Patients with liver disease undergoing non-hepatobiliary surgery

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Patients with liver disease undergoing non-hepatobiliary surgery have an increased risk of morbidity directly associated with their underlying liver dysfunction. They have greater transfusion requirements, higher infection risk, greater potential for organ dysfunction and experience longer hospital stays with higher mortality.

The prevalence of liver disease is rising in New Zealand. 10 % of the New Zealand population have chronic liver disease with 10% of these patients having cirrhosis (1). The largest causes in New Zealand are Hepatitis B and C and Alcoholic and Non Alcoholic Fatty Liver Disease (1). Anaesthetists will see an increase in non-hepatobiliary surgery for cirrhotic patients due to longer term survivals, an increasing disease burden and an aging affected population. Operative risk correlates with the severity of the underlying liver disease and the nature of the surgical procedure.

Knowledge of the perioperative implications for anaesthetising these patients is of relevance to prevent morbidity and mortality and enable improved outcomes.

Pre-operative Assessment

Assessment of the patient with liver disease presenting for non-hepatobiliary surgery should involve elucidation of the cause and nature of their disease. Disease severity should be assessed along with the presence of cirrhosis, portal hypertension, related complications and associated organ dysfunction.

It is important to risk stratify these patients before their surgery. Historically the Childs Pugh Scoring system was used to assess perioperative risk following hepatic and non-hepatobiliary surgery. The score comprises five variables and stratified into groups A (<7), B (7 to 9) and C (10-15) based on increasing severity (2).

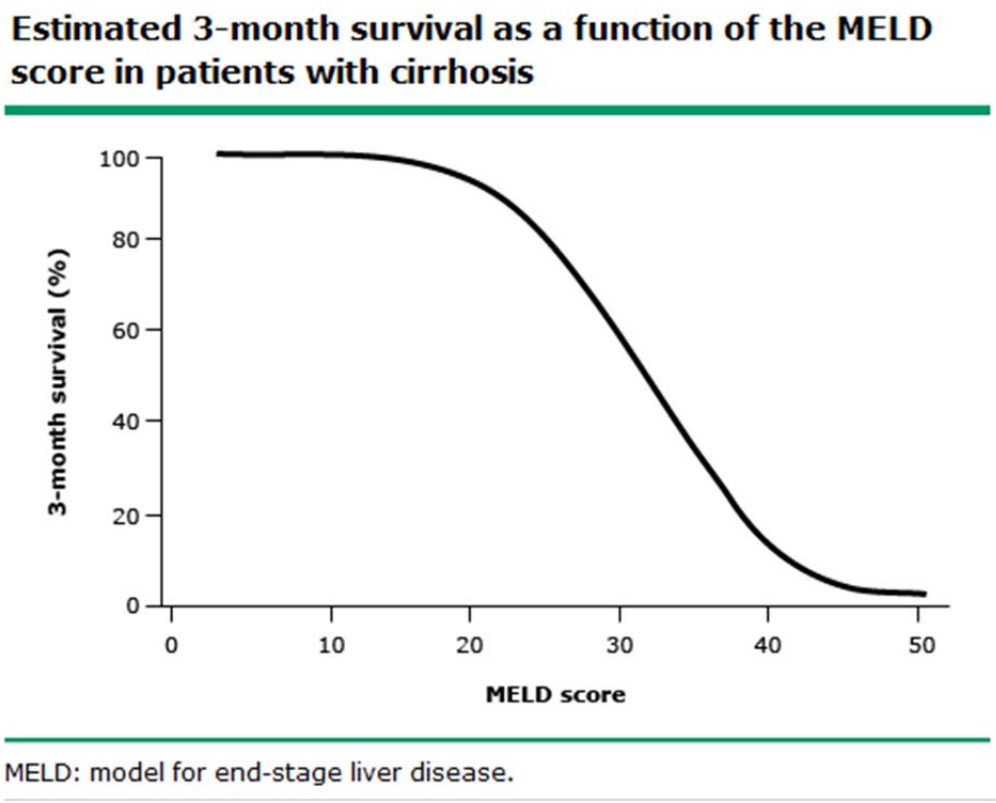
Child-Pugh classification of severity of cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

The Child-Pugh classes correlate with one- and two- year patient survival of:

Class A: 100 and 85%
Class B: 80 and 60%
Class C: 45 and 35%

The Child-Pugh score has been superseded by the more objective and accurate Model for End Stage Liver Disease (MELD) score which predicts post-operative mortality independent of the type of surgery. A higher MELD score is associated with a higher mortality and patients with MELD >15 should avoid elective non-essential surgery where possible (3). Most patients with MELD scores above 25 will die in hospital regardless of treatment and 3 month survival decreased exponentially beyond this (2), (4).



MELD: model for end-stage liver disease.

Thorough assessment of liver synthetic function, potential organ dysfunction and disease related complications is essential to ensure a stable intraoperative course and avoid perioperative morbidity. This is particularly important in the presence of portal hypertension where renal dysfunction, porto-pulmonary hypertension and hepato-pulmonary syndrome may be present increasing the likelihood of post-operative decompensation. Patients having acute or emergency surgery and those undergoing intra-abdominal surgery are at even higher risk independent of their underlying liver dysfunction.

Optimisation of coagulopathy and fluid and electrolyte abnormalities is important preoperatively to ensure a more stable intraoperative course. Nutritional assessment is very important and correction of protein-calorie malnutrition with nutritional support is beneficial.

Intraoperative Management

As with any patient, the choice of anaesthetic and level of monitoring should be tailored to the nature of surgery and overall patient assessment. The use of regional anaesthesia where possible allows a decrease in patient exposure to opioid analgesia avoiding possible respiratory depression and potential for worsening delirium or encephalopathy. When opioids are required fentanyl should be utilised preferentially as it's metabolism is not affected by hepatic dysfunction. Certain

Benzodiazepines such as midazolam or diazepam should be avoided or used with caution due to the potential for increased duration of action and worsening CNS depression/encephalopathy.

