EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Assessment of risk for non-hepatic surgery in cirrhotic patients

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Introduction

Patients with poorly compensated chronic liver disease (CLD), requiring surgical intervention form a unique group of surgical candidates. Though liver resection for hepatic tumours and liver transplantation (LT) are the most common surgical procedures performed in cirrhotic patients; these patients may frequently require other non-hepatic surgical procedures including surgery for abdominal wall hernia's, abdominal surgery for peptic ulcer disease, biliary, small bowel, colon, and pancreatic disease, and in addition cardiac, vascular, and orthopaedic surgery. Patients with compromised liver function are known to decompensate due to the stress of both anaesthesia and surgery, and in spite of significant advances in surgical and intensive care, perioperative mortality and morbidity continue to remain high [1–10].

Key Points

- Perioperative morbidity and mortality in CLD patients undergoing non-hepatic abdominal surgery remain high
- Stringent assessment and risk stratification in the preoperative period are essential for better outcomes
- Severity of liver disease, type of surgery and whether surgery is performed as a routine or emergency procedure are major determinants of outcomes
- CTP score and MELD score may be complementary rather than competitive in predicting short term outcomes
- Preoperative portal decompression (TIPSS) may help reduce operative bleeding and postoperative ascites

Keywords: Cirrhosis; Surgery; Outcomes; Scoring systems; Transjugular intrahepatic portosystemic shunt (TIPS).

Received 28 June 2011; received in revised form 8 March 2012; accepted 10 March 2012

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Abbreviations: CLD, chronic liver disease; LT, liver transplantation; CTP score, Child Turcotte Pugh score; MELD, Model for End stage Liver Disease; HCV, hepatitis C virus; HBV, hepatitis B virus; NAFLD, non alcohol related fatty liver disease; NASH, non alcoholic steatohepatitis; INR, international normalized ratio; ASA, American Society of Anesthesiologists; PHT, portal hypertension; TIPS, transjugular intrahepatic portosystemic shunt.

Studies reporting the occurrence of, and type of morbidity in patients with cirrhosis undergoing non-hepatic surgery have shown variable results; the reported in-hospital mortality rates after various non-transplant surgical procedures range from 8.3% to 25% (even in well selected cirrhotic patients) compared to 1.1% in non-cirrhotic patients [5,6]. Mortality is the consequence of a high rate of postoperative decompensation of cirrhosis (especially in cases of intra-abdominal surgery) and an increased risk of bacterial infection. In addition, the outcomes are known to be worse in patients undergoing surgery as an emergency procedure (e.g. for bleeding, perforation, incarceration) [6–10]. The wide variations in mortality rates can be attributed primarily to the varying degree of liver dysfunction, and in addition to different patient demographics, varied surgical diagnoses, different levels of expertise of the surgical anaesthesia and intensive care unit team and finally, reporting bias. The drawbacks of studies in literature include lack of control groups in most studies [2–5,7–10], comparison of morbidity and mortality for specific procedures rather than an overall assessment [11–19], small number of patients in some studies, and lack of sufficient details regarding severity of liver disease (i.e., CTP (Child Turcotte Pugh) or MELD (Model for End Stage Liver Disease) score) [6,7,18,20–23].

It is indeed difficult to significantly reduce the operative risk in decompensated CLD patients in most situations; hence it is of prime importance to assess these patients in the preoperative period and if possible predict the extent of risk of a surgical intervention. Retrospective studies have identified multiple clinical and laboratory variables that contribute to increased perioperative morbidity and mortality rates in CLD patients undergoing non-hepatic abdominal surgery [5,7–8]. Moreover, it has been shown that there is a correlation between the number of risk factors identified by multivariate analyses and the rate of perioperative complications [5]. However, the debate on the best method (scoring systems or non hepatic markers) and then the best individual parameters for risk assessment still continues.

This review explores methods that could best serve to assess patients with cirrhosis preoperatively and predict outcomes of non-hepatic surgery in them, particularly for the most common abdominal procedures. This knowledge could help in a better selection of patients, thus reducing postoperative mortality and morbidity; and at the same time explore the possibility of using preoperative interventions to further reduce these risks.

Pathophysiology

The worldwide prevalence of CLD is increasing due to the increasing incidence of hepatitis C (HCV), hepatitis B (HBV), alcohol-related and non-alcohol related fatty liver disease (NAFLD). Up to 10% of patients with cirrhosis are likely to undergo non-transplant surgery in the last 2 years of their life [24].

While some studies have shown that in expert hands, even major abdominal surgeries like pancreaticoduodenectomy for pancreatic tumours are safe in well compensated CLD patients [25], general anaesthesia and surgery may lead to drastic morbidity and high perioperative mortality in decompensated cirrhotic patients.

Severity of liver disease (degree of decompensation) is thus the most important factor predicting postoperative outcome. Secondary to the loss of hepatic reserve and because of other systemic derangements that are the result of liver dysfunction (such as hemodynamic impairments), patients with liver disease have an inappropriate response to surgical stress. These individuals are accordingly at an increased risk of bleeding, infection, postoperative hepatic decompensation, including hepatic coma or death. Therefore, the decision to perform surgery in these patients must be heavily weighed and careful patient selection is mandatory.

