Preoperative Evaluation and Management of Patients With Select Chronic Gastrointestinal, Liver, and Renal Diseases

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Abstract

Patients with chronic gastrointestinal, hepatic, and renal disease are frequently encountered in clinical practice. This is due in part to the rising prevalence of risk factors associated with these conditions. These patients are increasingly being considered for surgical intervention and are at higher risk for multiple perioperative complications. Many are able to safely undergo surgery but require unique considerations to ensure optimal perioperative care. In this review, we highlight relevant perioperative physiology and outline our approach to the evaluation and management of patients with select chronic gastrointestinal, hepatic, and renal diseases. A comprehensive preoperative evaluation with a multi-disciplinary approach is often beneficial, and specialist involvement should be considered. Intra-operative and postoperative plans should be individualized based on the unique medical and surgical characteristics of each patient.

GASTROINTESTINAL PHYSIOLOGY IN THE PERIOPERATIVE PERIOD

In the perioperative setting, alterations to gastrointestinal physiology can occur for a variety of reasons. These include expected and compensatory physiological changes, direct gut stimulation (mechanical effects from the surgery itself), medication effects, and effects due to the underlying gastrointestinal disease. Delayed gastric emptying and alterations in peristalsis may occur due to neurotransmitter effects (e.g., acetylcholine, serotonin, and dopamine) on the central nervous system, specifically the chemoreceptor trigger zone in the area postrema, dorsal pons, amygdala, and thalamus. These physiologic changes may lead to postoperative nausea and vomiting, interference with medication absorption from the gastrointestinal tract, and delayed advancement to an oral diet.

Effects of the surgical procedure on the gastrointestinal tract are most common in abdominal and pelvic surgeries, where the gut is directly manipulated or subjected to pressurization during pneumoperitoneum, resulting in postoperative gut hypomotility or reduced perfusion.
Furthermore, excessive fluid administered perioperatively has been associated with gut wall edema, which can contribute to the development of ileus.2-4

Patients with chronic liver disease may have difficulty metabolizing medications with high hepatic clearance such as opioids, ketamine, neuromuscular blockers (including rocuronium and vecuronium), sedatives (such as benzodiazepines), and amide local anesthetics.5,6 Chronic liver disease can lead to reduced protein synthesis (which can alter drug binding), impaired wound healing, and altered clotting factor production. Portal hypertension contributes to excess collateral circulation, splenic sequestration, and renal dysfunction. Vaso-dilation from impaired arterial autoregulation can be exacerbated by anesthetics, leading to hypotension.7

### TABLE 1. Acute Hepatic Diseases and Complications Associated With Significant Perioperative Riska

<table>
<thead>
<tr>
<th>Condition</th>
<th>Perioperative implications</th>
<th>Management considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute alcoholic hepatitis</td>
<td>Laparotomy associated with morbidity and mortality &gt;50%.</td>
<td>Studies predate modern medical management of liver disease. Resolution can take up to 12 weeks if patient abstains from alcohol. Once resolved, evaluate for baseline hepatic disease.</td>
</tr>
<tr>
<td>Acute liver failure (fulminant hepatitis)b</td>
<td>Mortality approached 85% before transplantation.</td>
<td>Medical management of liver disease takes precedence. Consider referral for liver transplantation.</td>
</tr>
<tr>
<td>Acute viral or drug-induced hepatitis</td>
<td>Diagnostic laparotomy associated with significant risk of morbidity (12% to 60%) and mortality (9.5% to 30%) in studies performed when that practice was common.</td>
<td>Underlying conditions are treatable or self-limited. Surgical risk may be reduced if delayed to allow hepatic recovery.</td>
</tr>
<tr>
<td>Severe extrahepatic complications (hepatorenal syndrome, hypoxemia, hepatopulmonary syndrome, portopulmonary hypertension, and cardiomyopathy)</td>
<td>Significant mortality risk exists even in non-perioperative settings.</td>
<td>Optimize medical therapy per clinical practice guidelines. Consider liver transplantation evaluation.</td>
</tr>
<tr>
<td>Coagulopathyc</td>
<td>Severe bleeding may not be controllable. Bleeding risk does not correlate with degree of coagulopathy due to upregulation of procoagulant factors.</td>
<td>Very limited data on outcomes in patients. Consider liver transplantation evaluation.</td>
</tr>
</tbody>
</table>

*aCompiled from resources noted in the reference list.9-12 
bDefined as the development of jaundice, coagulopathy, and hepatic encephalopathy within 26 weeks in a patient with acute liver injury in the absence of preexisting liver disease. 
cDefined as platelets <50,000 or international normalized ration >1.5.

