PERIOPERATIVE RISK FACTORS IN PATIENTS WITH LIVER DISEASE UNDERGOING NON-HEPATIC SURGERY

Chandra Kant Pandey, Sunaina Tejpal Karna, Vijay Kant Pandey, Manish Tandon, Amit Singhal, Vivek Mangla

Abstract

The patients with liver disease present for various surgical interventions. Surgery may lead to complications in a significant proportion of these patients. These complications may result in considerable morbidity and mortality. Preoperative assessment can predict survival to some extent in patients with liver disease undergoing surgical procedures. A review of literature suggests nature and the type of surgery in these patients determines the peri-operative morbidity and mortality. Optimization of premorbid factors may help to reduce perioperative mortality and morbidity. The purpose of this review is to discuss the effect of liver disease on perioperative outcome; to understand various risk scoring systems and their prognostic significance; to delineate different preoperative variables implicated in postoperative complications and morbidity; to establish the effect of nature and type of surgery on postoperative outcome in patients with liver disease and to discuss optimal anaesthesia strategy in patients with liver disease.

Key words: Cirrhosis; Liver disease; Perioperative risk

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SPECTRUM OF LIVER DISEASE

**Fatty liver and non-alcoholic fatty liver disease**

Nonalcoholic fatty liver disease is one of the most common cause of chronic liver disease worldwide. The rising prevalence rate is because of increasing epidemic of obesity and metabolic syndrome. Risk of developing postoperative complications or death is more postoperatively after hepatic resection if > 30% hepatocytes are affected with steatosis. However, < 30% steatosis is not associated with significantly increased risk of mortality[8].

**Obstructive jaundice**

Retrospective analysis of 373 patients with obstructive jaundice identified three risk factors for perioperative death: low hematocrit (< 30%), an elevated serum bilirubin (> 11 mg/dL), and a malignant cause of biliary obstruction. The mortality rate was 60% when all three were present whereas it was only 5% when none were present[25]. Hypoalbuminemia, azotemia, and cholangitis were also thought to increase the risk of death. These factors reflect the degree of biliary obstruction[8]. Long-standing biliary obstruction can lead to biliary cirrhosis, which may then influence the outcome of surgery. The reported mortality rate in patients with secondary biliary cirrhosis is 13% within 30 d of surgery[4]. In patients with acute cholangitis and choledocholithiasis, endoscopic decompression of the obstructed bile duct, in combination with intravenous antibiotics, is associated with lower morbidity and mortality than surgical decompression[40].

**Acute hepatitis**

Most literature regarding surgery in acute hepatitis is very old when laparotomy was part of diagnostic evaluation of patients with icterus[26]. Major elective surgery for a patient with suspected acute viral and alcoholic hepatitis should be deferred until the patient has recovered, the exception being life-saving emergency surgery.

**Acute liver failure**

Patients with acute liver failure (development of jaundice, coagulopathy and hepatic encephalopathy within 26 wk in a patient with acute liver injury in absence of pre-existing liver disease) are critically ill and any surgery other than liver transplantation is contraindicated[8].

**Chronic hepatitis**

Elective surgery has been reported to be safe in patients with chronic mild, asymptomatic chronic hepatitis[40]. However, in patients with symptomatic and histologically severe chronic active hepatitis, an increased risk is present especially in presence of impaired hepatic synthetic or excretory function, portal hypertension, and bridging or multilobular necrosis on liver biopsy[8].

**Cirrhosis**

In patients with chronic liver disease, outcomes correlate with underlying hepatocellular functions. Patients with well-compensated cirrhosis may have good health for years but once a complication such as variceal hemorrhage, ascites, hepatic encephalopathy, or jaundice develops, prognosis rapidly worsens. The mortality rate associated with various non-transplant surgeries ranges from 8.3% to 25% in comparison to 1.1% in non-cirrhotic patients[40].

