Chapter 8
Perioperative Critical Care of the Patient with Liver Disease Undergoing Nonhepatic Surgery

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Introduction

Patients with compensated liver disease are at increased risk of morbidity and mortality when undergoing anesthesia and surgery. Key concerns with hepatic decompensation include neurologic, cardiovascular, renal, respiratory dysfunction, coagulopathy, and infection.

Risk Assessment

Risk assessment is based on a combination of the severity of liver dysfunction, intensity of surgical stress, comorbidities, and functional status. Liver dysfunction comprises synthetic dysfunction and portal hypertension. The Childs-Turcotte-Pugh score and the model for end-stage liver disease (MELD) gauge severity of liver dysfunction. Although controversy exists as to which score is better [1], they complement each other and present the clinician with a more robust understanding. The patient's functional status should also be considered. The Charlson comorbidity index [2] correlates with morbidity and mortality after surgery in cirrhotics [3], but the impact may be obscured by the status of MELD and American Society of Anesthesiologists (ASA) [4] in multivariate analysis. The ASA predicts short-term morbidity and mortality [4] but has limited discrimination as patients with chronic liver disease will be at least status III. MELD and CTP correlate with long-term

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mortality, at 30, 90, and 365 days. Surgical stress is highest for intrathoracic, particularly cardiac and intra-abdominal procedures. However, procedures likely to result in significant blood loss and intraoperative hemodynamic instability should also be considered as high surgical stress. Surgery undertaken emergently increases this risk profile dramatically [5]. An online calculator is available to estimate the risk of major surgery in patients with cirrhosis. (http://www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/post-operative-mortality-risk-patients-cirrhosis)

Risk Mitigation

Hemodynamics and Renal Function

Liver injury which results from anesthesia and surgery is at least in part due to changes in hepatic hemodynamics. Increased hepatic venous resistance often coincides with decreased arterial perfusion pressure. Preoperative optimization requires assessment of the patient's cardiovascular status, renal function, and pulmonary function. Cirrhosis is associated with cardiomyopathy which is manifest by conduction abnormalities and diastolic dysfunction [6, 7]. Preoperative assessment with transthoracic echocardiography can be complemented by intraoperative transesophageal monitoring. In particular, right ventricular function can be assessed as intravascular volume and vasopressors are manipulated. Stress echocardiography is often used as a screen for hemodynamically significant coronary artery disease.

Patients with cirrhosis are often volume-overloaded with ascites and edema. Renal dysfunction is often masked as low creatinine and urea nitrogen may reflect sarcopenia and impaired ureagenesis rather than normal glomerular filtration rate (GFR). However, in early hepatorenal syndrome, the sodium avidity of the kidney indicates hypoperfusion, and echo demonstration of underfilling of the left ventricle will confirm intravascular volume contraction. This is often associated with significant arterial vasodilation which correlates with the severity of cirrhosis. Preoperative optimization includes restoration of perfusion pressure by increasing arterial tone and intravascular volume while controlling ascites and decreasing edema. Arterial vasodilation may reflect hypocalcemia and severe anemia as well as concomitant adrenal insufficiency [8, 9]. Hypoalbuminemia may be addressed with hyperoncotic albumin and judicious diuresis undertaken. Persistent arterial vasodilation may require vasopressor support. Terlipressin is not available in the United States but would be the first-choice agent in much of the world. Our preference is norepinephrine. Large-volume paracentesis may also be considered in an effort to optimize renal function once arterial tone and intravascular volume are optimized. The need for significant vasopressor support in advance of induction of anesthesia heralds an even higher risk of perioperative morbidity and mortality.

Electrolyte imbalance is common in cirrhosis. Hyponatremia, hypokalemia, hypomagnesemia, hypophosphatemia, and hypozincemia can be addressed preoperatively. Care should be taken to avoid exacerbating metabolic acidosis by administering hyperchloremic solutions. Balanced electrolyte solutions are commercially available. In addition, the relatively high chloride content of blood products including albumin can be counterbalanced by creating a solution of 0.45% sodium chloride with 50–75 mEq/L which is readily available and inexpensive. Over-rapid correction of hyponatremia which is associated with central pontine myelinolysis also can be avoided with this approach. Although colloid administration is controversial, patients with cirrhosis appear to benefit from albumin particularly in the settings of infection and renal failure. However, other colloids such as hydroxyethyl starch (Hetastarch) are associated with renal failure and relatively contraindicated in the setting.

