before surgery to make sure the medication is tolerated. Collaboration with cardiology is sometimes needed. Although not studied specifically in the perioperative setting, nonselective beta blockers in patients with cirrhosis can reduce portal hypertension and decrease the risk of decompensation in general. I consider carvedilol as the preferred nonselective beta blocker, but propranolol and nadolol are other options. If the patient has undergone a liver transplant, I offer comments about managing their posttransplant medications.

Additionally, I avoid routine use of blood products in an attempt to normalize a high INR. In particular, I would avoid fresh frozen plasma, which can lead to volume expansion. In addition, I recommend minimizing the use of opiates and benzodiazepines, which may worsen or precipitate hepatic encephalopathy. Although they are almost universally included in multimodal postoperative pain management protocols, I also strongly advise avoiding nonsteroidal anti-inflammatory drugs in patients with cirrhosis. Up to 2 g per day of acetaminophen is considered safe.

As for other considerations, if the patient's platelet count is unacceptably low, I consider a transfusion or a

thrombopoietin receptor agonist such as eltrombopag. Patients with a history of hepatic encephalopathy should continue lactulose or rifaximin, if applicable. It is important to plan how to prevent constipation postoperatively; I recommend documenting the number of bowel movements per day postoperatively, which may sound obvious but is not always done. It is also important not to restrict protein intake. Such intake was restricted in patients with cirrhosis in the past in an attempt to decrease risk of hepatic encephalopathy, but now it is known that adequate protein intake is extremely important for nutrition. For volume status, I recommend documenting the patient's daily weight and determining the need for diuretics on a case-by-case basis. These are some basic considerations in the preoperative setting to try to head off complications postoperatively.

Disclosures

Dr Johnson has no relevant conflicts of interest to disclose.

Suggested Reading

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