The underlying disease and nature of the surgical procedure are important determinants of postoperative outcomes. The morbidity and mortality risks are the highest in patients undergoing cardiac surgery (up to 31% perioperative mortality), and open abdominal surgeries like cholecystectomy (up to 17% perioperative mortality), gastric resection (up to 78% morbidity, 54% mortality) and colectomy (up to 48% morbidity, 24% mortality) [18]. The higher incidence of complications in abdominal surgery is probably explained by hepatic ischemia and an increased risk of intra-operative bleeding in the presence of portal hypertension (PHT), especially in patients with previous abdominal surgery and adhesions. Hemodynamic changes, characterized by increased cardiac output, splanchnic vasodilation, and decreased systemic vascular resistance, are common in patients with PHT, and these changes progress with worsening liver disease. Despite an increased cardiac output, perfusion may be impaired due to shunting of blood, and in addition, anesthetic agents may also reduce hepatic blood flow and decrease oxygen uptake by the liver and splanchnic organs. Hypotension, hypoxemia, hemorrhage and use of vasoactive drugs may further reduce hepatic oxygenation. Hepatic blood flow and liver function may be further compromised by catecholamine release and other neurohormonal responses [19,26,27].

Emergency surgery has also been shown to be associated with a higher morbidity and mortality (50% *vs.* 18%) as compared to elective surgery in several studies [3,7,23]. A study comparing the MELD and CTP scores in 40 cirrhotic patients who required either elective or emergency surgery with general anesthesia, found that emergency surgery was associated with significantly higher one- and three-month mortality rates. There was good correlation between the CTP and the MELD scores in predicting mortality, especially in the emergency surgery group [21].

In addition to the above, the etiology of cirrhosis in the patient is known to have a major influence on the postoperative outcome. A particularity of alcoholic cirrhosis is that the majority of patients with high disease severity indexes also have superimposed alcoholic hepatitis (most likely due to continued active alcohol consumption). Alcoholic hepatitis is a potentially reversible condition, which means that some of these patients are likely to improve within the first few months following discontinuation of alcohol. Hence, patients who have been abstinent for a prolonged period of time are likely to have better postoperative outcomes compared to those with continued alcohol abuse. It has also been shown that patients with HCV-related CLD undergoing liver resection (curative treatment) for hepatocellular carcinoma tend to do worse postoperatively as compared to those with HBV-related CLD, ethanol-related CLD or non-alcoholic steatohepatitis (NASH) [28,29].

Main indications for extrahepatic abdominal surgery in patients with cirrhosis: Associated morbidity, mortality, and alternatives to surgery

Gallstone disease

Prevalence of gallstone disease (GSD) in the cirrhotic patient is higher than in the general population, reaching 17–28%. Our center earlier reported the prevalence and incidence of significant complications of GSD in CLD patients [30]. We found that 17% of admitted CLD patients had cholelithiasis. In 22% of these patients, cholelithiasis caused cholecystitis, obstructive jaundice, or biliary pain, all the patients underwent a cholecystectomy. In the other 78%, cholelithiasis was asymptomatic, 20% of these patients died from liver failure, and the stones were discovered at necropsy. 14% had radiographically demonstrated stones that were not operated on, they had no complications on follow-up. In the remaining patients, the stones were discovered during portosystemic shunt procedures. Our study thus confirmed the high incidence of GSD in cirrhotic patients, and in addition, we found that complications of GSD requiring an emergency operation were associated with a higher risk of morbidity and mortality.

In a recent national study from the United States, the incidence of four index operations (cholecystectomy, colectomy, abdominal aortic aneurysm repair, and coronary artery bypass grafting) performed in CLD patients was studied over a 8-year period (from 1998 to 2005). Patients were grouped according to the presence of cirrhosis and PHT [23]. 22,569 patients with cirrhosis (of whom 4214 had PHT) underwent one of the four index operations. Patients with cirrhosis and those with cirrhosis complicated by PHT most frequently underwent cholecystectomy (63% and 58%, respectively). This was followed by colectomy, CABG and AAA repair, in that order. Hence, this study also concluded that GSD seems to be the most common extrahepatic disease that CLD patients have and are operated on.

Cirrhosis with cardiovascular disease is the main risk factor for postchlecystectomy mortality. In Child A and B patients, lap cholecystectomy (the preferred approach now) is feasible with 5–10% morbidity and 0–1% mortality [11,31]. On the contrary, for the Child C patient, cholecystectomy is associated with a prohibitive death rate of 23–50% [32]; severe liver failure, acute cholecystitis, and emergency surgery are common in this type of patient. Most authors agree that medical treatment should be offered in this situation. If the medical approach is unsuccessful, or should pyocholecystitis develop, percutaneous cholecystostomy could be a solution [33].

Three studies reported on the management of common bile duct (CBD) stones in cirrhotic patients. In the French association report, morbidity in 31 patients undergoing surgery for CBD stones was 29% with a mortality rate of 9.6%. Presence of CBD

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stones was an important factor with major impact on morbidity and mortality following surgery for gallstones in cirrhotic patients [34]. Two studies confirmed the benefits of endoscopic sphincterotomy (ES) over surgery for CBD stones [35,36], thus ES followed by elective laparoscopic cholecystectomy has become the gold standard for CBD stones. However, there is a 7% risk of mortality even with ES. Due to this, some centers have proposed balloon endoscopic sphincteroclasia to avoid risk of bleeding in cirrhotic patients, particularly Child C patients without secondary cholecystectomy [37].

Abdominal wall hernias

Umbilical and incisional hernias are more common in cirrhotic patients than in the general population. Abdominal distension caused by ascites and loss of muscle mass secondary to a poor nutritional status are the main risk factors. In the cirrhotic patient, the incidence of abdominal wall hernia is 16% and reaches 24% in the presence of ascites. More than half of all hernias are umbilical; the rate is 4-fold higher in patients with ascites [38].

In the series reported by the French Association of Surgery, which included 81 patients who underwent surgical treatment for umbilical hernia, overall mortality was 5%: 11% after emergency surgery for ruptured or strangulated umbilical hernia and 2% after elective surgery [39]. Mortality was zero in the two most recent studies reported by expert centers, including 39 and 40 patients respectively, undergoing surgery for umbilical hernia [15,40].