Neurologic Function

Hepatic encephalopathy develops with deteriorating liver function and worsening portosystemic shunting. It often heralds infectious complications or acute bleeding. Agitation, delirium, and altered nociception are typical. If the enteral route is available, we continue rifaximin and lactulose, and zinc if hypozincemia. We do not restrict protein but do occasionally use branched chain enriched formulae if encephalopathy is refractory to standard measures. We address environmental factors such as early mobilization of the patient out of bed, daylight during the daytime, and promote sleep hygiene with efforts to minimally disturb the patient at night. Local therapy such as repositioning, a heating pad, and/or lidocaine patch serve to minimize systemic narcotic requirements. Although we are hesitant to place epidural catheters in coagulopathic patients, regional anesthesia is often a very useful adjunct.

The metabolism of sedative hypnotics and narcotics is impaired in liver failure but unpredictably. We avoid benzodiazepines and minimize narcotics—treating as needed rather than with continuous infusions. Non-narcotic approaches are limited as nonsteroidal anti-inflammatory agents may increase the risk of GI bleeding. Acetaminophen is effective and can be administered parenterally if needed, but the total daily dose should be reduced in liver failure to 2 g. Ketamine is an excellent analgesic in small doses of 10–25 mg and does not cause respiratory depression or worsen hemodynamic instability. Gabapentin is an effective adjunct [10]. Even a single preoperative dose lowers narcotic requirements [11].

Hepatic encephalopathy seems to reduce the incidence of recall during anesthesia. Isoflurane and sevoflurane have minimal direct impact on hepatic function [12]. However, both may exacerbate arterial vasodilation and result in hypotension requiring vasopressors. Although the minimum alveolar concentration for volatile anesthetics is higher in chronic alcohol users, it is significantly lower in the setting of liver disease [13].

Pulmonary Function

Respiratory function may be impaired in cirrhosis because of mechanical factors such as ascites and chest wall edema as well as altered respiratory drive related to hepatic encephalopathy. Gas exchange may also be affected by atelectasis, pulmonary edema, and pneumonia. In the absence of radiographic abnormalities, the diffusing capacity is often low and reflects intrapulmonary shunting due to hepatopulmonary syndrome, which can be demonstrated with echocardiography using microbubbles. In addition to optimizing the patient's volume status preoperatively, discontinuation of tobacco smoking and management of obstructive airways with appropriate bronchodilation are imperative. Once intubated and mechanically ventilated, such patients are particularly prone to lung injury. Consequently, a lung-protective ventilating strategy should be undertaken with low tidal volumes (6 mL/kg IBW) and PEEP [14]. We use the ARDS-Net high PEEP protocol [15] to titrate PEEP and FiO_2 and start with the PEEP set at BMI/4. The duration of intubation and mechanical ventilation should be minimized. This requires minimizing sedation in the ICU changing intraoperative anesthetic management. We attempt extubation within 6 h, in the OR if possible. We use noninvasive ventilation with CPAP or BiPAP until the patient can mobilize out of bed and cough effectively. These patients often have impaired gastric motility. Aspiration of gastric contents is often a life-ending event, prompting us to routinely decompress the stomach with a gastric tube until the patient can protect the airway.

Nutrition

Malnutrition is common in liver failure [16], with muscle wasting and sarcopenia evident on exam and abdominal CT [17] even in obese patients with nonalcoholic fatty liver disease [18]. The MELD score fails to capture this comorbidity which correlates with weakness and risk of postoperative infection. Cirrhosis is a catabolic process which is difficult to reverse. However, if time permits, a trial of nutritional supplementation is indicated, with postpyloric placement of a small-bore feeding tube [19] if sufficient calories and protein cannot be reliably ingested per os. We aggressively treat hepatic encephalopathy rather than reduce protein. Vitamin deficiencies should be anticipated, particularly fat-soluble vitamins in cholestatic liver disease. Thiamine supplementation is indicated particularly in alcohol-induced liver disease.

Liver Support

The potential for improvement in liver function should be assessed. Patients with acute viral hepatitis or untreated autoimmune hepatitis or alcoholic hepatitis are likely to improve with supportive care, specific treatments, and time. In such

patients, elective surgery should be deferred. A combination of acute liver injury and the need for emergent surgery presents a high risk. There may be benefit for administration of N-acetylcysteine [20] .

Mechanical support for patients with liver failure is an area of intense interest. High-volume plasma exchange has recently been shown to be of benefit in acute liver failure [21]. Improvement in hemodynamics, encephalopathy, cholestasis, and ammonia levels results in acute or chronic liver failure in patients treated with MARS, although there is no improvement in survival [21, 22]. Data are insufficient to argue for routine prophylactic use or for attempted rescue with these approaches in the event hepatic decompensation occurs after surgery. The experience with other support devices such as ECMO and ventricular assist devices in liver failure has been dismal, and these interventions are unlikely to be of benefit.