ESTIMATING OPERATIVE RISK IN PATIENTS WITH LIVER DISEASE

**American Society of Anaesthesiologists physical status classification**

It is a six category physical status classification system to assess the physical state of the patient prior to selecting for anasthesia or performing surgery. Patients with severe liver disease are assigned a score of 3 or more. Even though, it generally correlates with perioperative mortality, this relationship is not perfect because of multiple factors influencing the perioperative outcome. This grading system is however not intended for use as a measure to predict operative risk.

In Cirrhotic patients, Teh et al[8] documented that an American Society of Anaesthesiologists (ASA) class of IV added the equivalent of 5.5 Model for End Stage Liver Disease (MELD) points to the mortality rate, whereas an ASA class of V was associated with a 100% mortality rate. The influence of the ASA class was greatest in the first 7 d after surgery, after which the MELD score became the principal determinant of outcome[8]. In this study, no patient under age 30 died, and an age greater than 70 added the equivalent of 3 MELD points to the mortality rate[8].

**The Child-Turcotte-Pugh scoring system**

The risk of postoperative mortality and morbidity correlate(s) well with the categorization of the patient as per the Child-Turcotte-Pugh (CTP) class of cirrhosis[2,3]. A total score of 5-6, 7-9 and > 9 co-relates with CTP classification A, B, and C respectively (Table 1).

In a retrospective analysis (from 1992 to 1999) of 40 patients with cirrhosis who underwent non-hepatic surgical procedures, the presence of tense ascites, low albumin value, deranged prothrombin time, activated partial thromboplastin time, together with the emergency of the operation, was significantly correlated with a mortality of 7.1% in Child’s class A, of 23% in class B, and of 84% in class C[30].

**MELD scoring system**

MELD score is utilized to prioritize organ allocation to the probable liver transplant recipients. The MELD score is considered objective and reliable because it is based on objective criteria, i.e., serum bilirubin, serum creatinine and international normalized ratio (INR). The score can be calculated by an online MELD calculator like the one at www.unos.org/resources[11].
MELD = 3.78×loge (bilirubin in mg/dL) + 11.2 × loge (INR) + 9.57 × loge (creatinine in mg/dL) + 6.43 (a bilirubin or creatinine value of less than 1.0 mg/dL is rounded to 1.0 mg/dL, and the maximum creatinine value allowed is 4.0 mg/dL).

Recent studies suggest that MELD could be used to stratify risk in patients undergoing non- transplant surgery. In a retrospective study of 140 patients with cirrhosis who underwent surgery, a 1% increase in mortality for each one-point increase in the MELD score from 5 to 20 and a 2% increase in mortality for each one-point increase in the MELD score above 20 was observed. MELD score < 10, 10-14, > 14 may correspond to CTP class A, B, C respectively.[12,13]

Patients with Child Turcotte Pugh class C cirrhosis and MELD scores > 14 are generally not considered for surgical intervention. Patients with Child Turcotte Pugh class B cirrhosis and MELD scores > 8-14 have an increased perioperative risk and the indication for surgery should be assessed carefully. In patients with Child Turcotte Pugh class A cirrhosis and MELD scores of ≤ 8, perioperative mortality is low.[14]

APACHE scoring system

The Acute Physiology, Age and Chronic Health Evaluation System (APACHE III) score can predict survival in cirrhotic patients admitted to an intensive care unit. Cirrhotic patients admitted to the medical intensive care unit are associated with high mortality rates. While both Child-Pugh and the APACHE II scores can satisfactorily predict the outcomes for critically ill cirrhotic patients, APACHE II is more powerful in discriminating the survivors from the non-survivors.[15]. However, it has not been studied specifically in cirrhotic patients undergoing surgery.

RISK FACTORS FOR COMPLICATION AND DEATH

Garrison et al.[14] did a retrospective analysis on 100 patients with cirrhosis who underwent abdominal operations. Porta-systemic shunts surgery were excluded. Procedures were primarily cholecystectomies, duodenal ulcer surgery, and other miscellaneous intra-abdominal surgeries. The results of the study are shown in the Tables 2 and 3.