### PERIOPERATIVE MANAGEMENT OF NON-CIRRHOTIC LIVER DISEASE

There are limited data on the perioperative management of non-cirrhotic chronic liver disease. Many previous studies were performed before modern surgical and diagnostic techniques.8 In patients with acute hepatic injury, perioperative morbidity and mortality is increased (Table 1).9-12 Although these results have not been replicated in modern cohorts, the preponderance of data suggest that the risks (e.g., infection, bleeding, clotting, wound healing, and wound fragility) of proceeding with elective surgery in these patients are significantly greater than the harm from delaying surgery.13 Patients needing urgent or emergency surgery should receive individualized care with input from surgical, hepatobiliary, and anesthesia specialists.
Patients with chronic, non-cirrhotic liver disease generally have a lower risk of perioperative complications compared with patients with cirrhosis.\textsuperscript{14,15} There are unique considerations that should be taken into account perioperatively due to the underlying physiology of the disease or its associated treatments (Table 2).\textsuperscript{16-21} Patients with chronic, active hepatitis without cirrhosis undergoing hepatic resection for hepatocellular carcinoma may be at higher risk for postoperative complications, such as death or liver failure, than those without active hepatitis.\textsuperscript{22} This may be due to decreased hepatic synthetic function and increased risk for portal hypertension.\textsuperscript{8}

**PERIOPERATIVE MANAGEMENT OF CIRRHOTIC LIVER DISEASE**

Patients with cirrhosis are at increased risk of perioperative complications, including...
bleeding, thromboembolism, poor wound healing, pulmonary complications, delirium, hepatic failure, renal dysfunction, and death. General perioperative risk assessment principles discussed in previous entries in this series should be applied. Early evaluation by a multispecialty team may be beneficial for patients being considered for elective or semi-urgent surgery. Patients being considered for urgent or emergency surgery may benefit from the expertise at a facility experienced in cirrhosis management, such as a transplant-based medical center.

Baseline Assessment
The primary goals of the baseline cirrhosis assessment are to identify the presence of complications of cirrhosis and evidence of portal hypertension. Perioperative risk correlates directly with the severity of the underlying liver disease, as seen in non-cirrhotic chronic liver disease. Because cirrhosis represents the final common pathway of various disease processes, there is less heterogeneous data and more evidence to guide preoperative evaluation. Nevertheless, it is still imperative to understand the underlying etiology and severity of the patient’s cirrhosis, as there may be disease-specific aspects with unique perioperative considerations (Table 2).

A focused history aims to identify the etiology, duration, and severity of cirrhosis, any previous or current interventions directed at the underlying cause, and the use of any medications or substances that could affect the liver perioperatively. An accurate medication history, including herbs and supplements, is essential. Complications of portal hypertension or decreased hepatic synthetic dysfunction, such as ascites, esophageal varices, renal dysfunction, hepatic encephalopathy, and coagulopathy have significant clinical impact in the perioperative setting and should be investigated as recommended by established clinical practice guidelines. Patients may not be aware of disease manifestations, so physical examination findings suggestive of portal hypertension (eg, ascites, shifting abdominal dullness, gynecomastia, spider angioma, caput medusae, splenomegaly, jugular venous distension, jaundice, edema, etc) should prompt further evaluation.

Preoperative diagnostic studies are useful in assessing hepatic function (Table 3). Many of these studies provide the information necessary to perform cirrhosis-specific perioperative risk stratification using tools such as the Model for End-Stage Liver Disease (MELD) score, Child-Turcotte-Pugh (CTP) score, or the Mayo Postoperative Surgical Risk calculator. Advanced imaging such as ultrasound or computed tomography can be helpful in patients with symptoms, examination findings, or laboratory abnormalities suggestive of cirrhotic complications. Invasive diagnostic procedures such as liver biopsy should be performed as indicated by clinical practice guidelines for general cirrhosis management. Markers that exclude clinically significant portal hypertension include a hepatic vein portal gradient less than 10 mm Hg, the absence of venous abdominal collaterals on cross-sectional imaging, the lack of esophageal varices on endoscopy, peripheral blood platelet count greater than 100,000/mL, and hepatic transient elastography values of less than 22 kPa. Overall, for patients with symptomatic, decompensated, or previously undiagnosed liver disease, our practice is to postpone any elective surgical procedure until further evaluation and optimization has been performed.

Perioperative Risk Assessment in Cirrhosis
The American Gastroenterology Association (AGA) recently published the first clinical practice guidelines on perioperative risk assessment in cirrhosis. These guidelines recognize the predictive performance of the MELD score, CTP score, Mayo Postoperative Surgical Risk Score, and the American Society of Anesthesiologists (ASA) score. The CTP score (Table 4) was initially developed to predict survival after esophageal resection for variceal bleeding. It grades ascites, encephalopathy, hypoalbuminemia, hyperbilirubinemia, and prothrombin time (subsequently modified to include international
The scores are summed and classified as A (score 5–6), B (score 7–9), and C (score 10–15). The MELD score was initially developed to predict mortality after transjugular portosystemic shunt placement.\textsuperscript{29} It incorporates bilirubin, INR, and creatinine into an equation that produces a score from 6 to 40 points. The MELD-Na, which adds serum sodium to the original MELD components, is currently used for organ transplant prioritization but has not been evaluated for perioperative risk assessment. The Mayo Postoperative Surgical Risk Score combines the original MELD with ASA status, age, and the underlying etiology of cirrhosis to provide a mortality estimate at 7 days, 30 days, 90 days, 1 year, and 5 years postoperatively.\textsuperscript{26} However, the study population was highly selective, excluding patients with significant nonhepatic comorbidities, which could affect generalizability and predictive value. Although the Mayo risk score derivation population included gastrointestinal, orthopedic, and cardiovascular surgeries, it has not been formally evaluated in other surgery types nor has it been validated outside of the institution where it was developed.