In patients with Child A or B cirrhosis, cure for inguinal hernia was achieved with acceptable morbidity (no major complications and four minor, readily correctable complications), 8% recurrence rate, and a mortality rate of 5.7% in a large series of 915 patients [41] .

Ammar *et al.* [42] reported results of a randomised control trial aimed at evaluating the use of polypropylene mesh to treat complicated umbilical hernias in cirrhotic patients. Forty patients each underwent a conventional fascial repair or mesh hernioplasty. Hernia recurrence was significantly less in the mesh hernioplasty group, no mesh exposure or fistulae were experienced, and there was no need to remove any of the meshes. The authors concluded that permanent mesh can be used in complicated hernias in cirrhotic patients with minimal wound-related morbidity and a significantly lower rate of recurrence.

Appendix and colorectal surgery

In a study by Tsugawa *et al.* [43], comparing outcomes of open appendectomy (OA) and laparoscopic appendectomy [LA] for acute appendicitis in CLD patients, postoperative pain and length of hospital stay were significantly lesser in the LA group, so were the number of wound infections and wound bleeding. The overall costs were similar. The authors concluded that LA may be superior to OA in terms of postoperative pain and postoperative complications for CLD patients.

Two large series have reported results of colorectal surgery (predominantly for diverticular disease and colorectal cancer) in CLD patients [44,45]. The reported mortality rate was 13–23% and morbidity was 46–51%. The factors predictive of perioperative mortality were elevated serum bilirubin levels, low prothrombin level, ascites (Child B and C patients), and emergency surgery. The outcomes are known to be worse in patients undergoing surgery as an emergency procedure (e.g., for intestinal obstruction, bleeding, perforation) [6–10]. In the emergency situation, colonic stenting for patients with intestinal obstruction and endoscopic management in patients with bleeding from an ulcer or tumour would be preferred to surgery.

In a recent study by Lian *et al.* [46], CLD patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) who underwent a restorative proctocolectomy have been studied. Most patients were Child Pugh class A or early B, and eight patients were on the orthotopic liver transplantation list. Indications for colectomy included dysplasia, failure or complications of medical therapy, cancer, and colonic perforation at colonoscopy. 82.6% of the patients developed postoperative complications, and 34.8% of the patients had worsening liver function. Two patients, both after total proctocolectomy/IPAA (ileal pouch-anal anastomosis), died of septic shock after pelvic abscess in the postoperative period. Two patients underwent transjugular intrahepatic portosystemic shunt (TIPS) procedure before total proctocolectomy/IPAA; none developed pelvic abscess or mortality. There were no differences in mortality or morbidity between patients who underwent an ileoanal pouch procedure or colectomy with ileostomy. The authors concluded that colectomy in patients with IBD complicated with cirrhotic PSC is associated with a high early postoperative morbidity rate. In addition, strategies to reduce pelvic sepsis should be adopted, especially after IPAA, because pelvic sepsis is associated with higher mortality and morbidity.

Gastric surgery

Peptic ulcers are more common in CLD patients, affecting 8–20% of them [16,47]. The mortality of emergency surgery for complicated peptic ulcer (bleeding or perforation) in CLD patients is very high ranging from 23% to 64%. Prognostic factors having an influence on mortality are CTP class and presence of ascites [3,16]. Laparoscopic suture of the perforated ulcer combined with proton pump inhibitors and endoscopic haemostatic techniques for bleeding ulcers have reduced the need for resectional surgery and reduced the mortality in the emergency setting.

Surgical treatment of gastric cancer in cirrhotic patients resulted in a morbidity rate of 20–26% and mortality of 0–10% in two studies from Japan [48,49]. The French study reported a mortality of 23%, significantly higher in patients with ascites and low serum albumin, and a morbidity of 56% [50]. The conclusions from these studies suggest that for CTP A and B patients, surgery is safe, but it would be preferable to propose type D1 dissection and to avoid dissection of the hepatic pedicle because of the risk of lymphatic ascites.

Pancreatic surgery

Sethi *et al.* [25] reported four patients with pancreatic tumours and well compensated cirrhosis, who successfully underwent pancreaticoduodenectomy with radical lymphadenectomy. They concluded that in expert hepatobiliary centers, pancreaticoduodenectomy is not contraindicated in patients with cirrhosis.

In a study that aimed at detailing the overall prevalence of pancreatic surgery in CLD [51], a total of 35 patients were included; 17 underwent surgery for chronic pancreatitis, three for acute pancreatitis, 14 for malignant tumours, and one for a benign tumour. The procedures included nine resections, including three distal pancreatectomies, two pancreaticoduodenectomies, two ampullectomies and two atypical resections for acute pancreatitis. Among the other 26 patients, seven underwent gastrojejunostomy, 13 had a bilioenteric bypass, and 10 underwent a pancreaticoenteric bypass. Overall morbidity was 51% and mortality was 20%. All three patients who had emergency procedures died, and all deaths occurred in patients in whom the gastrointestinal tract was opened. These findings suggested that endoscopic (stent, endoscopic cystogastrostomy, ampullectomy) and radiologic (percutaneous drainage of pancreatic abscesses) treatments should be preferred in cirrhotic patients with an inflammatory disease or tumour of the pancreas. The rare indications for resection should be reserved for elective procedures in Child Pugh A patients without elevated transaminases (as these were found to be independently predictive of death on univariate analysis).