Ziser et al.[16] reviewed the records of 733 patients with cirrhosis who underwent surgical procedures over an 11 years period (1980-1991) excluding liver transplantation. The mortality rate within 30 d of surgery was 11.6%. Long-term follow-up showed that most deaths occurred within the first few months after surgery, when many patients succumbed to pneumonia or renal insufficiency. Factors predictive of perioperative complications and of postoperative mortality are shown Table 4[16].

CUMULATIVE POWER OF RISK FACTORS

The probability of developing complications increased as the number of risk factors increased. About 9.3% risk of complications with 1 risk factor, 14.5% risk with 2 factors, 33.5% risk with 3 factors, 63.0% risk with 4 or 5 factors, 73.3% risk with 6 factors, 100% risk with 7 or 8 factors[9].

Aranha et al.[17] studied a series of patients undergoing cholecystectomy. As a single quantitative measure of the severity of cirrhosis, they employed the prothrombin time. They used the criterion for the same major surgical procedure with the same surgical and anaesthetic team. Results are presented in Table 5.

Teh et al[9] analyzed 772 patients with cirrhosis who underwent major digestive (586), orthopedic (107) or cardiovascular surgery (79). The control group included patients with cirrhosis without any surgical procedures and those with cirrhosis and undergoing minor surgeries. The authors concluded that MELD score, ASA class and

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**Table 1** Child-turcotte-pugh scoring system

<table>
<thead>
<tr>
<th>Variables</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy grade</td>
<td>None</td>
</tr>
<tr>
<td>Asites</td>
<td>Absent</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>3.5</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>1-4</td>
</tr>
</tbody>
</table>

**Table 2** Preoperative variables and mortality rates of survivors and non-survivors of abdominal surgery

<table>
<thead>
<tr>
<th>Preoperative variables</th>
<th>Percent of mortality if factors present</th>
<th>Percent of mortality if factors absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child class</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>A</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>58</td>
<td>10</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>57</td>
<td>10</td>
</tr>
<tr>
<td>Bilirubin &gt; 3 mg/dL</td>
<td>62</td>
<td>17</td>
</tr>
<tr>
<td>Albumin &lt; 3 mg/dL</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>Prothrombin time &gt; 1.5 s above control</td>
<td>63</td>
<td>18</td>
</tr>
<tr>
<td>White blood cell count &gt; 10 000</td>
<td>54</td>
<td>19</td>
</tr>
</tbody>
</table>

**Table 3** Preoperative variable associated with mortality

<table>
<thead>
<tr>
<th>Preoperative variable</th>
<th>Mortality in percent if present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary failure</td>
<td>100</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>92</td>
</tr>
<tr>
<td>Requirement of &gt; 2 antibiotics</td>
<td>82</td>
</tr>
<tr>
<td>Renal failure</td>
<td>73</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>66</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>86</td>
</tr>
<tr>
<td>Required second operation</td>
<td>81</td>
</tr>
<tr>
<td>Positive cultures</td>
<td>64</td>
</tr>
<tr>
<td>Blood requirement &gt; 2 units</td>
<td>69</td>
</tr>
<tr>
<td>Blood requirement &lt; 2 units</td>
<td>22</td>
</tr>
</tbody>
</table>

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age were predictors of mortality. Thirty-day mortality ranged from 5.7% (MELD score < 8) to more than 50% (MELD score > 20). The relationship between MELD score and mortality persisted throughout the 20-year postoperative period[9].

Nature of surgery

The nature of surgery is an important determinant of postoperative complications. Emergency surgery is associated with a higher morbidity and mortality than elective surgery. Mansour et al[11] reported that emergency surgery is associated with higher mortality than elective surgery: a 22% vs 10% for patient in child class A; 38% vs 30% for those in child class B; and 100% vs 82% for those in child class C.

Neeff et al[12] analyzed perioperative mortality in non-hepatic general surgical procedures in 138 patients with liver cirrhosis. About 49% (68) of the patients underwent emergency operations. There was 27.5% (38 deaths in 138 cases) of overall perioperative mortality (within 30 d of surgery) out of which 8.7% were in elective surgery (6/70) and 47% (32/68) were in emergency surgery. The similar results have also been shown by Kim et al[13] in a study of 53 patients with chronic liver disease who underwent emergency surgery with general anesthesia. They reported 35.8% mortality (19 out of the 53). Five deaths (9.4%) occurred within one month of surgery.

