



Opinion

The imperative for an updated cirrhosis surgical risk score

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ABSTRACT

The burden of cirrhosis is increasing, as is the need for surgeries in patients with cirrhosis. These patients have increased surgical risk relative to non-cirrhotic patients. Unfortunately, currently available cirrhosis surgical risk prediction tools are non-specific, poorly calibrated, limited in scope, and/or outdated. The Mayo score is the only dedicated tool to provide discrete post-operative mortality predictions for patients with cirrhosis, however it has several limitations. First, its single-center nature does not reflect institution-specific practices that may impact surgical risk. Second, it pre-dates major surgical changes that have changed the landscape of patient selection and surgical risk. Third, it has been shown to overestimate risk in external validation. Finally, and perhaps most importantly, the score does not account for differences in risk based on surgery type. The clinical consequences of inaccurate prediction and risk overestimation are significant, as patients with otherwise acceptable risk may be denied elective surgical procedures, thereby increasing their future need for higher-risk emergent procedures. Confident evaluation of the risks and benefits of surgery in this growing population requires an updated, generalizable, and accurate cirrhosis surgical risk calculator that incorporates the type of surgery under consideration.

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Cirrhosis results in significant morbidity, mortality, and healthcare costs [1], and inadequate surgical risk stratification is an increasingly salient contributor to this burden. Non-alcoholic steatohepatitis, alcohol use disorder, and an aging hepatitis C population [1–4] have led to a growing population of patients with cirrhosis or advanced fibrosis, many of whom develop surgical indications over time. Furthermore, cirrhosis confers an increased surgical risk relative to the general population [5], likely related to poor wound healing, impaired hepatorenal medication clearance [6], and increased predilection toward bleeding, among other factors. Given this risk, a multidisciplinary pre-operative evaluation is critical to improve patient surgery selection and optimize outcomes. This assessment may be shared by gastroenterologists, hepatologists [6], surgeons [7], and anesthesiologists [8]. However, currently-available risk stratification tools are non-specific, poorly calibrated, based on single-center cohorts, and/or outdated. An accurate risk score must be specific to patients with cirrhosis and the modern surgical procedures they may undergo.

Although pre-operative risk stratification is a cornerstone of surgical management, existing clinical tools do not capture cirrhosis

physiology appropriately. For example, the widely used American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) surgical risk calculator does not include cirrhosis as an input, nor does it address the spectrum of decompensated disease. The only ACS NSQIP cirrhosis-related variable is ascites within 30 days of surgery [9], and the score accuracy has not been assessed broadly in patients with cirrhosis [10]. While the American Society of Anesthesiologists (ASA) physical status classification system has been associated with surgical risk in cirrhosis [11], it does not provide discrete post-operative mortality predictions, and again is not specific to cirrhosis surgical risk.

The model for end-stage liver disease (MELD) and Child-Turcotte-Pugh (CTP) scores are perhaps the most commonly applied risk scores in the field of chronic liver disease. With respect to surgical risk prognostication, however, the literature is divided as to the utility of the MELD and the CTP scores. MELD has been linearly associated with increased 30-day postoperative mortality [12], and several studies demonstrated its superiority over CTP in predicting surgical risk [13,14]. In contrast, several studies support the superiority of CTP scoring in predicting surgical mortality [8,15,16], however more recent literature has noted an overall weaker association between CTP class and postoperative mortality among a realistic cohort where few CTP Class C patients underwent surgery [17]. In the context of elective surgeries, a comparison between

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MELD and CTP scores showed no association with postoperative death or decompensation for either score [18]. Ultimately, the roles of MELD and CTP in surgical risk assessment are limited, especially as neither was designed to be a comprehensive cirrhosis surgical risk prediction tool. Furthermore, CTP suffers from subjectivity in assessment of ascites and hepatic encephalopathy, as well as a narrow score range which limits its ability for granular prediction.