Tense ascites may reduce the Functional Residual Capacity (FRC), complicate ventilation and increase the risk of aspiration. Rapid Sequence Induction (RSI) may be indicated and drainage of ascites will aid ventilation. Severe liver disease is associated with reduced plasma cholinesterase activity and prolonged neuromuscular block following suxamethonium is possible, though rarely a problem clinically. Atracurium and cisatracurium are the muscle relaxants of choice in liver disease due to metabolism through Hoffman's degradation. Rocuronium onset time is longer with a prolonged recovery time in cirrhotic patients. A number of small studies have shown Sugammadex can safely reverse neuromuscular blockade after rocuronium in patients with liver dysfunction however, appropriate dosing is necessary and reversal may not be as rapid as in patients with normal liver function (5), (6).

The presence of clinical coagulopathy may warrant preoperative correction and acquisition of blood and component products depending on severity, nature of surgery and anticipated blood loss. The preoperative INR has no predictive value and point-of-care testing with thromboelastography is useful for guidance of component therapy. This should always be used in conjunction with clinical findings. Thrombocytopenia is common in portal hypertension due to sequestration and decreased thrombopoietin production. Platelet function should be assessed as thrombocytopenia alone is not an indication for platelet therapy. In situations of severe thrombocytopenia with associated dysfunction treatment options include platelet transfusions, splenic embolisation and splenectomy. Recombinant thrombopoietin and other thrombopoietic agents are currently under investigation in clinical trials. Prevention of hypothermia is especially important in patients with liver disease to prevent coagulopathy. The operating room temperature should be increased and patient and fluid-warming devices should be used.

Intraoperative haemodynamic stability can be challenging due to underlying low systemic vascular resistance, blunted chronotropic and inotropic responses in cirrhotics and challenging fluid status arising from hypoproteinaemia and resultant decreased effective plasma volume. Hepatic blood flow decreases during anaesthesia and is normally compensated with increased hepatic arterial flow. Cirrhotic patients have decreased ability to increase hepatic arterial flow. Their liver perfusion and oxygenation rely on stable haemodynamics which must be preserved to avoid worsening liver dysfunction. Vasodilatory hypotension should be treated with appropriate intravascular volume expansion and administration of a vasoconstrictor. 4% Albumin is an acceptable volume expander particularly given the underlying hypoalbuminaemic states of many of these patients. Fluid resuscitation can be challenging as excessive administration can lead to increased cardiac filling pressures leading to hepatic congestion, pulmonary oedema, and resulting respiratory failure. Renal perfusion should be optimised as these patients are high risk for concomitant renal dysfunction which greatly increases morbidity and further complicates fluid balance.

Intraoperatively strict attention must be paid to monitoring glucose levels. Multiple factors affect glucose levels, including the inflammatory response to surgery, steroid administration, hepatic dysfunction, altered glycogen stores, and insulin resistance in liver failure. Hyponatraemia is often present and must be corrected to ensure prevention of encephalopathy. Rapid correction should be avoided to prevent central pontine myelinolysis.

Post-operative Care

The postoperative care of patients with liver disease begins with appropriate placement. This is determined by the severity of the patient's disease, associated co-morbidities and the nature and course of surgery. Admission to a High Dependency Unit or Intensive Care Unit should be considered for any high risk or high MELD patient even in the setting of uneventful surgery. Where encephalopathy and altered GCS is present preoperatively, a period of post-operative ventilation should be considered due to potential for lack of airway protection.

Where possible a multidisciplinary team approach should be adopted to postoperative care with involvement of gastrointestinal physicians for ongoing follow up and monitoring of liver function. Attention should be paid to the potential for specific manifestations of liver disease including

encephalopathy, renal dysfunction, wound infections and sepsis especially in the presence of ascites and malnutrition. Ongoing monitoring for postoperative coagulopathy is essential with bleeding possible not only from surgical sites but gastrointestinal sources also. Hypoxia and hypotension should be avoided and are poorly tolerated, contributing to worsening liver and neurological dysfunction.

Dietician involvement with maintenance of caloric and low protein nutrition is important. The pre-emptive use of laxatives / enemas and avoidance of hypovolemia or hyponatraemia will minimise potential for encephalopathy.

Analgesia should be provided with regional and simple analgesics where feasible. Opiates are generally tolerated in patients with compensated liver disease but must be used with caution in patients with hepatic dysfunction due to risk of respiratory depression and possible encephalopathy arising from accumulation and prolonged effects. When necessary, opioid analgesia should preferentially be in the form of fentanyl due to its renal excretion. Oral opiates if required should be administered at reduced doses or with increased time intervals to prevent accumulation. NSAIDs should be avoided due to risk of nephrotoxicity, gastrointestinal bleeding and platelet dysfunction.

Antiviral therapy

Antiviral therapy is now halting the progression of hepatitis C and B liver cirrhosis and saving a number of patients from transplant. Patients who present for elective surgery with undiagnosed cirrhosis secondary to hepatitis should have surgery deferred and be referred to hepatologists for consideration of antiviral therapy prior to surgery. This will markedly improve their liver synthetic reserve and reduce their in-hospital morbidity and mortality. Hepatitis B requires four weeks treatment (Entecavir) whilst hepatitis C requires 12 weeks (Viekira Pak/Harvoni). Whilst hepatitis B antiviral therapy suppresses viral disease new antiviral treatments are available that cure hepatitis C. In both diseases antivirals can be utilised for treatment of decompensated cirrhosis, even resulting in reversal of cirrhosis and improvement in portal hypertension (7), (8).

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