Type of surgery

The morbidity and mortality risks are highest in patients undergoing cardiac and open abdominal surgeries including cholecystectomy, gastric resection, colectomy and hepatic resection[12]. The contributing factors proposed were laparotomy causing a greater reduction in liver blood flow and therefore more severe hepatic ischemia, and increased risk of intra-operative bleeding in the presence of portal hypertension especially in patients with previous abdominal surgery and adhesions.

Abdominal wall surgery

Patients with both cirrhosis and ascites have a 20% risk of developing umbilical hernia. Eker et al[14] conducted a prospective study to assess safety and efficacy of elective umbilical hernia repair in cirrhotic patients with ascites in 2011. The following data were collected prospectively for all patients: Child-Pugh-Turcotte classification, MELD score, kidney failure, cardiovascular comorbidity, operation-related complications, and duration of hospital stay. They concluded that elective umbilical hernia repair is safe and it is the preferred approach in cirrhotic patients with ascites.

Park et al[15] compared 30-d mortality among the different CTP classes, and between those with or without refractory ascites in 53 cirrhosis patients who underwent hernia repair. Seventeen patients were in CTP class A, 27 in class B, and 9 in class C. The median follow-up duration was 24 mo. Authors concluded that hernia surgery could be performed safely in CTP class A and B with low rate of recurrences, and there was no definitive increase in the operative risk in class C. Refractory ascites did not increase operative risk and recurrence rate[16].

Open abdominal surgery

The risk of surgery in patients with cirrhosis is based on studies of abdominal surgery. Neeff et al[17] have documented that perioperative mortality was higher after intra-abdominal than after abdominal wall operations (35% vs 8%, P = 0.001). Beveler et al[18] analyzed fifty-three adult patients with histologically proven cirrhosis undergoing abdominal surgery. Total 13 patients (25%) had poor outcomes including 9 deaths (17%). “Model for end-stage liver disease” score and plasma hemoglobin levels lower than 10 g/dL were found to be independent predictors of poor outcomes. A MELD score of 14 or greater was a better clinical predictor of poor outcome than CTP C. Authors concluded that patients with cirrhosis and hac-

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Table 4  Factors predictive of perioperative complications and of postoperative mortality

<table>
<thead>
<tr>
<th>Predictor of complications</th>
<th>Predictor of mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh class B and C</td>
<td>Male gender</td>
</tr>
<tr>
<td>Ascites</td>
<td>Child-Pugh class B and C</td>
</tr>
<tr>
<td>Etiology of cirrhosis other than primary biliary cirrhosis</td>
<td>Etiology of cirrhosis other than primary biliary cirrhosis</td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td>Ascites</td>
</tr>
<tr>
<td>Preoperative infection</td>
<td>Preoperative infection</td>
</tr>
</tbody>
</table>
| Chronic obstructive pulmonar
disease | Respiratory surgery |
| Preoperative upper gastrointestinal bleed | American Society of Anaesthesiologists physical status IV and V |
| Invasiveness of surgical procedure | Intravenous hypotension (20% decrease of baseline blood pressure for 10 min or more) |
| Intraoperative hypotension (20% decrease of baseline blood pressure for 10 min or more) | American Society of Anaesthesiologists physical status IV and V |

Table 5  Mortality rates in patients undergone cholecystectomy with or without cirrhosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with normal liver function</td>
<td>1%</td>
</tr>
<tr>
<td>Patients with cirrhosis (PT &lt; 2.5 s than control)</td>
<td>9%</td>
</tr>
<tr>
<td>Patient with cirrhosis (PT &gt; 2.5 s than control)</td>
<td>83%</td>
</tr>
</tbody>
</table>

PT: Prothrombin time.
moglobin levels lower than 10 g/dL should receive corrective blood transfusions before abdominal surgery.

Patients undergoing non transplant surgery with MELD scores lower than 10 had survival rate of 99% at 7 d, 96% at 30 d, and 92% at 90 d but survival rates were significantly lower with MELD scores of 10 or more[23].

