Pre-surgical risk assessment in patients with cirrhosis

R. Martin Mateos[1,2], I. García de la Filia Molina[1], A. Albillos[1,2]

(1) Gastroenterology department. Hospital Universitario Ramón y Cajal. Madrid, Spain ; (2) Instituto Ramón y Cajal de Investigación Clínica (IRYCIS). Universidad de Alcalá. Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd).

Abstract

Over the last decades, significant improvements in the clinical management of patients with cirrhosis have increased their life expectancy. Thus, indications for surgical procedures other than liver transplantation are becoming more frequent. However, patients with advanced liver disease are at high risk of perioperative morbidity and mortality. This is the consequence of multiple factors that include the presence of portal hypertension, alterations on hemostasis and coagulation, the immune dysfunction that entails an increased risk of infections, and the impaired synthesis of proteins that impacts on the nutritional status and the wound healing. Surgical outcomes are not only determined by the severity of the liver disease, but also by the type of surgery and the presence of other comorbidities. Different models to predict mortality have been proposed, including the MELD score, the Child-Pugh classification, the hepatic venous pressure gradient, and the Mayo postoperative mortality risk calculator, among others. Multidisciplinary committees including surgeons, anesthesiologists, hepatologists, critical care physicians and other specialties involved in each case, should assess individually the risk-benefit of the surgical procedure, also considering patient`s expectations and will. (Acta gastroenterol. belg., **2020**, 83, **449-453**).

Keywords : cirrhosis, surgery outcomes, perioperative risk assessment, model for end-stage liver disease.

Introduction

Indications for surgical procedures other than liver transplantation are increasing in patients with chronic liver diseases. The development of better treatments in specific areas such as chronic hepatitis C or hepatocellular carcinoma (1), along with the continuous advances in the management of portal hypertension-related complications, have contributed to increase their life expectancy. Accordingly, we are now facing clinical scenarios where indications for urgent or elective abdominal, cardiovascular or oncologic interventions not related with the liver disease, have to be carefully assessed.

Despite significant advances in the clinical management of patients with cirrhosis, any surgical procedure entails a high risk of complications and mortality. Indeed, the estimated mortality is 2-10 times higher than in patients without cirrhosis (2). However, outcomes are improving over the time, thanks to a better selection of the surgical candidates by using specific tools for risk assessment, and a careful optimization of patient´s condition before the surgery. This has been translated into a decreasing mortality for abdominal surgery from 30% in cohorts analyzed from 1975-1982 (3), to 7% for patients with cirrhosis studied from 2002-2008 (4).

Currently available data aiming to predict mortality and to identify factors associated with a high postoperative risk are limited. This is because most of the studies are retrospective, no-randomized, no-controlled, and performed relatively long time ago, which may not reflect the current standard of care and recent technical advances. In addition, the number of patients who undergo certain types of surgeries is small, and candidates are usually highly selected, which entails selection bias and potential confounders (2).

This review intends to summarize the current knowledge about the perioperative evaluation and management of patients with cirrhosis, aiming to provide specific tools and recommendations for the optimal selection and conditioning of candidates before surgery.

Factors contributing to the perioperative surgical risk in patients with cirrhosis

The severity of the liver disease critically impacts the prognosis, and, thus, mortality and complications rise in parallel to the grade of portal hypertension and liver dysfunction.

First, specific immune alterations are associated with cirrhosis at its different stages. The immune dysfunction is featured by persistent systemic inflammation and progressive immune deficiency (5). All these modifications are collectively known as cirrhosis-associated immune dysfunction (6), and are responsible for the high risk of infections in these patients, both at baseline conditions, and, more importantly, at the time of the surgery. On the other hand, the progression of cirrhosis alters the architecture of the liver replacing parenchymal cells by scar tissue. The loss of hepatocytes decreases the synthesis of proteins leading to sarcopenia and malnutrition, and hindering the wound healing and the physical recovery (7).