To date, the Mayo risk score is the only tool designed to specifically estimate cirrhosis surgical risk, providing discrete post-operative mortality predictions at 7 days, 30 days, 90 days, 1 year, and 5 years [12]. This score was developed from a single-center cohort of major cardiovascular, orthopedic, and abdominal surgeries from 1980 to 2004. While the score marks an improvement over other options, it has several important limitations. First, given its single-center nature, the score may not reflect institution-specific practices that impact surgical risk. Second, major advances in the surgical field, including an increased adoption of endovascular and minimally invasive techniques, have changed the landscape of patient selection and associated surgical risk. Third, the score is inadequately calibrated. The sole external validation study for the Mayo score demonstrated good discrimination but significant overestimation of risk. Indeed, the actual 1-year post-operative mortality in this study was significantly lower than that predicted by the Mayo score (8.9% versus 22.6%, $p < 0.01$) [11]. Finally, and perhaps most importantly, the score does not account for procedure-specific risks. A recent study of the National Inpatient Sample database demonstrated that surgery type significantly impacts post-operative risk in patients with cirrhosis [19]. For example, major abdominal surgery had a ten-fold increased in-hospital mortality risk compared to major orthopedic surgery (odds ratio 8.27, 95% confidence interval 5.96–11.49). This highlights the primacy of surgery type in estimating post-operative risk.

The clinical consequences of inaccurate prediction and overestimation of surgical risk are significant. Patients with cirrhosis who might actually have acceptable surgical risk are likely being denied elective surgery. This compounds a risk-aversion phenomenon where elective procedures are deferred until a surgical indication becomes emergent. This is important, as both single-procedure [20,21] and multi-procedure [18] studies of patients with cirrhosis demonstrate uniformly higher mortality with emergent versus elective surgery. A common example of this scenario in patients with cirrhosis is the abdominal hernia, which often presents in the setting of ascites and elective operative management is rarely pursued. Instead, surgical intervention is typically reserved for a complication such as incarceration, a high-mortality scenario. A more accurate and better-calibrated risk prediction tool would therefore be expected to promote lower-risk elective surgeries and limit higher-mortality surgeries, thereby reducing post-operative mortality overall.

As suggested above, a clinically useful novel cirrhosis surgical risk score must overcome the limitations of the currently available prediction tools. To date, surgical risk stratification in cirrhosis has come from case reports and small series of isolated, disparate procedures such as infrarenal aortic aneurysms [22], subdural hematomas [23], head and neck flaps [24], and others [25–28]. Only a dataset that includes a diverse set of surgeries, sourced from a large, multi-center cohort will enable the development of an accurate surgical risk score that incorporates surgical procedure type. Furthermore, these data must post-date the Mayo score in order to reflect modern surgical advances that have occurred in the ensuing 15 years. This includes endovascular techniques [29,30] that have revolutionized cardiothoracic surgery, which historically carried the highest mortality rates in patients with cirrhosis [31]. Derivation and validation of an updated, generalizable, and accurate cirrhosis surgical risk calculator will enable physicians and surgeons to confidently weigh the risks and benefits of surgery

in this growing population, with the ultimate goal of minimizing both short- and long-term morbidity and mortality. Until that point, even the best efforts of providers may result in misguided management.

Abbreviations

ACS NSQIP	American College of Surgeons National Surgical Quality Improvement Program
ASA	American Society of Anesthesiologists
CTP	Child–Turcotte–Pugh
MELD	model for end-stage liver disease

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Conflicts of interest

The authors have no conflicts of interest to disclose.