**COLORECTAL SURGERY**

Nguyen et al[24] studied patients undergoing colorectal surgery. The mortality in patients with cirrhosis and cirrhosis with portal hypertension was significantly higher than in patients with no cirrhosis (14% and 29% vs 5%, respectively). del Olmo et al[25] studied 135 patients with liver cirrhosis undergoing different types of non-hepatic surgeries and compared the outcomes to those without cirrhosis. Patients with cirrhosis demonstrated the increased need for intraoperative transfusion, mean length of hospital stay, postoperative complications (50.4% vs 29.1%) and the mortality rate (16.3% vs 3.5%). In a multivariate analysis it is demonstrated that high CTP score, duration of surgery and postoperative complications were independently associated with mortality in patients with cirrhosis[26].

**CHOLECYSTECTOMY: OPEN OR LAPAROSCOPIC**

Patients with cirrhosis who have incidental gallstones on ultrasonography should not undergo cholecystectomy unless the gallstones are symptomatic due to the possible deterioration of liver function post-operatively. Besides there is common concern whether an open or closed procedure should be done in these patients.

Poggio et al[27] retrospectively analyzed 50 patients who had undergone cholecystectomy for symptomatic gallstone disease. The procedure was open in half of the patients and laparoscopic in the other half. The study concluded that laparoscopic cholecystectomy is associated with statistically significant reductions in operating room time, blood loss, and length of hospital stay and is safe in patients with cirrhosis and offers advantages over an open surgical approach. Thus, laparoscopic cholecystectomy should be recommended for patients with liver disease without decompensation.

**LAPAROSCOPIC CHOLECYSTECTOMY**

Laparoscopic cholecystectomy carries a low mortality rate. Yeh et al[28], in one of the largest retrospective analyses, reported that, out of 226 patients with cirrhosis (Child-Pugh class A or B) who underwent laparoscopic cholecystectomy, only two died (0.88%). The reported mortality is low, but this figure is still significantly higher than in non-cirrhotic controls (0.01%). Suman et al[29] found that a preoperative MELD score of 8 or more had 91% sensitivity and 77% specificity in predicting 90-d morbidity and suggested this as the cutoff mark for considering patients with cirrhosis for laparoscopic cholecystectomy.

**CARDIAC SURGERY**

In 2 retrospective series of patients who underwent surgery requiring cardiopulmonary bypass, low mortality rates of 0% (0/10) and 3% (1/31) were observed in those with Child class A cirrhosis but rates were markedly increased in those with Child class B (42%-50%) and C (100%, n = 52) cirrhosis. In addition, more than 75% of Child class B and C patients experienced hepatic decompensation[27,28]. Increased mortality was also predicted by an increased MELD score. The best cutoff values for predicting mortality and hepatic decompensation were found to be a score greater than 7 in the CTP system and a score greater than 13 in the MELD system.

In 2007, Filsoufi et al[29] studied 27 patients with cirrhosis who underwent cardiac surgery. Patients were in CTP class A (n = 10), B (n = 11), and C (n = 6) and mean MELD score was 14.2 ± 4.2. Operative mortality was 26%. The mortality according to the CTP class was 11%, 18% and 67% for class A, B, and C respectively. No mortality occurred in patients who had revascularization without cardiopulmonary bypass. Major postoperative complications occurred in 22%, 56% and 100% for CTP class A, B, and C, respectively. Authors suggested that cardiac surgery can be performed safely in patients with CTP class A and selected patients with class B. Operative mortality remains high in class C patients.

In addition to an elevated CTP or MELD score, clinically significant portal hypertension is a contraindication to cardiothoracic surgery. Portal decompression with TIPS placement may make the risk acceptable if the CTP and MELD scores remain low[30]; however, elevated right-sided cardiac pressures from cardiac dysfunction and pulmonary hypertension are absolute contraindications to TIPS placement.

In general, the least invasive option of angioplasty with or without stent placement should be considered whenever feasible in a patient with advanced cirrhosis who requires coronary artery revascularization.

