Editorial

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A step forward to accurately predict mortality in cirrhotic patients undergoing elective surgery: The role of the hepatic venous pressure gradient

Rosa Martin Mateos[1], Haripriya Maddur[2,*]

[1]*Gastroenterology Department, Hospital Universitario Ramón y Cajal, Universidad de Alcalá, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain;* [2]*Division of Gastroenterology and Hepatology, Northwestern University Feinberg School of Medicinem, Chicago, IL, United States*

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There has been a significant increase in the number of surgical procedures performed in cirrhotic patients.[1] This is the consequence of critical improvements in diagnosis, treatment and long-term clinical management, which have led to improved prognosis and expanded life expectancy in patients with chronic liver disease. Despite improvements in lifespan, the need for surgery in such patients portends a high risk of postoperative complications and increased mortality.[2] Therefore, a careful assessment of the risk/benefit ratio when considering elective surgery is necessary. Unfortunately, this is not an easy task.

There are a multitude of factors related to end-stage liver disease that increase surgical risk and concomitant complications, including the presence of collaterals and varices, which increase the likelihood of portal hypertensive related bleeding. Other factors include impaired wound healing related to synthetic dysfunction and malnutrition, and a higher risk of infection as a consequence of cirrhosis-associated immune dysfunction. Less commonly appreciated is the thrombotic risk as a consequence of coagulation abnormalities.[3] Finally, portal hypertension challenges hemodynamic management, thus increasing susceptibility to cardiovascular and renal complications.

Aiming to accurately predict mortality and determine perioperative outcomes in this clinical setting, different scoring systems have been proposed. The American Society of Anesthesiology (ASA) has developed the most widely used classification system based on presurgical physical status and comorbidities.[4] High ASA class is associated with a very high risk of mortality in cirrhosis, however, this classification lacks specific criteria to evaluate severity of liver disease. The Child-Turcotte-Pugh (CTP) and the model for end-stage liver disease (MELD) scores are the most commonly used criteria to assess the severity of cirrhosis, and demonstrate a good correlation with post-surgical outcomes.[5,6] A specific formula combining MELD, ASA class, and age was proposed in 2007 by the Mayo Clinic group.[7] The Mayo postoperative surgical risk score allows for mortality prediction at different time points (30, 90 and 365 days), independent of the type of surgery. This score shows better accuracy than its components individually, and it has become one of the strongest tools to evaluate the preoperative risk in cirrhotic patients.

Despite the aforementioned efforts directed at improving the selection of surgical candidates, preoperative evaluation of cirrhotic patients in clinical practice remains challenging. Regarding the Mayo risk score specifically, it does not differentiate between emergent versus elective surgery and, therefore, cannot be broadly applied. Moreover, different types of surgical modalities are associated with varying risks (*i.e.* open versus laparoscopic and cardiovascular, abdominal wall and orthopedic surgery, amongst others). Due to the imprecision of currently available surgical prognostication scoring systems in patients with chronic liver disease, other modalities to assess risk are needed.

In this issue of *Journal of Hepatology*, Dr. Reverter *et al.* approach this clinical question by evaluating the prognostic role of the hepatic venous pressure gradient (HVPG) in cirrhotic patients undergoing elective extrahepatic surgery.[8] The authors found that ASA class, high-risk surgery (open abdominal or cardiovascular interventions) and HVPG, were independently associated with 1-year mortality. Regarding HVPG specifically, a HVPG >16 mmHg was associated with increased mortality, with a value >20 mmHg identifying a very high-risk population.

This is the first prospective, multicenter study that accurately evaluates the role of portal hypertension with hemodynamic studies. The direct and quantitative measuring of HVPG enables risk stratification, and overcomes the limitations of previous investigations that assess the presence of portal hypertension by indirect markers, such as ascites, splenomegaly or previous variceal bleeding, amongst others.[2] This is particularly relevant as patients who lack traditional surrogate markers of portal hypertension (*i.e.* thrombocytopenia or varices) were still found to have elevated HVPG (>10 mm) in this study, thus increasing the risk of surgical complications.[9,10]

Regarding the perioperative clinical management of cirrhotic patients undergoing elective surgery, an important unsolved

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* Corresponding author. Address: Division of Gastroenterology and Hepatology, Northwestern University Feinberg School of Medicinem, Chicago, IL, United States.
E-mail address: hmaddur@nm.org (H. Maddur).

question is the role of the preemptive placement of a transjugular intrahepatic portosystemic shunt (TIPS). Although some authors have suggested potential benefits in selected surgical candidates,[11] the lack of strong evidence and potential complications preclude its recommendation as a standard of care.[1] In the study from Reverter and colleagues, only two patients with previous TIPS and one with a surgical portosystemic shunt were included, and therefore, the role of preemptive TIPS cannot be addressed. However, the authors provide specific HVPG values associated with a high risk of post-surgical mortality and complications. These cut-offs may be considered for future studies attempting to answer this controversial question.

MELD and CTP scores were higher in the group of patients that did not survive 1 year after surgery, but these variables were not associated with a significant risk of post-surgical mortality in the multivariate analysis. This is striking, considering that several previous studies claim otherwise.[5,12] As the authors argue, one explanation may be that the study includes a quite homogeneous cohort of patients with mild to moderate disease (mean MELD 11.1 ± 3, 59% CTP A). However, one limitation of the study, the sample size, may also play a role. Although the study aimed to include 200 patients, data were reported on 140 patients due to a slow inclusion rate. It may be speculated that the sample size was not large enough to show significant differences for MELD and CTP, but sufficient to find the strong predictive value of the HVPG.

The smaller than predicted sample size also precluded stratification by different types of surgery. However, the study size was sufficient to stratify patients as having had low and high-risk procedures. As expected, this study demonstrated that those patients undergoing high-risk surgery had a higher 1-year mortality than those undergoing low risk surgery. Unfortunately, the over representation of abdominal interventions hinders obtaining reliable data about other specific types of surgery, such as cardiovascular or pulmonary procedures, which should be addressed in future larger prospective cohorts. Moreover, the results of this study should be interpreted in the context of the absence of a control group.

The evidence provided by Reverter *et al.* support the use of HVPG for the presurgical assessment of patients with cirrhosis. The utility of HVPG is best suited for scenarios in which surgery is non-emergent, to allow for preoperative HVPG measurement. Thus, one of the limitations of this modality is that it cannot be obtained in emergency situations or in facilities where HVPG is not available. In addition, the risk of performing an invasive procedure for risk stratification purposes should also be considered.

Nonetheless, the study by Reverter and colleagues demonstrates for the first time the predictive role of the HVPG in cirrhotic patients undergoing elective extrahepatic surgery, and provides evidence for risk stratification based on specific cut-offs. Based on these results, HVPG should be considered in the preoperative assessment of patients undergoing elective surgery. Larger studies with a greater representation of decompensated patients are needed to corroborate these findings.

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2019.09.001.

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