Another aspect involved in the high rate of intra procedure and postoperative complications, are the

Correspondence to : Agustín Albillos, Carretera de Colmenar Km 9100, Madrid, Spain.
E-mail : agustin.albillos@uah.es

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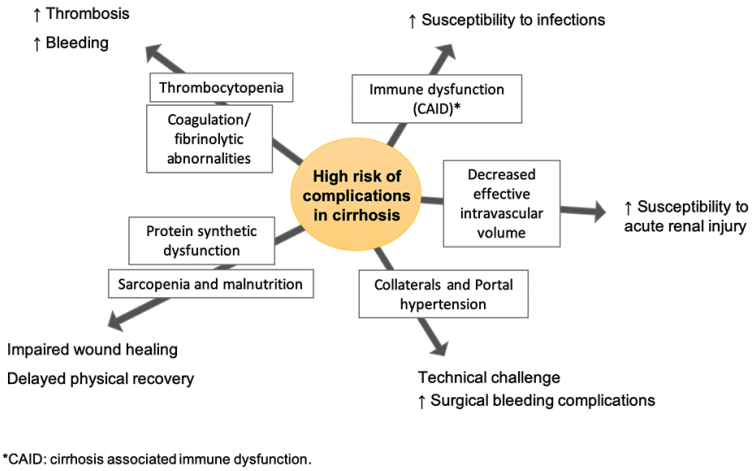

Figure 1. — Factors associated with an increased risk of mortality and complications in patients with cirrhosis undergoing surgical procedures.

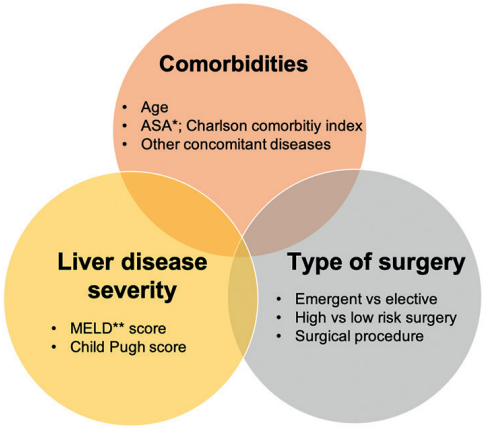

Figure 2. — Preoperative factors associated with the surgical risk in cirrhotic patients

alterations in the hemostasis and coagulation present in cirrhosis. The liver dysfunction entails deficits of both, procoagulant and anticoagulant factors (8), which results in a higher risk of bleeding and thrombosis. In addition, severe thrombocytopenia and low fibrinogen levels are common, and further increase the risk of hemorrhage. Significant portal hypertension also challenges the hemodynamic management and the fluid balance, thus increasing the susceptibility to cardiovascular and renal dysfunction. Finally, the presence of collaterals and varices not only increases the risk of bleeding, but also compromises the technical approach to the area of the intervention (Figure 1).

Tools for predicting the surgical risk in patients with cirrhosis

The overall risk of mortality and complications, depends on multiple variables related to the patient (comorbidities and severity of the liver disease) and the surgery (type and urgency) (Figure 2). Aiming to predict the surgical outcomes in different clinical situations, several scores have been proposed (Table 1). They provide additional information to the physicians and the surgical team in order to decide if the surgery can be performed safely, should be delayed until liver transplantation or clinical improvement, or should not be performed at all due to the high risk of futility.

To assess the severity of the liver disease, the Child-Pugh (CP) score and the model for end-stage liver disease (MELD) have been traditionally used in the clinical practice. CP score assess 5 components (encephalopathy, ascites, bilirubin, albumin and INR), and classifies the severity of the liver disease in 3 stages (A-C) (9). It has been shown that the CP score has a good correlation with mortality after surgery (10). Child class C cirrhotic patients have very poor perioperative outcomes and are not generally considered as candidates for elective surgery (11). The MELD score, on the other hand, is based on the serum creatinine, bilirubin and the international normalized ratio (INR) (12). MELD score predicts 30-day mortality with an acceptable accuracy (c-statistic 0.72), and is considered one of the most important predictors of perioperative mortality in cirrhosis (13). Scores higher than 15 are associated with a high risk of complications and mortality, and, thus, surgery indications for these patients have to be carefully evaluated.