Morisaki et al[31] conducted a retrospective study in 42 cirrhotic patients undergoing cardiovascular surgeries, of which 30 were CTP class A and 12 were CTP class B. Hospital morbidity occurred in 13 patients (31.0%), including 4 who died in-hospital. The MELD score was evaluated in 25 patients. Significant differences in hospital morbidity were identified for platelet count (8.7 ± 3.8 vs 12.1 ± 4.2 × 10^4/microL), MELD score (17.8 ± 5.3 vs 9.8 ± 4.9), operation time (370 ± 88 vs 313 ± 94 min), and cardiopulmonary bypass time (174 ± 46 vs 149 ± 53 min) in univariate analyses (P < 0.005). Platelet count, operation time, and age were significantly associated with hospital morbidity in multivariate analyses (P < 0.005). They concluded that careful consideration of operative indications and methods are necessary in cirrhotic patients with low platelet counts or high MELD scores. A high incidence of in-hospital morbidity is pre-
dicted in patients with platelet counts of less than $9.6 \times 10^{4}/\text{microL}$ or MELD scores exceeding 13.

**UROSURGICAL PROCEDURES**

Thirty patients with liver cirrhosis who underwent transurethral resection of the prostate (TURP) were compared to 150 patients without liver cirrhosis. There was 6.7% mortality at 30 d in cirrhotic group compared to 2% mortality in patients without cirrhosis. This study indicates that TURP in patients with liver cirrhosis is associated with increased mortality[32].

**PULMONARY PROCEDURES**

Liu et al[33] retrospectively analyzed 59 adults with cirrhosis undergoing chest tube placement. Variables that were investigated included reason for chest tube placement, complications developing while having the tube in place, and outcome. Their results demonstrated that out of 59 subjects 3 were classified as having CTP class A cirrhosis, 31 as CTP class B cirrhosis, 25 as CTP class C cirrhosis. Indications for having a chest tube placed were hepatic hydrothorax ($n = 24$), pneumothorax ($n = 9$), empyema ($n = 8$), video-assisted thoracotomy (VAT $n = 7$), non-VAT ($n = 5$), and hemothorax ($n = 3$). Serum total bilirubin levels, presence of porto-systemic encephalopathy, and CTP C classification were predictors of mortality. Mortality was seen in 5 out of 31 CTP class B subjects (16%), and in 10 out of 25 CTP class C subjects (40%).

In a retrospective analysis of 37 patients with co-morbid cirrhosis who underwent curative surgery for primary lung cancer, occurrence of postoperative complications like liver failure, bleeding and critical infection were studied to determine the factors predicting liver cirrhosis-related complications in the early postoperative period[34]. Liver cirrhosis related complications occurred in seven of the 37 patients (18.9%). Transient liver failure occurred in two patients (5.4%) after pulmonary resection. Acute intra thoracic bleeding occurred in four cases (10.8%). Two patients died (5.4%) due to sepsis. Preoperative total bilirubin ($P < 0.05$), and indocyanine green retention rate at 15 min ($P < 0.05$) were significantly higher in patients with liver failure. Only serum value of total bilirubin was an independent risk factor ($P < 0.05$) by multivariate analysis. In predicting death from infection, only preoperative nutritional status was a significant risk factor ($P < 0.05$). It was suggested that to avoid postoperative cirrhosis related complications, preoperative preparation to improve their liver function and nutrition status is essential.

**TRAUMA**

Trauma patients found to have cirrhosis at laparotomy are at increased risk for morbidity and mortality. In one study, the overall mortality rate was 45%, significantly higher than of a matched control population (24%)[35]. Mortality and morbidity rates were increased even for patients considered to have relatively minor trauma. The authors recommended that trauma patients found to have cirrhosis at laparotomy be admitted to the intensive care unit for close monitoring and aggressive management irrespective of the severity of their injuries.

**ANESTHESIA**

The risk of surgery cannot be separated from the risk of anesthesia. Sedatives, narcotics, and intravenous induction agents are generally well tolerated in patients with compensated liver disease but must be used with caution in patients with decompensated hepatic dysfunction, because they may cause prolonged depression of consciousness and precipitate hepatic encephalopathy.