There are unique strengths and limitations with each of the above scoring systems.\textsuperscript{7} The CTP score incorporates clinical factors in addition to laboratory values. Two of these factors, ascites and encephalopathy, are subjectively graded, which increases interobserver variability. Scores are grouped into risk classes, which do not reflect the continuous (rather than categorical) nature of risk. The MELD score incorporates only laboratory measures of hepatic dysfunction but does not capture other hepatic complications, such as ascites. The Mayo risk score showed improved predictive performance over the MELD in the derivation study, in part by incorporating clinical factors.\textsuperscript{26} However, the study population was highly selective, excluding patients with significant nonhepatic comorbidities, which could affect generalizability and predictive value. Although the Mayo risk score derivation population included gastrointestinal, orthopedic, and cardiovascular surgeries, it has not been formally evaluated in other surgery types nor has it been validated outside of the institution where it was developed.

Current studies generally show better performance of the MELD score than CTP score in modern cohorts, but this is not definitive.\textsuperscript{7} For example, some patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Clinical utility</th>
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<tbody>
<tr>
<td>CBC</td>
<td>Anemia; thrombocytopenia</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Abnormalities may be seen due to cirrhosis or complications of its treatment</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Necessary component of MELD score</td>
</tr>
<tr>
<td>Albumin</td>
<td>Assessment of hepatic synthetic function</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>May reflect active hepatitis; often low/normal in cirrhosis due to reduction in number of hepatocytes</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>Necessary component of MELD score</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Necessary component of MELD score</td>
</tr>
<tr>
<td>B vitamins</td>
<td>Deficiencies common in cirrhosis</td>
</tr>
<tr>
<td>Zinc</td>
<td>Deficiencies common in cirrhosis; may impact wound healing</td>
</tr>
<tr>
<td>Selenium</td>
<td>Deficiencies common in cirrhosis; may impact wound healing</td>
</tr>
<tr>
<td>Thromboelastogram</td>
<td>Functional test of coagulopathy that better correlates with bleeding risk and can identify interventions to reduce bleeding risk</td>
</tr>
<tr>
<td>Elastography</td>
<td>Lower stiffness associated with lower risk of portal hypertension</td>
</tr>
<tr>
<td>EGD</td>
<td>Test of choice for screening for esophageal varices</td>
</tr>
<tr>
<td>Ultrasound/CT/MRI</td>
<td>Can demonstrate objective evidence of portal hypertension and sarcopenia</td>
</tr>
<tr>
<td>Handgrip strength</td>
<td>Objective measure of frailty</td>
</tr>
<tr>
<td>Densitometry</td>
<td>Objective measure of sarcopenia</td>
</tr>
</tbody>
</table>

\*CBC = complete blood count; CT = computed tomography; EGD = esophagogastroduodenoscopy; MELD = Model for End-stage Liver Disease; MRI = magnetic resonance imaging.
with severe ascites have relatively preserved hepatic synthetic function leading to a discrepancy between the CTP and MELD scores. The AGA recommends using both systems to overcome this limitation. A limitation with both scoring systems is that they do not incorporate surgery-specific factors, such as the type of surgery or the need for emergency surgery. Table 5 lists surgeries with uniquely associated risk in patients with cirrhosis.

Perioperative mortality risk increases continuously. However, there is no universal cutoff where surgery is absolutely contraindicated. Patients with CTP class A or MELD score less than 10 points can typically undergo elective surgery safely. Patients with MELD score from 10 to 15 points or CTP score of class B may be able to safely undergo elective surgery depending on the degree of portal hypertension and the specific surgery being considered. Multiple studies of different surgery types have shown an increased risk in patients with a MELD score greater than 15 points; mortality may be as high as 50% at 90 days postoperatively. Patients with CTP class C cirrhosis or MELD greater than 20 points have a very high risk of perioperative morbidity and mortality, and the AGA recommends against elective surgery in this population.

Postoperative liver failure is a potential indication for liver transplantation, although eligibility for liver transplantation is ideally determined preoperatively. The AGA recommends delaying non-urgent surgery to facilitate this evaluation in patients with a MELD score greater than 15 points or a liver-related 3-month postoperative mortality risk greater than 15%. Delaying elective surgery until after liver transplantation should also be considered in this population. Patients with severely advanced cirrhosis who develop an urgent or emergent surgical need may encounter a situation of medical futility; Teh et al identified a 100%

| TABLE 5. Surgeries Associated With Increased Risk in Patients With Cirrhosisa |
|-----------------------------|-------------------------------------------------------------------|
| Procedure                   | Complications                                                    |
| Hepatic resection           | Elevated risk of postoperative hepatic failure                    |
| Cholecystectomy             | Elevated risk of mortality and conversion to open procedure       |
| Abdominal wall hernia repair| Poor wound healing and dehiscence in the presence of ascites      |
| Cardiovascular surgery      | Technically complex management of extracorporeal circulation; increased morbidity and mortality if MELD >7 |
| Bariatric surgery           | Roux-en-Y gastric bypass may make liver transplant technically complicated |