A case-control study by Warnick *et al.* [52] compared outcomes in 32 cirrhotic patients (30 CTP A and 2 CTP B) *vs.* matched controls (operated patients without cirrhosis) undergoing pancreatic resection surgery. In their study, patients with cirrhosis experienced significantly more complications especially major complications (47 *vs.* 22%; $p = 0.035$) requiring reoperation (34 *vs.* 12%; $p = 0.039$). These patients also had a significantly prolonged hospital and ICU stay, and required twice as many transfusions. Overall, three patients died following surgery, one with Child A (3% of all Child A patients) and two with Child B cirrhosis. The authors concluded that pancreatic surgery is associated with an increased risk of postoperative complications in patients with liver cirrhosis, and is therefore not recommended in patients with Child B cirrhosis. In Child A cirrhotic patients the mortality is, however, comparable to non-cirrhotic patients. In addition, due to the demanding medical efforts that these patients require, they should be treated exclusively in high-volume centers.

Risk stratification: What could be the ideal method to predict risk and outcomes?

Scoring systems for liver function? CTP score or MELD?

The CTP and MELD scores have been the prognostic scoring models predominantly used for assessing the severity of liver disease and for risk stratification.

The CTP score includes five parameters, three of them being objective (serum bilirubin, serum albumin, and prothrombin time), and two subjective (presence of ascites and encephalopathy) [53]. The score ranges from 5 to 15, and patients are further classified into three CTP classes, A (CTP score 5–6), B (CTP score 7–9), and C (CTP score 10–15).

Based on studies published to date, it has been suggested that elective surgery is tolerated well in CTP A patients, it is permissible with good preoperative preparation in CTP B patients (except those undergoing major hepatic resection or cardiac surgery) and contraindicated in CTP C patients. Two of the most important studies, carried out 13 years apart, reported nearly identical results: perioperative mortality rates for patients undergoing surgery were 10% for CTP A, 30% for CTP B, and 80% for CTP C patients [3,7]. With respect to cardiac surgery, the combined mean mortality for CTP class A, B, and C was 5.2%, 35.4%, and 70%, respectively. Hence, the risk of mortality in patients with Child class B and C is comparatively high.

Table 1. Mortality rates associated with specific types of surgery in patients with cirrhosis [3,7,18,20,44,55,71,98]. Includes emergency and elective procedures. Adapted from: Friedman LS. "Surgery in the patient with liver disease". Trans Am Clin Climatol Assoc 2010;121:192–204.

Type of surgery	Mortality				
	Overall (%)	Child-Pugh class			MELD score
		A (%)	B (%)	C (%)	
Appendectomy	9	n.a.	n.a.	n.a.	n.a.
Cardiac	16-17	0-3	42-50	100	n.a.
Cholecystectomy	1-3	0.5	3	n.a.	<8 = 0% ≥8 = 6%
Colorectal cancer surgery	12.5	6	13	27	n.a.
Esophagectomy	17	n.a.	n.a.	n.a.	n.a.
Major abdominal surgery	26-30	10	30-31	76-82	n.a.

n.a., not available.

Table 1 lists the mortality rates associated with specific types of surgery in patients with cirrhosis stratified according to the CTP scores. The overall operative mortality rates are maximal in patients undergoing major open abdominal and cardiac surgery, and these surgeries are contraindicated in Child C patients.

In recent years, the MELD score has been utilized to prioritize organ allocation in patients awaiting LT. This score has also been used to predict risk of mortality following surgery in CLD patients. A MELD score 0–11 correlates with 5–10% 90-day mortality, a score of 12–25 with 25–54% mortality rate, and scores greater than 26 with a 90% postoperative mortality rate [20–22,54]. Unlike the CTP score, which has subjective components, the MELD score is considered more objective as it relies solely on laboratory values, serum bilirubin, creatinine, and international normalized ratio (INR). Northup *et al.* [54] noted in their study that there was approximately a 1% increase in mortality risk per MELD point below a score of 20, whereas there was a 2% increase in mortality risk per MELD point over 20. The c statistic of the MELD score for predicting 30-day mortality was found to be 0.72 in the whole population of patients undergoing surgery and 0.8 in the subgroup with intra-abdominal surgery. The mean MELD score for patients dying was significantly different from patients who survived the non-hepatic surgical intervention in this study. Also, in other studies, a MELD score of at least 8 was shown to predict an increased risk of postoperative complications, including death in patients undergoing cholecystectomy [55].

Both CTP and MELD have been correlated with outcome of patients with CLD. Several investigators gave birth to a "battle for supremacy" between the CTP and MELD score to predict outcomes of non-hepatic surgery in cirrhotic patients [20–22,54,56]. Befeler *et al.* [56] also showed the superiority of the MELD score for extrahepatic general surgery in a group of 53 patients. MELD score and plasma hemoglobin levels less than 10 g/dl were found to be independent predictors of poor outcomes in this study. A MELD score of 14 or greater was a better clinical predictor of poor outcome than CTP class C (77% sensitivity, 80% specificity, 56% positive predictive value and 91% negative predictive value). Teh *et al.* [18] in the largest retrospective study of predictors of perioperative mortality in patients with cirrhosis undergoing abdominal, orthopaedic, and cardiovascular surgery found that the MELD score, patient's age, and ASA class were statistically

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significant predictors of mortality on multivariate analysis. Whereas the ASA class was the best predictor of 7-day postoperative mortality, the MELD score was the best predictor of 30-day, 90-day, and long-term postoperative mortality for all types of surgery. An important finding of this study was that the relative risk of 30- and 90-day mortality increased by 14% with each 1-point increase in the MELD score. MELD score, along with patient age and ASA class, was proposed as principal factor for risk stratification.

For now, clinicians should probably determine both the Child's class and the MELD score to estimate 30- and 90-day postoperative mortality and morbidity rates in patients with cirrhosis. The CTP score includes additional important parameters like ascites and portosystemic encephalopathy, which are not included in the MELD score; on the other hand, the MELD score includes creatinine which is an estimate of the renal function that is often deranged in cirrhotic patients. The two scores should be considered complementary rather than mutually exclusive, since using both would give a better insight on the status of liver disease and degree of decompensation.