The Child and MELD scores provide information about the severity of the liver disease, but do not consider other factors such as the type of surgery or the presence of concomitant comorbidities. In this regard, the Mayo postoperative mortality risk calculator may provide more specific results, and inform about the predicted mortality at different time-points (7, 30 and 90 days, 1 and 5 years) (14). This score can be easily calculated using an online tool (https://www.mayoclinic.org/medical-professionals/transplant-medicine/calculators/post-operative-mortality-risk-in-patients-with-cirrhosis/itt-20434721). The results are based on a retrospective analysis of

Table 1. — **Predictive models for assessing the preoperative risk in patients with cirrhosis**

Predictive Model	Definition	Proposed cut-offs indicating high risk of mortality and complications	References
Child Pugh Score	Encephalopathy grade (none: 1; stage 1–2: 2, stage 3–4: 3), ascites (absent: 1; moderate: 2; severe: 3), serum albumin (g/dL) (>3.5: 1; 2.8–3.5: 2; <2.8: 3), total bilirubin (mg/dL) (<2: 1; 2–3: 2; >3: 3) and INR (<1.7: 1; 1.7–2.3: 2; >2.3 :3) Points: 5–6 (class A), 7–9 (class B), 10–15 (class C)	Child C (≥10) (mortality rates up to 76%)	3, 9, 10
MELD Score	3.78 x ln (serum bilirubin)(mg/dL) + 11.2 x ln (INR) + 9.57 x ln (serum creatinine)*(mg/dL) + 6.43	MELD >15	12, 13, 14
ASA classification	1 (healthy patient), 2 (mild systemic disease), 3 (severe not life-threatening systemic disease), 4 (severe systemic disease that is a constant threat to life), 5 (absence of expectation to survive without surgery), 6 (brain-dead patient)	ASA class ≥III	14, 15, 16
Mayo Postoperative Mortality Risk Calculator	Probability of mortality calculated by: Age, ASA score (3 for compensated cirrhosis, 4 for decompensated cirrhosis), bilirubin (mg/dl), creatinine (mg/dl), INR, etiology of cirrhosis (alcoholic/ cholestatic or viral/other)	MELD>8 HR 1.12 (1.09-1.16) ASA IV HR 2.26 (1.08-1.37) Age HR 1.22 (1.64-3.11) (mortality 1 year after surgery)	14
HVPG	HVPG >16 mmHg: High risk (HR >2.5); HVPG >20 mmHg: Very high risk (HR 5.67)	HVPG >16mmHg –High risk >20 mmHg - Very high risk of death (44%)	16

MELD, Model for End-Stage Liver Disease ; ASA, American Society of Anesthesiologists ; HVPG, hepatic vein pressure gradient ; INR, international normalized ratio ; HR: hazard ratio. * 4 mg/dl in patients on renal replacement therapy.

772 patients with cirrhosis who underwent abdominal, orthopedic or cardiovascular surgeries. The etiology of the liver disease, the type of surgery, the ASA Class (American Society of Anesthesiologists classification) (15), the Charlson comorbidity index, and whether it was an urgent or an elective procedure, were studied among other variables. The multivariable analysis showed that the ASA class, the MELD score and the age can predict the risk of mortality independently of the procedure performed.

Recently, a nomogram based on the ASA class, the type of surgery (low or high-risk), and the hepatic venous pressure gradient (HVPG), has been proposed to predict 1-year mortality in cirrhotic patients undergoing elective extrahepatic surgery (16). HVPG values higher than 16 mmHg, and specially >20 mmHg, identified a subgroup of patients at very high risk of death (44%).

Risk stratification according to specific types of surgeries

Elective vs emergency interventions

Different studies have shown that patients undergoing emergency interventions present worse surgical outcomes as compared to those subjected to elective procedures. The risk of postoperative mortality is 4 to 10 times higher, and complications are 5 to 7 times more frequent in this population (2). This is due to the fact that the clinical condition of patients requiring emergency interventions is usually more severe, and there is no time enough to optimize patient´s situation before the intervention.