<p>| TABLE 4. Child-Turcotte-Pugh Classification for Severity of Cirrhosisa |
|-----------------------------|-------------------------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Clinical and lab parameters</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>None, Mild to moderate, Severe</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None, Mild to moderate (grade 1 or 2), Severe (grade 3 or 4)</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>&gt;3.5, 2.8-3.5, &lt;2.8</td>
</tr>
<tr>
<td>Bilirubin, mg/dL</td>
<td>&lt;2, 2-3, &gt;3</td>
</tr>
<tr>
<td>Prothrombin time prolongation</td>
<td>&lt;4, 4-6, &gt;6</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>&lt;1.7, 1.7-2.3, &gt;2.3</td>
</tr>
</tbody>
</table>

| aTotal score obtained by adding points for each parameter: Class A, 5-6 points; class B, 7-9 points; class C, 10-15 points. |
90-day mortality rate in patients with cirrhosis and an ASA status of 5. Advanced care planning is crucial to ensure patients' wishes are identified.

**PERIOPERATIVE MANAGEMENT OF CIRRHOTIC COMPLICATIONS**

**Infection**

Preoperative infections such as pneumonia or spontaneous bacterial peritonitis are associated with increased postoperative mortality in patients with cirrhosis. Spontaneous bacterial peritonitis can present subtly, and diagnostic paracentesis is recommended for any patient with ascites who suffers a clinical deterioration. Empiric antimicrobial therapy appropriate for the suspected site of infection should be initiated early and tailored based on the results of cultures.

**Ascites**

Ascites can be managed via restricting dietary sodium and using diuretics such as furosemide and spironolactone. Symptomatic ascites is best treated with a large-volume paracentesis followed by the intravenous administration of 6 to 8 g albumin per liter of ascitic fluid removed. Large-volume paracentesis should ideally be performed the day before the planned surgery, as this could help to decrease infection risk (especially spontaneous bacterial peritonitis), decrease abdominal girth, improve ventilatory mechanics, and achieve better overall volume control. Thoracentesis is recommended for patients with hepatic hydrothorax if the effusion is affecting ventilatory mechanics. Intravenous fluid and blood products should be used in a goal-directed manner (such as targeting a mean arterial pressure of >65 mm Hg or a hemoglobin of >7 g/dL) as excessive resuscitation may lead to extracellular volume overload and increase portal venous pressure. Although transjugular intrahepatic portosystemic shunts may be used to treat medically refractory ascites or recurrent variceal bleeding, their role in reducing the risk of perioperative complications has been poorly studied. There are inconsistent data on reducing blood transfusions and limited data on complications such as hepatic encephalopathy. The AGA currently does not recommend placement of preoperative transjugular intrahepatic portosystemic shunt unless it is indicated independent of surgical status.

**Coagulopathy**

Patients with cirrhosis are at risk for both bleeding and thrombosis. These risks are difficult to predict due to variations in pro- and anticoagulant factors. Reduced platelet counts and impaired production of clotting factors (except factor VIII, which is also produced in vascular endothelial cells) and fibrinogen contribute to bleeding risk, whereas reduced protein C and S levels and activation contribute to thrombotic risk. Vascular endothelial dysfunction leads to increased von Willebrand factor production, which is accompanied by an increase in factor VIII. The INR counterintuitively does not correlate with bleeding risk. Rather, pro-coagulant effects dominate in later stages of cirrhosis due to reduced protein C activity, increases in factor VIII levels, and increased platelet aggregation mediated by Von Willebrand factor. Low fibrinogen levels (<120 mg/dL) are associated with increased bleeding risk. Platelet counts greater than 50,000/µL are adequate in most patients undergoing invasive procedures, although platelet counts greater than 100,000/µL are recommended for intracranial or intraspinal procedures and neuraxial anesthesia.

Regarding coagulopathic changes associated with cirrhosis, there are several potential treatment agents that could be used in the perioperative setting. Cryoprecipitate infusion to satisfy fibrinogen levels is reasonable for patients with hypofibrinogenemia, although controlled trials have not shown the clinical efficacy of replacement strategies. Vitamin K may be helpful in cases of malnutrition or biliary obstruction. Fresh frozen plasma transfusion based on INR alone is not recommended as it does not reduce bleeding and the additional volume may worsen portal hypertension. Thrombopoietin analogues have not been approved...
for use in cirrhosis. However, thrombopoietin receptor agonists have been approved for thrombocytopenia due to cirrhosis from hepatitis C (eltrombopag) and cirrhosis from any cause (avatrombopag and lusutrombopag) in patients with platelet counts less than 50,000/µL before invasive procedures. Although these agents were effective in raising platelet counts, bleeding events were not reduced and thrombotic events still occurred. Until further data are available, thrombopoietin receptor agonists should be used cautiously; the AGA recommends limiting their use to selected patients with platelet counts less than 50,000/µL undergoing procedures with high risk for bleeding.7

Because of the above-stated changes in various coagulation factors, patients with cirrhosis are often found to be at increased risk for perioperative bleeding and thromboembolic events simultaneously. A recent meta-analysis showed an increased risk for venous thromboembolism in patients with cirrhosis, particularly in men.38 As a result, patients with cirrhosis should be considered for venous thromboembolism prophylaxis guided by existing practice guidelines,59 which should be tailored accordingly. Consideration could be given for the use of sequential compression devices as well as unfractionated heparin (given its reversibility and shorter duration of activity).

