Is MELD the best prognostic score in acute variceal bleeding? The jury is still out

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Title: A MELD-based model to determine risk of mortality among patients with acute variceal bleeding

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Summary

Variceal bleeding as a complication of portal hypertension carries significant morbidity and mortality, despite improvement in the therapeutic approaches available [1,2]. Risk stratification for mortality and early re-bleeding is important for the delivery of effective therapy in a timely manner [1].

Several risk factors for acute variceal bleeding (AVB) have been identified as poor prognostic factors, namely: hepatic encephalopathy, Child-Pugh class, model for end-stage liver disease (MELD) score, shock, renal failure, infection, hepatocellular carcinoma, active bleeding at the time of endoscopy, presence of portal vein thrombosis and hepatic venous pressure gradient (HVPG) >20 mmHg [3].

These factors have been combined in prognostic models that are used for risk stratification. The Augustin [4] and D'Amico [5] models were specifically developed to predict survival in AVB but are seldom used because of lack of external validation. The MELD score is fairly consistent in predicting 3-month survival in patients with cirrhosis and is used to prioritize organ allocation in patients waiting for liver transplantation [6]. Some studies have shown that MELD is a clinically useful model in predicting prognosis in AVB [7,8].

Risk stratification is important for treatment decisions. A recent study showed that emergency transjugular intrahepatic portosystemic shunt (TIPS) in individuals with HVPG >20 mmHg improved survival and reduced re-bleeding [9]. The feasibility of obtaining HVPG measurements in a clinical setting is however limited to tertiary centers. Following that study, Garcia Pagan *et al* showed that early TIPS

is associated with improved survival in patients with Child Pugh B and active bleeding at endoscopy or Child Pugh C [10]. A drawback with the Child-Pugh classification is a subjective variability in the assessment of ascites and encephalopathy [3]. In fact, a recent trial has shown that both the Child-Pugh classification and active bleeding at endoscopy were assessed inconsistently [11].

The current study assessed and compared the performance of the D'Amico and Augustin models, MELD and Child-Pugh to predict 6-week mortality in patients with AVB, both in terms of discrimination and calibration [3]. Discrimination relates to a model's capacity to rank patients in order of their risk of getting an outcome and therefore predicts how frequently a patient with a higher score will get the outcome compared to a patient with a lower score. Calibration looks at the agreement between a predictive model's expected and observed outcome and allows a judgment on which model is more accurate at predicting the outcome for a given individual. The authors prospectively studied 178 patients with variceal bleeding over a 3-year period and reported an overall 6-week mortality of 16%. MELD had the best discrimination for mortality with an AUROC of 0.79, although this was not statistically significant compared to the other models assessed [3]. The discriminatory ability was similar to previous studies by Bambha and Cerqueira, which both found an AUROC of 0.76 [7,8], and is somewhat suboptimal. As there was a significant mis-calibration, the authors re-calibrated MELD and validated this in 2 external series of patients with AVB. They also calculated a predicted mortality for each MELD value according to the updated MELD-based model [3]. A MELD score of 11 was associated with a 5% risk of mortality and a MELD score of 19 was associated with a 20% mortality rate.

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Conflict of Interest: None

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Opinion

Although important, this study did not conclusively address the need for accurate prognostication in AVB. This could be due to shortcomings in design or to inherent limitations of MELD as a predictive score in this setting.

The MELD-based model was not consistent and indeed over-predicted mortality for high MELD values in one of the validation sets. All of the patients in that cohort received antibiotics compared to 71% of the second validation cohort, while such information was not available for the derivation cohort [3]. Given the well-documented association of infection and bleeding and the effects of antibiotics on outcome, these improved outcomes could have resulted from the universal use of antibiotics [12]. Therefore, the suboptimal management of AVB puts into question the whole model re-calibration.

Moreover, potential factors that could be added to MELD and increase the predictive ability of the model, such as the patient's hemodynamic status or active bleeding at endoscopy, were not taken into account or analysed. A study by Bambha *et al* demonstrated that endoscopic evidence of active bleeding had a 10-fold greater risk of mortality within 6 weeks in patients with a MELD score >18, compared to patients with a MELD <18 who had no active bleeding at endoscopy [7]. The current study also didn't take into account blood transfusion requirements, which was found significant at cut-offs of 2 [8] and 4 units [7] in other studies. It should also be noted that in the current study 72/178 patients had a prior variceal bleeding. The authors made no mention of when the prior bleeding occurred compared to the incident bleeding. If this group is actually at greater risk of bleeding, then one could argue that the MELD score would not capture this.

An important consideration in all studies assessing MELD or Child-Pugh scores in patients with AVB is that such scores potentially increase in the acute setting due to factors such as underlying infection and hypovolemia and therefore might significantly differ from the baseline scores. For instance, adequate fluid resuscitation might improve creatinine and therefore the MELD score. Likewise, sepsis and the acute decompensating event would increase the bilirubin and INR. The re-calibrated MELD score in the current study did not show improved discrimination compared to other studies, and had a borderline AUROC of 0.79. Risk stratification and clinical trials in high-risk patients require better discrimination for valid conclusions on efficacy. This begs the question of whether the re-calculation of MELD at 48 h after admission, after initial endoscopy, antibiotics and adequate resuscitation would be a better predictor of mortality.

Therefore, further studies are needed to better stratify and identify high-risk patients with AVB that would benefit from additional interventions. Although the re-calibrated MELD is promising, it is still far from ideal in discriminating patients who are at high risk of dying.

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