Hepatic resection for hepatocellular carcinoma

Surgical resection is considered for patients with cirrhosis who present a very early or early stage hepatocellular carcinoma, as defined by the Barcelona Clinic Liver Cancer group (BCLC) criteria. This applies for patients with preserved liver function (Child A without ascites), excellent performance status (ECOG-PS 0), solitary nodules <3cm and no evidence of clinically significant portal hypertension (17). Clinically significant portal hypertension may be defined by a HVPG <10 mmHg, or by the absence of esophageal varices on endoscopy, abdominal collaterals on imaging, platelets > 100,000/μL and a transient elastography < 23 kPa. In these patients, the estimated survival is higher than 60% at 5 years, and the postoperative mortality is reasonably low (<3%). However, 70% may have a tumor recurrence during the first 5 years after the surgery (18).

Cholecystectomy and abdominal wall hernia repair

Laparoscopic cholecystectomy is associated with lower mortality rates and complications than open laparotomy in patients with cirrhosis (19), and thus, this should be the preferred approach when technically possible. Of note, a frequent finding in patients with advanced liver disease is the fibrotic thickening of the gallbladder wall, which should not be confused with a sign of acute cholecystitis. On the other hand, the presence of ascites predisposes to hernias in the abdominal wall. Incarcerated hernias are the most common indication for emergency surgery in cirrhosis, and result in higher mortality and morbidity as compared with the elective hernia repair (20). A tight control of the ascites, before and after the intervention, is key in these situations. The use of diuretics, large-volume paracentesis or a transjugular intrahepatic portosystemic shunt (TIPSS), may be required as recommended in the current clinical guidelines (21).

Bariatric surgery

The worldwide increasing prevalence of non-alcoholic steatohepatitis (NASH), is contributing to expand the indications of bariatric surgery in patients with chronic liver disease (22,23). Bariatric surgery in these patients is associated with an increased risk of death compared with those who undergo bariatric surgery without NASH (24). Regarding the technical approach, restrictive procedures, such as the sleeve gastrectomy, should be preferred over malabsorptive techniques (gastric by-pass) in patients with advanced liver disease. However, in those with decompensated cirrhosis or significant portal hypertension, liver transplantation should be considered instead. A few observational studies have addressed the impact and safety of bariatric surgery at the time of transplantation (25), however, no specific recommendations in this regard can be made yet.

Cardiovascular procedures

Cardiovascular surgery entails a very high risk of complications and mortality in cirrhosis (26). Limited data are available due to the small number of highly selected patients considered for these procedures. Multivariable analysis has revealed that MELD score is an independent factor associated with in-hospital mortality in open-heart surgery with cardiopulmonary bypass (27). In these cases, a MELD score higher than 13.5 is highly predictive of the risk of death, with an optimal cut-off value of 13.5. Recently, Peeraphatdit T. et al have compared outcomes following transcatheter *vs* surgical aortic valve replacement for severe aortic stenosis in patients with advanced liver disease (28). The authors found that both procedures have acceptable and comparable short-term outcomes, and, again, MELD score was the best predictor of long-term survival in this context.

Conclusion and prospects for future research

Surgical procedures entail a higher risk of complications and mortality in patients with cirrhosis. However, the number of indications is increasing due to an improved survival and patient care. The decision of whether to perform the intervention or wait until liver transplantation or clinical improvement should be carefully assessed. Multidisciplinary committees should evaluate each case individually, considering different factors such as the severity of the liver disease, the presence of other comorbidities and the type of surgery. Different models and scores for risk assessment have been proposed in this context, and may be helpful for the decision-making process.

Future research should address the limitations of currently available data. In this regard, prospectively controlled studies with larger cohorts of patients should be pursue. Randomized clinical trials may be performed if ethically acceptable. Results should also consider the level of expertise of the surgical and medical team involved. Finally, stratification by specific types of surgery may provide more accurate information about the outcomes, contributing to to personalize the decision-making process.

Conflict of interest

All authors declare no conflicts of interest relevant to this manuscript.

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