Blood levels of narcotics that undergo high first-pass extraction by the liver, increase as hepatic blood flow decreases. Elimination of benzodiazepines that undergo glucuronidation (e.g., oxazepam, lorazepam) is unaffected by liver disease, whereas the elimination of those that do not undergo glucuronidation (e.g., diazepam, chloral hydrazine) is prolonged in liver disease. Long acting narcotics and sedatives should (therefore) be avoided in cirrhotic patients. However, the use of various narcotics like Fentanyl, Sufentanil and sedatives like Oxazepam, Lorazepam, in conjunction with anesthetics is recommended, because their actions are less prolonged in patients with liver disease[36].

Anesthesia can affect the liver functions by reducing its blood flow. In healthy volunteers, hepatic blood flow decreases by 35%-42% in the first 30 min of induction of anesthesia[37]. Studies in animals have shown that under the conditions of stress, hepatic blood flow increases to compensate for the reduced portal blood flow but patients with liver disease, especially cirrhosis under the influence of anesthesia cannot compensate for the reduced portal blood flow, which may cause hepatic dysfunction[38]. The anesthetic agents Halothane and Enflurane reduce hepatic arterial blood flow. These effects are minimal with Isoflurane.

Acute hepatitis associated with the administration of halothane is believed to be caused by immune sensitization to trifluoroacetylated liver proteins formed by oxidative metabolism of halothane by cytochrome P450 2E1 in genetically predisposed persons[39]. With this notable exception, few data suggest that either the choice of anesthetic agent or mode of administration (inhaled or spinal) influences surgical outcome in patients with liver disease[40].

Inhalational agents Isoflurane, Desflurane and Sevoflurane undergo hepatic metabolism, extent of which is 0.2% for isoflurane, 2%-4% for Enflurane, and 20% for Halothane[41] presumably, this leads to a lesser incidence of drug-induced hepatitis. Therefore, Isoflurane has become the inhalation agent of choice in patients with liver disease.

Propofol is an excellent anesthetic agent of choice in patients with liver disease, because it retains a short halflife even in patients with decompensated cirrhosis[42].
The volume of distribution of non-depolarizing muscle relaxants is increased in patients with liver disease, and therefore larger doses may be required initially to achieve adequate neuromuscular blockade. The actions of neuromuscular blocking agents may be prolonged in patients with liver disease because of reduced pseudo-cholinesterase activity, decreased biliary excretion, and larger volume of distribution. Atracurium and cisatracurium are the preferred muscle relaxants in patients with liver disease because neither the liver nor the kidney is required for their elimination. Doxacurium is the preferred muscle relaxant in longer procedures such as liver transplantation, as it is metabolized by the kidney.

No correlation could however be established in patients with cirrhosis undergoing cardiac surgery and hepatic decompensation or mortality between the use of Enflurane, Isoflurane, Fentanyl, Sufentanil, Midazolam or Morphine (29). The type of anesthetic management either general anesthesia, regional anesthesia, or monitored anesthesia care did not affect the mortality in one of the largest reported series of 733 patients (30).

CONCLUSION

The literature on patients with liver disease undergoing surgical procedures emphasizes that CTP status and MELD score correlates well with the perioperative morbidity and mortality and are reasonably good predictors of the operative risk. Various open abdominal and even cardiac surgeries can be performed in patients of Child A status and MELD score < 8 with low perioperative mortality. In patients with Child C status and MELD score > 14, elective surgeries other than liver transplant should be avoided. Acute liver failure is a contraindication for any surgical intervention other than liver transplant. Surgery in acute hepatitis should be deferred till it resolves. Laparoscopic and abdominal wall surgeries can be safely performed as compared to open abdominal surgeries in patients of cirrhosis with Child A and B status. Emergency procedure carries significantly higher risk of perioperative mortality and morbidities in patients with cirrhosis irrespective of their Child status or MELD score. The type of anesthetic management either general anesthesia, regional anesthesia, or monitored anesthesia care do not have correlation with mortality.

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