Are individual markers of organ function better than a single scoring system?

While large populations of patients seem to be correctly prognosticated using one or both of the grading systems (CTP and MELD), it is evident that not all pathophysiologic conditions can be taken into account by any single score. In addition, not considering acuity of patient presentation and operative course may limit the ability of CTP and MELD scores to predict perioperative outcome [56].

Some individual markers of organ function may help in preoperative assessment, though there is no strong evidence yet to suggest that individual risk factors are better than either CTP or MELD scores in assessing risk. In addition to parameters included in the CTP and MELD scores, presence of PHT, hyponatremia, infection, anemia, and malnutrition are other recognised individual risk factors. Semi-quantitative liver function tests including galactose elimination capacity, aminopyrine breath test, indocyanine green (ICG) clearance, and monoethylglycinexylidide test (MEGX) have also been proposed to risk-stratify patients with cirrhosis undergoing surgery, but these are not available universally and hence not used routinely in clinical practice.

Tables 2 and 3 summarise important series in literature, which studied the morbidity and mortality associated with various non-hepatic intra-abdominal surgical procedures and tried to identify prognostic factors.

Preoperative interventions: Could they help make the surgery safer?

Transjugular intrahepatic portosystemic shunt (TIPS)

The high morbidity and mortality after surgery in cirrhotic patients is related to a great extent to the degree of PHT and the occurrence of liver insufficiency in the postoperative period. Preoperative portal decompression would seem to be a logical approach to facilitate abdominal surgery and hopefully to improve postoperative survival in these patients. TIPS reduces the portosystemic gradient thus reducing the risk of bleeding, and also helps reduce ascites, which is a significant cause of postoperative morbidity in these patients. TIPS placement is much less invasive as compared to surgical shunts and it is possible to do this procedure in patients with decompensated cirrhosis (Child B) also, hence making it an option in this group of patients [57].

Table 2. Series in literature on morbidity and mortality of non-hepatic abdominal surgery in patients with cirrhosis.

Authors Journal year; [Ref.]	Type of surgery	Morbidity (%)	Mortality (%)	Risk factors for morbidity/mortality
del Olmo JA *et al.*, World J Surg. 2003; [6]	Non-hepatic abdominal surgery	50	16.3	~ Preoperative CTP score ~ Duration of surgery ~ Presence of postoperative general complications
Mansour A *et al.*, Surgery 1997; [7]	Non-hepatic abdominal surgery	45	50 in emergent, 18 in elective surgery	~ Emergency surgery ~ Preoperative Child-Pugh class
Zarski *et al.*, Gastroenterol Clin Biol 1988; [86]	Extrahepatic digestive surgery	37	23	~ Child-Pugh score esp. hypoalbuminemia
Wong R *et al.*, J Am Coll Surg. 1994; [97]	Abdominal extrahepatic surgery	28 (major)	18	~ Emergency surgery ~ Gastric procedures ~ Transfusion of FFP, platelets
Telem *et al.*, Clin. Gastro. Hepatol. 2010; [87]	Abdominal extrahepatic surgery	43	7	~ MELD ≥15 ~ Serum albumin ≤2.5 ~ Emergency surgery ~ Blood transfusions
Neeff H *et al.*, J. Gastrointest. Surg. 2011; [88]	Non-hepatic general surgery	-	35 after intra-abdominal procedures	~ Emergency surgery ~ Child-Pugh class ~ ASA class ~ Intraoperative transfusions ~ Preoperative sodium <130

PHT, portal hypertension; BP, blood pressure; ASA, American Society of Anesthesiologists.

Table 3. Series in literature on morbidity and mortality in specific surgeries in patients with cirrhosis.

Author, Journal year; [Ref.]	Type of surgery	Morbidity (%)	Mortality (%)	Risk factors for morbidity/mortality
Lehnert T *et al.*, Ann Surg 1993; [16]	Peptic ulcer surgery	-	~ 29 in elective ~ 35-64 in emergency	~ Preoperative Hb <12 g/L ~ Systolic BP <100 mmHg ~ Prothrombin time <60% ~ Presence of PHT
Metcalf AM *et al.*, Dis Colon Rectum 1987; [89]	Colorectal surgery	24	48	Encephalopathy, ascites, anemia, hypoalbuminemia
Meunier K *et al.*, Dis Colon Rectum 2008; [90]	Colorectal surgery	77	26	~ Preoperative ascites ~ Postoperative infections
Nguyen GC *et al.*, Dis Colon Rectum 2009; [91]	Colorectal surgery	-	In-hospital 14 for cirrhotics, 29 for cirrhotics with PHT	~ Presence of PHT ~ Emergent/urgent surgery
Martinez JL *et al.*, Surg Endosc 2004; [92]	Laparoscopy assisted colorectal surgery	29	0	-
Lee JH *et al.*, World J Gastroenterol 2005; [93]	Gastric cancer	39.4	3.8	~ Child-Pugh class B, C
Jang HJ *et al.*, Dig Dis Sci. 2008; [94]	Gastric cancer	39	9	~ Child-Pugh class B, C
Carbonell AM *et al.*, Hernia 2005; [95]	Abdominal wall hernias	16.5	2.5	~ Co-morbidities – functional impairment, CHF, renal failure, nutritional deficiencies, PVD ~ Emergency surgery
Mc Kay A *et al.*, Hernia 2009; [96]	Umbilical hernia repair	21	2.7	~ Child-Pugh class ~ Emergency surgery

PHT, portal hypertension; BP, blood pressure; CHF, congestive heart failure; PVD, peripheral vascular disease.