References

- [1] Peery AF, Crockett SD, Murphy CC, Lund JL, Dellen ES, Williams JL, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the united states: update 2018. *Gastroenterology* 2019;156, <http://dx.doi.org/10.1053/j.gastro.2018.08.063>, 254–272.e11. [PMID: 30315778].
- [2] Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. *Clin Gastroenterol Hepatol* 2019, <http://dx.doi.org/10.1016/j.cgh.2019.07.060> [PMID: 31401364].
- [3] Kim D, Li AA, Perumpail BJ, Gadiparthi C, Kim W, Cholankeril G, et al. Changing trends in etiology-based and ethnicity-based annual mortality rates of cirrhosis and hepatocellular carcinoma in the united states. *Hepatology* 2019;69:1064–74, <http://dx.doi.org/10.1002/hep.30161> [PMID: 30014489].
- [4] Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the united states: a population-based study. *J Clin Gastroenterol* 2015;49:690–6, <http://dx.doi.org/10.1097/MCG.0000000000000208> [PMID: 25291348].
- [5] Friedman LS. The risk of surgery in patients with liver disease. *Hepatology* 1999;29:1617–23, <http://dx.doi.org/10.1002/hep.510290639> [PMID: 10347099].
- [6] Northup PG, Friedman LS, Kamath PS. AGA clinical practice update on surgical risk assessment and perioperative management in cirrhosis: expert review. *Clin Gastroenterol Hepatol* 2019;17:595–606, <http://dx.doi.org/10.1016/j.cgh.2018.09.043> [PMID: 30273751].
- [7] Farnsworth N, Fagan SP, Berger DH, Awad SS. Child–Turcotte–Pugh versus MELD score as a predictor of outcome after elective and emergent surgery in cirrhotic patients. *Am J Surg* 2004;188:580–3, <http://dx.doi.org/10.1016/j.amjsurg.2004.07.034> [PMID: 15546574].
- [8] Ziser A, Plevak DJ, Wiesner RH, Rakela J, Offord KP, Brown DL. Morbidity and mortality in cirrhotic patients undergoing anesthesia and surgery. *Anesthesiology* 1999;90:42–53, <http://dx.doi.org/10.1097/00000542-199901000-00008> [PMID: 9915311].
- [9] Biliomaria KY, Liu Y, Paruch JL, Zhou L, Kmiecik TE, Ko CY, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. *J Am Coll Surg* 2013;217, <http://dx.doi.org/10.1016/j.jamcollsurg.2013.07.385>, 833–842.e1. [PMID: 24055383].
- [10] Zaydfudim VM, Kerwin MJ, Turrentine FE, Bauer TW, Adams RB, Stukenborg GJ. The impact of chronic liver disease on the risk assessment of ACS NSQIP morbidity and mortality after hepatic resection. *Surgery* 2016;159:1308–15, <http://dx.doi.org/10.1016/j.surg.2015.11.020> [PMID: 26747226].
- [11] Kim SY, Yim HJ, Park SM, Kim JH, Jung SW, Kim JH, et al. Validation of a Mayo post-operative mortality risk prediction model in Korean cirrhotic patients. *Liver Int* 2011;31:222–8, <http://dx.doi.org/10.1111/j.1478-3231.2010.02419.x> [PMID: 21134111].
- [12] Teh SH, Nagorney DM, Stevens SR, Offord KP, Therneau TM, Plevak DJ, et al. Risk factors for mortality after surgery in patients with cirrhosis. *Gastroenterology* 2007;132:1261–9, <http://dx.doi.org/10.1053/j.gastro.2007.01.040> [PMID: 17408652].
- [13] Befeler AS, Palmer DE, Hoffman M, Longo W, Solomon H, Di Bisceglie AM. The safety of intra-abdominal surgery in patients with cirrhosis: model for end-stage liver disease score is superior to Child–Turcotte–Pugh classification in predicting outcome. *Arch Surg* 2005;140:650–4, <http://dx.doi.org/10.1001/archsurg.140.7.650>, discussion 655 [PMID: 16027329].
- [14] Delis S, Bakoyannis A, Madariaga J, Bramis J, Tassopoulos N, Dervenis C. Laparoscopic cholecystectomy in cirrhotic patients: the value of MELD score and Child–Pugh classification in predicting outcome. *Surg Endosc* 2010;24:407–12, <http://dx.doi.org/10.1007/s00464-009-0588-y> [PMID: 19551433].