Portal Hypertension

Portal venous pressures and the transhepatic venous pressure gradient correlate with severity of cirrhosis and may be reflected in the degree of thrombocytopenia. Liver injury, perhaps due to ischemia or associated with acute inflammation, will increase resistance to portal flow. If portal flow is maintained despite higher resistance, portal pressures will rise. This will increase ascites production and will increase the risk of gastrointestinal and intra-abdominal hemorrhage. Preoperative placement of intrahepatic shunts (TIPS) has been advocated as a way of reducing the morbidity associated with portal hypertension [23]. However, small studies have failed to show benefit of preoperative placement of TIPS [24]. Furthermore, TIPS in advanced liver disease (MELD >14 or CTP "C") is associated with more rapid hepatic decompensation and is relatively contraindicated, particularly if liver transplantation is not an option. If a TIPS is placed, a period of 6–8 weeks should elapse before proceeding with surgery. This will allow decompression of the splanchnic vasculature. It also will allow hepatic decompensation to manifest, perhaps avoiding death after elective surgery.

Hemostasis

The coagulopathy of liver disease includes depressed procoagulant and anticoagulant factors as well as thrombocytopenia. However, qualitative platelet dysfunction and unchecked fibrinolysis may also be factors. In addition, infection (even if low-grade) results in tissue inflammation and activation of coagulation pathways. Renal failure may exacerbate impaired platelet function. Conventional measures of coagulation often exaggerate the procoagulant factor deficiency with prolonged prothrombin time and INR. Fibrinogen levels can be assessed, but laboratory turnaround is often too slow to be of benefit. As a consequence, patients are transfused plasma, which may result in volume overload and increased hepatic congestion without

effectively treating the coagulation deficit. Thromboelastography (TEG) offers real-time analysis of the patient's coagulation and guides more focused blood product transfusion [25]. Rotational thromboelastography is an emerging alternative. Hyperfibrinolysis can be recognized by TEG, but low-grade fibrinolysis likely often contributes to the bleeding diathesis in decompensated liver disease. ε-Aminocaproic acid (Amicar) is effective and safe in reversing hyperfibrinolysis [26]. Prophylactic use during surgery and in the ICU might be considered in the cirrhotic at high risk for bleeding.

Infection

Liver failure is an immune-incompetent state. Postoperative infection is a feared complication, and the risks increase with the severity of liver disease and attendant comorbidities such as malnutrition, ascites, and renal failure. Perioperative antimicrobial prophylaxis for skin organisms may be augmented to cover bowel pathogens. Fungal pressure in these patients is high, and we have a low threshold for including antifungal agents such as fluconazole or micafungin. Accumulation of low protein (high serum—ascites albumin gradient, SAAG) with impaired opsonization of pathogens is a particular risk. Peritoneocentesis with supplemental albumin to maintain intravascular volume will decrease risk of infection and abdominal wound dehiscence. Ascitic neutrocytosis resolves rapidly (48 h) after surgery, and a rising ascites WBC thereafter may herald peritonitis [27]. We have a low threshold to include infection in the differential for any manifestation of hepatic decompensation. Cultures from all available sites, cell counts with differentials of ascites, and other drainage from surgical sites and stool leukocytes with *C. difficile* toxin assay are done if indicated. We minimize central venous and arterial access. We have a low threshold to initiate antimicrobial coverage—bacterial and fungal—with a commitment to discontinue in the absence of proven pathogen or site of infection. Procalcitonin may be misleading as a marker of infection as it is elevated in liver injury. However, elevated procalcitonin levels associated with infection diagnosed by other means will fall with effective therapy but may not normalize.

End of Life

Improvements in surgical and anesthesia techniques mean that even high-risk patients are offered surgery, and they survive to reach the ICU. There, some will fare well. However, many suffer significant morbidity, and of these a high proportion die. This chapter has addressed risk mitigation strategies. It is vital that the patient and family understand that the options available to manage hepatic decompensation are limited. Realistic expectations must be established prior to surgery. An intensivist familiar with the perioperative management of such patients may be of particular

value in this discussion. Prior to proceeding with surgery, the discussion should include when inappropriate medical care will be withheld. A practical example for discussion might be the patient who develops postoperative hepatic decompensation with intractable hemorrhage, for whom further surgical intervention is futile and will not benefit from continued blood product administration. Likewise, cardiac resuscitation in this setting is rarely medically appropriate. Even the candidate accepted for liver transplantation who acutely decompensated after nonhepatic surgery is unlikely to be transplanted successfully. This slim chance should not be used to provide medically inappropriate care.

Conclusion

Surgery and anesthesia present significant risks of increased morbidity and mortality to the patient with liver disease. Risk assessment mandates an understanding of the cause and severity of liver disease, medical comorbidities, functional status of the patient, and the surgical stress of the planned procedure. Risk mitigation can be undertaken in elective case. Likewise, supportive strategies can be employed when emergent surgery precludes robust optimizations. Preoperative management includes counseling about the possible outcomes and the appropriate constraint of medical options to ensure best patient care.

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