We previously introduced the concept of preoperative TIPS to increase safety of abdominal surgery in patients with severe PHT [58]. Seven cirrhotic patients with PHT were planned for the following surgical interventions; colonic, gastro-oesophageal, renal, and aortic procedures in three, two, one, and one patient, respectively. Because PHT was a relative contraindication for surgery in these patients, a "two-step strategy" was used: first, TIPS to control PHT, followed by abdominal surgery at least 1 month later. The TIPS procedure was successfully performed in all patients without complications. The hepatic venous pressure gradient decreased from 18 ± 5 to 9 ± 5 mmHg (p <0.01). All patients were operated on with a delay ranging from 1 month to 5 months after TIPS (2.9 ± 1.3 months; median 3 months). Patients with cancer were operated on at 1 month post TIPS procedure. The planned operation was performed in six of the seven patients. One patient with cancer of the cardia could not undergo the planned procedure because of intra-abdominal tumor dissemination detected at exploratory laparotomy. Intraoperative transfusion was necessary in only two of the six patients. One patient died, 36 days after resection of a left colon cancer. We concluded that the proposed two-step strategy in cirrhotic patients with severe PHT could decrease morbidity and mortality after abdominal surgery.

This concept was further used by Gil *et al.* [59] in three cirrhotic patients with severe PHT who had abdominal tumours (colonic, gastric, and pancreatic tumours, respectively) requiring surgical resection. In their small series, they concluded that TIPS reduced the portosystemic gradient and the varices around the tumoral area thus helping reduce bleeding and possible morbidity due to the same. Schlenker *et al.* [60] also proposed that preparation of patients with cirrhosis and PHT for elective surgery using preoperative TIPS decreased the risk of perioperative morbidity and mortality. Seven patients underwent gastric, colonic, urological, and gynaecological surgeries with limited blood loss and no operative mortality. However, since there was no comparison group in this study, it was difficult to determine which complications could be best prevented using preoperative TIPS.

Vinet *et al.* [61] in their study evaluated the clinical outcomes of 18 patients with cirrhosis who underwent non-hepatic abdominal surgery after preoperative TIPS placement, a mean of 72 days before surgery. TIPS induced a marked mean decrease in portohepatic gradient from 21.4 (±3.9) mmHg to 8.4 (±3.4) mmHg. Cirrhotic patients (n = 17) who underwent elective abdominal surgery without preoperative TIPS placement were used as the control group. Though the authors concluded that the preoperative placement of TIPS had no positive effect on operative blood loss, short and long term survival outcomes; it is of note that the mean CTP score was significantly higher in the TIPS group (7.7 *vs.* 6.2), indicating that these patients were more decompensated compared to controls. One would expect the more decompensated patients to have a worse outcome following major surgery.

Table 4. Important parameters to look for and manage appropriately in patients with cirrhosis planned for non-hepatic surgery.

System	Pathology	Assessment	Management
Abdomen	Ascites Increased risk of abdominal wound dehiscence, abdominal wall herniation, respiratory compromise, spontaneous bacterial peritonitis (SBP)	Check response to diuretics, pulmonary function tests, diagnostic ascitic tap	~ Low sodium diet and diuretics with careful monitoring of creatinine and electrolyte levels ~ Large volume paracenthesis for uncontrolled ascites with albumin ~ Antibiotics for SBP
Renal	Renal insufficiency/hepatorenal syndrome (HRS) due to drugs, infections, gastrointestinal bleed	Renal function tests, creatinine clearance, DTPA scan	~ Avoid nephrotoxic drugs, contrast agents for diagnostic studies ~ Combination of terlipressin, albumin in HRS ~ Optimal fluid, electrolyte status
Central nervous system	Hepatic encephalopathy (HE)	Clinical assessment, arterial ammonia levels	~ Use of lactulose, metrogyl, branched chain amino acids ~ Treat infections, avoid diuretics, constipation, CNS depressants, azotemia
Pulmonary	Hydrothorax, hepatopulmonary syndrome (HPS), portopulmonary hypertension (PPH)	~ Chest imaging ~ Bubble ECHO/MAA scan for HPS	~ Optimize pulmonary functions ~ Intravenous epoprostenol, sildenafil has also been tried perioperatively
Cardiac	Cardiomyopathy	~ Dobutamine stress ECHO ~ ACC and AHA guidelines for non-cardiac surgery	Beta blockers in perioperative period
Homeostasis	Electrolyte disorders (esp. hyponatremia)	Regular electrolyte profile and arterial blood gases	Slow correction of serum sodium with fluid restriction, discontinuation of diuretics
Nutrition	Malnutrition, hypoalbuminemia, muscle wasting, increased need for postoperative ventilation	Methodical nutritional assessment	~ Preoperative nutritional build-up (high carbohydrate/lipid content, low in amino acid) ~ Vitamin B1 in alcoholics
Other systems	Anaemia and coagulopathy	Intraoperative thrombo-elastogram	Appropriate blood products perioperatively to maintain desired INR (<1.5), haemoglobin (>9 g%), platelet (>50,000/mm^3) levels
	Glucose intolerance	Laboratory testing	Insulin infusion
	Gastroesophageal varices	Endoscopy, portal pressure measurements	Beta blockers, variceal banding
	Concurrent infections	Screening	Antibiotic prophylaxis
	Autoimmune hepatitis patients developing stress-induced insufficiency	Serum cortisol levels	Stress-dose steroids preoperatively

Kim *et al.* [62] reported results of surgery in patients with a previously placed patent TIPS. Twenty-five cirrhotic patients with a patent TIPS underwent abdominal (n = 19) or cardiothoracic (n = 6) surgery at a single center. Thirty-two percent of surgeries were emergent, 24% were urgent, and 44% were elective surgeries. Postoperatively, severe ascites developed in 29% and encephalopathy in 17% of cases. During a median follow-up of 33 months, actuarial 1-year patient survival was 74%. The three patients (12%) who died during their hospitalization all had MELD scores ⩾25 and had undergone emergency surgery. Though, this study did not have a control group, the conclusion was that portal decompression via TIPS may allow selected cirrhotic patients to safely undergo major surgery with an acceptable rate of short-term morbidity and mortality.