Encephalopathy

Multiple perioperative factors increase the risk for hepatic encephalopathy, including analgesics, protein catabolism, hypovolemia, electrolyte disturbances, bleeding, infection, constipation, and ileus. The diagnosis of encephalopathy (defined as transient cognitive impairment in the setting of cirrhosis, presenting as a spectrum of neurological or psychiatric abnormalities) is made clinically, although a serum ammonia level may be helpful if there is uncertainty. An evaluation for potential precipitating factors should be completed; most common etiologies include infection, electrolyte disorder, gastrointestinal bleeding, constipation, medication side effect, and dehydration.40 Treatment includes minimizing sedating medications, optimizing volume status, electrolyte repletion, controlling infection and bleeding, and ensuring an adequate bowel regimen. Oral or rectal lactulose titrated to two to three bowel movements a day is commonly recommended.40 Rifaximin can be used as second line therapy. Treatment response should be monitored clinically; trending ammonia levels is not recommended.

Malnutrition

Protein depletion, micronutrient deficiency, electrolyte derangement, and malnutrition are frequently seen in cirrhosis. The prevalence of protein-calorie malnutrition increases with increasing severity of liver disease. Alcohol consumption further exacerbates catabolism, leading to greater malnutrition. Malnutrition and sarcopenia are associated with higher rates of perioperative morbidity and mortality in patients with cirrhosis who undergo abdominal surgery or liver transplantation. Although prospective evidence is limited in malnourished patients with cirrhosis, observational evidence from other malnourished populations would suggest delaying elective surgery to optimize nutritional status if sarcopenia (via detection of muscle mass loss in radiographic studies) or decreased muscle function (via exercise testing or 6-minute walk testing) is identified.41 Changes in glucose metabolism have perioperative implications in cirrhosis. Hepatic glucose production decreases due to reduced hepatic glycogen storage and an inability to increase gluconeogenesis to compensate. This results in a metabolic state similar to prolonged starvation after an overnight fast. Fasting should be kept to a minimum perioperatively and glucose monitoring is advisable. Enhanced recovery after surgery protocols are encouraged.41 Specialized diets or regimens have not shown consistent benefit over standard regimens in adults. Calorie requirements are similar to non-cirrhotic patients, but protein needs are increased. Approximately 1.2 to 1.5 g protein/kg body weight/day is recommended to facilitate nitrogen balance and protein accretion. Protein restriction should
be avoided as it increases catabolism and does not reduce the risk of encephalopathy. Enteral nutrition is preferred over parenteral nutrition in patients unable to tolerate oral intake. There may be benefit to initiating parenteral therapy if oral intake will be delayed more than 12 to 24 hours postoperatively. Percutaneous endoscopic gastric tubes are associated with a higher risk of complications in patients with ascites or varices. If necessary, nasogastric or nasojejunal tubes are preferred over percutaneous gastric tubes for most patients.41

Renal Dysfunction
Renal dysfunction directly correlates with mortality risk in cirrhosis, as shown by its inclusion in the MELD score. Common causes of postoperative renal dysfunction in cirrhosis include intravascular volume depletion, acute tubular necrosis, and hepatorenal syndrome.16 Avoiding nephrotoxic agents and ensuring adequate intravascular volume are recommended.7 The use of albumin, especially after large-volume paracentesis or as part of the treatment for spontaneous bacterial peritonitis, can help maintain renal perfusion, although trials have not shown universal benefit of colloid over crystalloid fluids.42 Renal function should be closely monitored postoperatively. The cause of deteriorating renal function should be rapidly identified; a targeted workup could include a complete blood count, serum extended electrolytes (including calcium, magnesium, and phosphorus), urinalysis with microscopy, urine electrolytes, and a renal ultrasound. If hepatorenal syndrome is identified, rapid treatment is vital as this condition is often fatal if not treated. Vasoactive medications may be necessary to treat hepatorenal syndrome and early specialist consultation should be considered in such cases.16

Medication Management
Significant alterations in drug metabolism, protein binding, and elimination occur in cirrhosis, increasing the risk of medication toxicity. General principles include starting at lower doses with longer dosing intervals, particularly for sedating medications such as opioids and benzodiazepines. Short-acting medications are preferred to long-acting medications, especially in the early perioperative period.13 Hydromorphone and fentanyl have favorable hepatic metabolism compared to other opioids. Acetaminophen is safe in cirrhosis at doses of up to 2 g per day.7 Nonsteroidal anti-inflammatory medications are generally avoided to lessen the risk for kidney injury and platelet dysfunction in the setting of coagulopathy. All current anesthetic agents may be safely used in the setting of acute or chronic liver disease.