- [15] Neeff H, Mariaskin D, Spangenberg H-C, Hopt UT, Makowiec F. Perioperative mortality after non-hepatic general surgery in patients with liver cirrhosis: an analysis of 138 operations in the 2000s using Child and MELD scores. *J Gastrointest Surg* 2011;15:1–11, <http://dx.doi.org/10.1007/s11605-010-1366-9> [PMID: 21061184].
- [16] Peng Y, Qi X, Guo X. Child-Pugh versus MELD score for the assessment of prognosis in liver cirrhosis: a systematic review and meta-analysis of observational studies. *Medicine* 2016;95:e2877, <http://dx.doi.org/10.1097/MD.0000000000002877> [PMID: 26937922].
- [17] Telem DA, Schiano T, Goldstone R, Han DK, Buch KE, Chin EH, et al. Factors that predict outcome of abdominal operations in patients with advanced cirrhosis. *Clin Gastroenterol Hepatol* 2010;8:451–7, <http://dx.doi.org/10.1016/j.cgh.2009.12.015>, quiz e58 [PMID: 20036761].
- [18] Hoteit M-A, Ghazale A-H, Bain A-J, Rosenberg E-S, Easley K-A, Anania F-A, et al. Model for end-stage liver disease score versus Child score in predicting the outcome of surgical procedures in patients with cirrhosis. *World J Gastroenterol* 2008;14:1774–80, <http://dx.doi.org/10.3748/wjg.14.1774> [PMID: 18350609].
- [19] Mahmud N, Fricker Z, Serper M, Kaplan DE, Rothstein KD, Goldberg DS. In-Hospital mortality varies by procedure type among cirrhosis surgery admissions. *Liver Int* 2019;39:1394–9, <http://dx.doi.org/10.1111/liv.14156> [PMID: 31141306].
- [20] Choi SB, Hong KD, Lee JS, Han HJ, Kim WB, Song TJ, et al. Management of umbilical hernia complicated with liver cirrhosis: an advocate of early and elective herniorrhaphy. *Dig Liver Dis* 2011;43:991–5, <http://dx.doi.org/10.1016/j.dld.2011.07.015> [PMID: 21872542].
- [21] Gray SH, Vick CC, Graham LA, Finan KR, Neumayer LA, Hawn MT. Umbilical herniorrhaphy in cirrhosis: improved outcomes with elective repair. *J Gastrointest Surg* 2008;12:675–81, <http://dx.doi.org/10.1007/s11605-008-0496-9> [PMID: 18270782].
- [22] Marrocco-Trischitta MM, Kahlberg A, Astore D, Tshionbo G, Mascia D, Chiesa R. Outcome in cirrhotic patients after elective surgical repair of infrarenal aortic aneurysm. *J Vasc Surg* 2011;53:906–11, <http://dx.doi.org/10.1016/j.jvs.2010.10.095> [PMID: 21215574].
- [23] Chen C-C, Chen S-W, Tu P-H, Huang Y-C, Liu Z-H, Yi-Chou Wang A, et al. Outcomes of chronic subdural hematoma in patients with liver cirrhosis. *J Neurosurg* 2018;130:302–11, <http://dx.doi.org/10.3171/2017.8.JNS171103> [PMID: 29393757].
- [24] Kao H-K, Chang K-P, Ching W-C, Tsao C-K, Cheng M-H, Wei F-C. The impacts of liver cirrhosis on head and neck cancer patients undergoing microsurgical free tissue transfer: an evaluation of flap outcome and flap-related complications. *Oral Oncol* 2009;45:1058–62, <http://dx.doi.org/10.1016/j.oraloncology.2009.07.010> [PMID: 19726221].
- [25] Perkins L, Jeffries M, Patel T. Utility of preoperative scores for predicting morbidity after cholecystectomy in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2004;2:1123–8, [http://dx.doi.org/10.1016/S1542-3565\(04\)00547-6](http://dx.doi.org/10.1016/S1542-3565(04)00547-6) [PMID: 15625658].
- [26] El Nakeeb A, Sultan AM, Salah T, El Hemaly M, Hamdy E, Salem A, et al. Impact of cirrhosis on surgical outcome after pancreaticoduodenectomy. *World J Gastroenterol* 2013;19:7129–37, <http://dx.doi.org/10.3748/wjg.v19.i41.7129> [PMID: 24222957].
- [27] Lopez-Delgado JC, Ballus J, Esteve F, Betancur-Zambrano NL, Corral-Velez V, Mañez R, et al. Outcomes of abdominal surgery in patients with liver cirrhosis. *World J Gastroenterol* 2016;22:2657–67, <http://dx.doi.org/10.3748/wjg.v22.i9.2657> [PMID: 26973406].
- [28] Hayashida N, Shoujiama T, Teshima H, Yokokura Y, Takagi K, Tomoeda H, et al. Clinical outcome after cardiac operations in patients with cirrhosis. *Ann Thorac Surg* 2004;77:500–5, <http://dx.doi.org/10.1016/j.athoracsur.2003.06.021> [PMID: 14759426].
- [29] Murashita T, Matsuda H, Domae K, Iba Y, Tanaka H, Sasaki H, et al. Less invasive surgical treatment for aortic arch aneurysms in high-risk patients: a comparative study of hybrid thoracic endovascular aortic repair and conventional total arch replacement. *J Thorac Cardiovasc Surg* 2012;143:1007–13, <http://dx.doi.org/10.1016/j.jtcvs.2011.06.024> [PMID: 21783209].
- [30] Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet* 2015;385:2477–84, [http://dx.doi.org/10.1016/S0140-6736\(15\)60308-7](http://dx.doi.org/10.1016/S0140-6736(15)60308-7) [PMID: 25788234].
- [31] Suman A, Barnes DS, Zein NN, Levinthal GN, Connor JT, Carey WD. Predicting outcome after cardiac surgery in patients with cirrhosis: a comparison of Child-Pugh and MELD scores. *Clin Gastroenterol Hepatol* 2004;2:719–23 [PMID: 15290666].