In the study by Lian *et al.* [46], among the CLD patients with IBD who underwent restorative proctocolectomy, two patients underwent TIPS before total proctocolectomy/IPAA; both patients did well in the postoperative period, none developed a pelvic abscess or sepsis, which was the major cause of mortality in their series.

In summary, it is true that at present there is not enough evidence clearly supporting the use of TIPS before major abdominal surgery in cirrhotic patients with severe PHT. Though a randomised, controlled trial comparing outcomes in adequately matched groups (with respect to CTP class and type of surgery) will give the final answer to the debate on whether preoperative TIPS is beneficial or not, such a trial is difficult to design and undertake.

Child A and early Child B patients (CTP score 5–7) [MELD score ⩽25] with moderately well preserved liver function, yet having significant ascites, extensive abdominal varices, or both may be ideal candidates for preoperative TIPS. The MELD score was originally developed to predict short term mortality in patients undergoing TIPS, before being adopted by UNOS for prioritizing organ allocation. With regard to its original utilization, a MELD score <8 predicts good outcome after TIPS and a score >18 predicts poor outcome, with best outcomes seen in patients with scores <14. Avoidance of TIPS is generally recommended in patients with a MELD score >24, unless the procedure is used as a measure of last resort to control active variceal bleeding.

Being a minimally invasive procedure, TIPS is not associated with too many procedural complications in expert hands. Complications like hepatic encephalopathy are the bane of TIPS, but these are known to occur more commonly in severely decompen-

Table 5. Recent reports on results of laparoscopic cholecystectomy in patients with liver cirrhosis (includes emergency and elective procedures).

Author, year [Ref.]	Number of patients (n)	Child-Pugh classification			Morbidity (n)	Mortality (n)
		A	B	C		
Morino M *et al.*, 2000 [77]	33	27	4	2	0	0
Fernandes NF *et al.*, 2000 [11]	48	38	10	0	4	0
Clark JR *et al.*, 2001 [79]	25	14	9	2	0	0
Yeh CN *et al.*, 2002 [31]	226	193	33	0	15	2
Cucinotta E *et al.*, 2003 [78]	22	12	10	0	14	0
Puggioni A *et al.*, 2003 [81]	400	265	73	6	10	5
Curro G *et al.*, 2007 [76]	50	35	15	0	15	0

sated (Child C) patients. The placement of TIPS should be done at least 2–4 weeks prior to the proposed surgical procedure because, even though the drop in the portosystemic gradient is immediate, the resolution of ascites (largely dependent on natriuresis) takes some time. Consequently, a cirrhotic patient needing emergent surgery would not benefit from TIPS.

Preparing a cirrhotic patient for surgery

Common pathology in chronic liver disease patients to be looked for and managed preoperatively

Table 4 shows the common complications and morbid conditions that frequently co-exist in patients with CLD, they need to be identified and adequately treated in order to ensure a smooth operative and postoperative course. Primary issues to anticipate and address include manifestations of acute liver decompensation including encephalopathy, acute renal failure, coagulopathy, adult respiratory distress syndrome, and sepsis [63,64]. In addition, cardiovascular and nutritional status, and fluid and electrolyte balance need to be optimized so as to decrease perioperative death and complications after surgery.

In general, it is accepted that converting a Child C patient to Child B preoperatively could help survival after surgery [65]. Coagulopathy and thrombocytopenia should be corrected with replenishment of vitamin K, administration of fresh-frozen plasma (FFP), and possibly cryoprecipitate transfusions to reduce a prothrombin time within 3 s of normal time and to achieve a goal of platelet counts >50,000/mm^3. Infection, diuretics, metabolic alkalosis, constipation, CNS depressants, hypoxia, sepsis, azotemia, or gastrointestinal bleeding in the pre/postoperative periods may induce encephalopathy. Thus, correction of electrolyte imbalance, treatment of infection, branched chain amino acid therapy, and restriction of sedatives help prevent encephalopathy [66,67].

With respect to the etiology of cirrhosis, patients with autoimmune hepatitis on daily steroids should receive stress-dosed steroids before surgery. D-penicillamine can impair wound healing; patients taking it for Wilson disease should decrease their dose for 1–2 weeks pre and postoperatively. As mentioned before, CLD patients with a history of alcohol abuse are at increased risk of other complications, including poor wound healing, bleeding, delirium, and infections. Patients who have continued to actively drink are at risk for withdrawal. Unless the surgery is imminent, patients with alcoholic hepatitis should have medical management and be stabilised, or should undergo alternative, less invasive procedures in an emergency situation.

Role of laparoscopic surgery in patients with cirrhosis

Cirrhosis was once considered to be a contraindication for the laparoscopic approach. A major difference of open and laparoscopic procedures is the creation of pneumoperitoneum for visualisation of the abdominal cavity. Theoretically, for reasons cited above, pneumoperitoneum is considered unsafe for abdominal surgery in CLD patients as they already have varying degrees of alterations in hepatic blood flow and general haemodynamics. However, within the limits of our literature search, no report of hepatic failure attributable to laparoscopy alone in a cirrhotic patient was found. Also, current literature has increasingly shown that the use of laparoscopy in the treatment of various disease specific and disease non-specific surgical conditions in cirrhotic patients is safe and offers many advantages [68–71].

Some authors have advocated modifications in operative techniques to help minimise the morbidity in CLD patients undergoing laparoscopic procedures. Friel *et al.* [72] advocated the use of open technique using Hassan's trocar for access, to prevent inadvertent puncture of an umbilical varix, whereas placement of the trocar in the right paramedian position when umbilical varix is already present was proposed by Schiff [73]. In addition, certain modifications in the surgical technique have been suggested to make particular procedures safer as detailed below.