Patients who have received a liver transplant deserve special attention with respect to medication management to avoid compromising immunosuppression or inducing toxicity. The prescribed regimen should be identified, ideally with goal drug levels. In most cases, post-transplantation immunosuppressive medications should be continued preoperatively as closely as possible to their normal schedule. Calcineurin inhibitors such as tacrolimus and cyclosporine are prescribed to most patients after liver transplantation and have several properties that can lead to altered drug levels perioperatively. They are metabolized by CYP3A4/5 enzymes; any new medications should be screened for potential drug interactions. In addition, disruptions in gastrointestinal motility can affect absorption, with increased absorption potentially occurring in situations that prolong transit time (eg, ileus, opioid use). Monitoring trough levels of calcineurin inhibitors postoperatively is reasonable and a liver transplantation expert should be consulted if significant drug level alterations are anticipated or identified.43

MANAGEMENT OF INFLAMMATORY BOWEL DISEASE IN THE PERIOPERATIVE SETTING
Patients with inflammatory bowel disease (IBD) require careful preoperative evaluation, with particular focus on assessment of disease severity and current activity, potential IBD-related complications (nutritional deficiencies, anemia, venous thromboembolic [VTE] risk, and chronic pain), and
IBD-specific medication management. Recommended perioperative IBD management depends on whether the patient is undergoing gastrointestinal surgery or non-gastroenterological surgery.

In non-gastroenterological surgery, assessment for an IBD flare is a key element of the preoperative evaluation. Pertinent history includes the presence of fevers, chills, bowel habit change, oral intake, weight loss, bleeding, pain level, and current medications. Preoperative inflammatory markers (such as erythrocyte sedimentation rate or C-reactive protein) may assist the clinical evaluation. In the case of elective and non-urgent surgery, patients with suspected active or flared IBD should be referred to their gastroenterologist as part of the preoperative assessment. All patients with IBD merit preoperative laboratory studies to include a complete blood count, metabolic panel, and serologic nutritional markers (eg, albumin and prealbumin) if there is concern for malnutrition.

If severe malnutrition is present, surgery should be delayed for nutritional optimization. Weight loss greater than 10%, albumin less than 3 g/dL, and body mass index less than 18.5 kg/m² are associated with postoperative complications. In mild cases, patients should be referred to a dietician to optimize oral nutrition. In cases of severe malnutrition unresponsive to optimized oral nutrition, patients may require enteral (preferred route) or parenteral nutrition.

Anemia is the most common systemic complication of IBD and is usually due to iron deficiency. Alternatively, it may be related to chronic systemic inflammatory burden, malabsorption, other nutritional deficiencies, and gastrointestinal blood loss. If anemia is present, evaluation for gastrointestinal blood loss and nutritional deficiencies is required. Patients with iron deficiency anemia should be given iron supplementation, although the optimal timing, route of administration, and effect on perioperative transfusion requirements are unknown.

Patients with IBD are at increased VTE risk in both inpatient and outpatient settings, highlighting the need for aggressive perioperative VTE prophylaxis. The presence of IBD is incorporated into the commonly used Caprini risk assessment model, which guides perioperative VTE prophylaxis in many non-orthopedic surgeries. Patients with IBD undergoing gastroenterological and non-gastroenterological surgery should receive prophylaxis based on current clinical guidelines for VTE prevention in both orthopedic and non-orthopedic surgery. Because of the additional VTE risk associated with IBD, some practices extend postoperative VTE prophylaxis to 30 days in patients undergoing gastroenterological surgery.

In individuals with IBD and chronic abdominal pain or taking opioids, a pain management plan and associated expectations should be addressed preoperatively. If possible, it is ideal to wean opioids before surgery due to increased risk for postoperative constipation, ileus, respiratory complications, and possible increased risk for overall mortality. Involvement of pain medicine specialists is beneficial.

Chronic corticosteroids and other immunosuppressive medications are frequently used in IBD treatment. Associated perioperative concerns, due to the use of chronic corticosteroids or other immunosuppressants, include impaired wound healing, infection, hyperglycemia, fluid retention, and delirium. In patients receiving chronic corticosteroids who are undergoing gastroenterological surgery, there may be concerns about increased risk of intra-abdominal sepsis and anastomotic healing. In general for non-gastroenterological surgery, the lowest dose of corticosteroids should be used and need for supplemental steroids addressed on a case-by-case basis. Perioperative glucocorticoid supplementation is based on both surgery type and patient-specific factors (including steroid dose and duration of therapy). Purine analogues including azathioprine and 6-mercaptopurine are generally held the day of surgery but otherwise continued throughout the perioperative timeframe. Aminosalicylates can be continued through surgery, unless there is concern for renal insufficiency.
patients undergoing non-gastroenterological surgery, biologics are typically held preoperatively (length of time depends on the specific medication) and surgery should occur at the end of the dosing cycle. Biologics are typically resumed 2 weeks postoperatively or after wound healing is complete. The decision to hold these medications is complex and must be balanced with the potential risk of IBD flare. Risks should be discussed with the patient and the primary gastroenterologist. The evidence regarding continuation of biologic agents in patients undergoing gastroenterological surgery for IBD is mixed and depends on the surgical procedure, the severity and type of underlying disease, and other factors. This is best deferred to the patient’s gastroenterologist.