Laparoscopic cholecystectomy in cirrhotic patients

Open cholecystectomy (OC) in cirrhotic patients continues to be associated with high rates of morbidity (5–30%) and mortality (7–25%) compared to 0.5–1% mortality in non-cirrhotics [74,75]. With increasing experience, several centers across the world have demonstrated that laparoscopic cholecystectomy (LC) is safe and effective with fewer complications compared to OC [11,31,76–79,81] (Table 5).

Specifically, LC is associated with less intraoperative bleeding and shorter duration of hospital stay and fewer postoperative complications. It is also particularly useful in LT candidates since it is associated with fewer postoperative adhesions [11].

Certain problems may be encountered during laparoscopic cholecystectomy in patients with a cirrhotic liver. There may be difficulty with traction of the liver, inadequate exposure of the hilum, adhesions around the gallbladder and the hilum with difficulty in identifying anatomical landmarks as well as increased vascularity of the gallbladder bed. The use of additional ports, as well as performance of retrograde cholecystectomy or modified subtotal cholecystectomy in cases of severe inflammation leaving the back wall of the gallbladder on the liver bed in selected cases, can be helpful [79]. The use of mechanical compression from introduced surgical sponges to achieve haemostasis with additional haemostatic modalities such as oxidized cellulose, topical haemostatic agents, application of ultrasonic energy via a harmonic scalpel and the use of argon beam coagulator, which can be inserted through an operative port, have also been described [72].

Palanivelu *et al.* [80] reported their experience with 265 laparoscopic cholecystectomies in Child–Pugh A and B cirrhotic patients, with symptomatic gallstones. There was no mortality; in 15% of patients, postoperative deterioration in liver function occurred. They concluded that a modification of subtotal cholecystectomy should be practiced, depending on the risk factors present, to avoid complications in these high risk cirrhotic patients.

A meta-analysis of LC in cirrhotic patients, [81] was inconclusive in recommending LC for CTP class C patients due to inconclusive data in most of the studies reviewed. It is not clear whether many surgeons consider the risks of morbidity and mortality to be so high as to withhold even emergency surgeries in these patients or that the data on this group of patients are not included in the different publications. It would seem that indications for surgery in these patients should be limited to emergencies such as cholecystectomy for acute cholecystitis. Even in such instances, percutaneous drainage of the gallbladder and other conservative procedures may suffice [82].

Laparoscopic hernia repair in cirrhosis

In a report of 14 cirrhotic patients who underwent laparoscopic incisional and umbilical hernia repair, Giulio *et al.* [68] observed that though open repair in cirrhotic patients has significant recurrence rates and frequent wound infections, laparoscopic repair yields less morbidity and fewer recurrences. The study further highlighted that the preservation of the anterior abdominal wall in laparoscopic repair avoided the interruption of collateral veins, which are not infrequently distended in cirrhotic patients.

Successful laparoscopic repair of recurrent incarcerated umbilical hernia in a cirrhotic patient with refractory ascites has also been reported [83]. In the report, the authors used dual mesh prosthesis and advocated meticulous sterile fashion of mesh insertion and fixation. This is important since ascitic fluid infection, which may occur after surgery may affect the hernia mesh repair. The possibility of mesh migration due to the ascitic fluid can be reduced by placing the mesh in a preperitoneal space [84].

Other laparoscopic procedures in cirrhotic patients

Cobb *et al.* [69] reported 52 laparoscopic procedures performed on 50 cirrhotic patients These procedures, including cholecystectomies, splenectomies, colectomies, diagnostic laparoscopies, ventral hernia repairs, Nissen fundoplication, Heller's myotomy, gastric bypass and radical nephrectomy, had a morbidity rate of 16% but no mortality.

Tsugawa *et al.* [43] had earlier compared open and laparoscopic appendectomies among patients with liver cirrhosis. They reported fewer complications with the laparoscopic approach.

Gentileschi [85] reported a successful laparoscopic suture closure and placement of an omental patch for treatment of a perforated gastric ulcer with peritonitis in a severely cirrhotic patient (Child C) with PHT.

To summarise, laparoscopy in cirrhotic patients is associated with a definite risk, yet is not significant enough to contraindicate the procedure in these patients. Many studies have also shown that laparoscopy is not only safe in carefully selected cirrhotic patients but also has many advantages over the various open procedures. However, its safety in Child-Pugh's class C patients is not yet proven hence surgery in such patients may be limited to conservative procedures in emergency cases.

Conclusions

The perioperative morbidity and mortality following non-hepatic surgical procedures in patients with cirrhosis are significant, with mortality rates of up to 50% reported following surgery in patients with decompensated CLD. Stringent assessment of these patients for co-morbidities and risk stratification in the preoperative period is essential if their outcomes are to be improved. Considering both, the Child score and MELD score to prognosticate these patients as regards short term outcomes seems to be necessary as of now.

Three factors essentially determine the extent of surgical risk; degree of decompensation (higher MELD and CTP score), whether the surgery is performed as an emergency procedure or electively, and the nature/type of surgery. Since PHT is an added risk factor for non-hepatic abdominal surgery, preoperative portal decompression may help reduce the difficulty of the surgical procedure especially as regards intraoperative bleeding, and may also reduce morbidity and mortality by decreasing the ascites if done relatively well in advance of the planned procedure. Though evidence and safety to support the approach in all eligible CLD patients are not strong enough at this point in time, the concept of a two-stage strategy initially proposed and used by us may help improve perioperative outcomes following non-hepatic abdominal surgery in well selected patients with compensated cirrhosis and severe PHT.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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