RENA L PHYSIOLOGY IN THE PERIOPERATIVE PERIOD
Renal function can be affected during the perioperative period due to hemodynamic changes and medication selection, leading to a reversible decrease in renal blood flow and secondary decrease in glomerular filtration rate. Renal blood flow may be indirectly affected by anesthesia-related sympatholysis and intraoperative hypotension. The physiologic response to surgery further impacts renal perfusion as catecholamines released in response to noxious stimuli activate the renin-angiotensin system as well as directly constrict the renal circulation, thus directly decreasing renal blood flow. During surgery, there is additional antidiuretic hormone release, which promotes fluid retention and transient hyponatremia. In patients with pre-existing renal impairment, consideration should be given to the direct renal effects of medications as well as renal clearance of medication. Most medications can be used safely in patients with renal disease, although some require dose adjustments based on renal function.

FLUID MANAGEMENT IN THE PERIOPERATIVE PERIOD
The ideal preoperative fluid management strategy continues to be debated. Traditional liberal fluid strategies are associated with intravascular expansion and improved end organ perfusion. This strategy, however, is associated with a higher incidence of volume overload complications, including interstitial edema and poor tissue healing. More restrictive fluid strategies have also been used. These have been successful in reducing the length of hospital stays, but have been associated with an increased incidence of acute kidney injury. Most current enhanced recovery after surgery protocols incorporate the use of goal-directed fluid management in the perioperative period, wherein the goal is to maintain tissue perfusion without causing the deleterious effects of volume overload. This is achieved by closely matching intravenous fluid therapy to predetermined hemodynamic goals.

PERIOPERATIVE ASSESSMENT AND MANAGEMENT OF PATIENTS WITH END-STAGE RENAL DISEASE
Preoperative Assessment for Patients With End-stage Renal Disease
The perioperative management of patients with chronic kidney disease is covered in a separate entry in this perioperative series. Patients with end-stage renal disease (ESRD) (glomerular filtration rate less than 15 mL/min or dialysis-dependent) require special perioperative consideration. These patients have a significantly higher risk of perioperative morbidity and all-cause mortality spanning multiple types of surgery, likely related to an increased rate of cardiovascular disease, electrolyte disturbances, and blood pressure lability. A large retrospective cohort study using the American College of Surgeons National Surgical Quality Improvement Program database compared patients with ESRD with matched controls undergoing common general surgery procedures. End-stage renal disease was associated with increased mortality (odds ratio, 9.05; 95% CI, 4.09 to 20.00), as well as increased rates of return to the operating room, postoperative infection, and pulmonary complications. End-stage renal disease is not a contraindication to elective surgery, but
special preoperative planning and counseling is indicated.

During the preoperative assessment, the patient’s renal function and regular dialysis regimen should be clarified and the plan for perioperative dialysis discussed. In particular, it is useful to know the patient’s current dry weight to help assess volume status in the perioperative period. Whether the patient continues to produce urine should also be established as this may influence medication decisions. Residual renal function, with even minimal urine production, is associated with better prognosis; as such, it is worthwhile to preserve any renal function, if at all possible.65

The preoperative physical examination should include a volume assessment and evaluation of the dialysis access site to ensure there is no evidence of infection. Preoperative labs should include a complete blood count (to assess for anemia) and a full set of extended electrolytes, including calcium, phosphorus, and magnesium (to help guide perioperative dialysis).

**Perioperative Management of Patients with ESRD**

**Timing of Dialysis.** Dialysis is necessary to correct electrolyte abnormalities (particularly potassium and urea), acid-base imbalance, and volume status. The goal is to reach the patient’s dry weight before surgery. For patients on hemodialysis, it is recommended that patients dialyze 12 to 24 hours before elective surgery, ideally the day before surgery.66 Logistically, elective surgical procedures should not be scheduled on Monday as most outpatient dialysis centers are closed on Sunday. There is no evidence to suggest that an additional hemodialysis session (besides the normal routine) improves outcomes. If dialysis must be performed within 4 to 6 hours of surgery, heparin should be avoided to decrease perioperative bleeding risk.66,67 For patients on peritoneal dialysis, some nephrologists recommend increasing the dialysis time for a few days to a week before surgery in anticipation that postoperative peritoneal dialysis may be delayed or complicated by ileus or constipation. This may be achieved by adding an additional exchange per day for patients on continuous ambulatory peritoneal dialysis or adding an additional couple of hours on the cycler for patients on continuous cycling peritoneal dialysis.68,69 However, there are no published data on the outcomes of this practice, and increased preoperative peritoneal dialysis is not uniformly endorsed.

**Hyperkalemia.** In the perioperative setting, hyperkalemia is the electrolyte derangement of greatest concern, given the potential effects on cardiac membrane stability. It is prudent to check the plasma potassium level on the day of surgery to re-evaluate an unexpectedly elevated potassium level because pseudohyperkalemia can result from mechanical trauma related to venipuncture, prolonged tourniquet time, or blood drawn through the intravenous line. Although there is no clear consensus regarding an ideal preoperative potassium level, it is recommended that potassium be less than 5.5 mEq/L before elective surgery.66 In the case of nonelective surgery, patients with hyperkalemia should have a preoperative electrocardiogram (ECG). In their usual sequence of appearance, hyperkalemia results in peaked T waves, prolonged PR intervals, loss of the P wave amplitude, widening of the QRS complex, sine wave configuration, and eventually ventricular fibrillation and asystole.70 Serum potassium greater than 6.5 mEq/L is usually associated with ECG changes, although it is also possible for a patient to directly enter ventricular fibrillation or asystole without prior ECG disturbances.70 Furthermore, it has been recommended that a patient be dialyzed preoperatively if there are any hyperkalemia-associated ECG changes or if the serum potassium is greater than 6.0 to 6.2 mEq/L.71

**Anemia.** Before elective surgery, the goal is to bring hemoglobin to target levels using erythropoiesis-stimulating agents (ESAs) and intravenous iron supplementation to reduce the need for red blood cell transfusion. It is particularly important to minimize transfusions in patients anticipating
renal transplantation given the concern for alloimmunization and subsequent increased risk of graft rejection. Patients with anemia are at risk for bleeding. Lower concentrations of red blood cells result in positioning of platelets within the bloodstream further from the subendothelium, which makes them less likely to induce clotting. Red blood cells release adenosine diphosphate and thromboxane A2, which trigger platelet aggregation, and are reduced in the setting of anemia. Therefore, it is recommended that hemoglobin and iron studies be assessed and optimized with ESAs and iron supplementation before elective surgery. The 2012 Kidney Disease Improving Global Outcomes guidelines recommend achieving a hemoglobin between 10 and 11.5 g/dL, transferrin saturation greater than 30%, and ferritin greater than 500 ng/mL. If hemoglobin is less than 10 g/dL and transferrin saturation and ferritin are not above these goals, iron should first be repleted before initiating the ESA. Typically, 1000 mg intravenous iron is given as a single dose or as repeated smaller doses at consecutive hemodialysis sessions. Transferrin saturation and ferritin levels can be rechecked 1 week after the last iron infusion.

Coagulation Abnormalities. Patients with ESRD are at increased risk of bleeding. There are several underlying reasons for this, including uremia-induced platelet dysfunction, abnormal platelet-endothelial interaction, and anemia. Therefore, preoperative dialysis is important to reduce urea levels and reduce platelet dysfunction. However, heparin should be avoided if dialysis is performed within 4 to 6 hours of surgery. As noted above, optimizing hemoglobin to target levels also decreases bleeding risk.

Desmopressin, which assists platelet aggregation by increasing release of von Willebrand factor, can be considered for patients with a history of excessive bleeding. This can be given intravenously, subcutaneously, or intranasally immediately before or during surgery. The intravenous and the subcutaneous dose is 0.3 µg/kg and the intranasal dose if 3 µg/kg. Desmopressin takes effect in approximately 1 hour and lasts for at least 4 hours. However, there is no clear evidence that desmopressin significantly impacts clinical outcomes and there is some potential increased risk of thrombotic events.

Malnutrition. Malnutrition is common in ESRD, in part related to changes in taste and appetite, loss of nutrients during hemodialysis, dialysis-induced catabolism, inflammation, and dietary restrictions. Before elective surgery, it is recommended that nutritional status be assessed and optimized orally as much as possible. Surgical patients with a body mass index less than 18.5 kg/m², more than 10% weight loss within 6 months, or 5% over 3 months are considered to be malnourished as per the European Society for Parenteral and Enteral Nutrition guidelines. Involving a dietician is especially helpful in these circumstances. Oral nutritional supplements are preferred over intravenous supplements. Renal specific supplements that are high protein, low volume, and have reduced potassium and phosphorus are preferred in patients with a history of hyperkalemia, hyperphosphatemia, or volume overload.

CONCLUSION

Patients with chronic gastrointestinal, hepatic, or renal disease are at risk for multiple perioperative complications and require a comprehensive preoperative evaluation. A multidisciplinary approach is often beneficial and specialist involvement should be considered. The intraoperative and postoperative plans should be individualized based on the unique medical and surgical characteristics of each patient.

POTENTIAL COMPETING INTERESTS

The authors report no potential competing interests.
Abbreviations and Acronyms: AGA, American Gastroenterology Association; ASA, American Society of Anesthesiologists; CTP, Child-Turcotte-Pugh (score); ECG, electrocardiogram; ESA, erythropoiesis-stimulating agent; ESRD, end-stage renal disease; IBN, inflammatory bowel disease; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; NGS, non-gastroenterological surgery; VTE, venous thromboembolism

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REFERENCES