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Reply to Risk Stratification in Acute Variceal Bleeding: Child-Pugh vs MELD

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We appreciate the interest and discussion provided by Dr Reverter and colleagues regarding our multicenter U.S. prospective cohort of patients with cirrhosis presenting with acute variceal hemorrhage¹. We agree that improved prognostication in variceal hemorrhage is essential in order to properly stratify and manage these patients both in clinical practice and in clinical research.

While our primary intent was to report on relevant clinical outcomes using a contemporary, prospective cohort of U.S. patients with acute variceal hemorrhage who received standard of care, we also aimed to investigate the accuracy of known prognostic models, Child-Turcotte-Pugh (CTP) and MELD, in predicting 6-week mortality and we were particularly interested in validating the recently published MELD model that had been ‘recalibrated’ specifically for variceal hemorrhage by Reverter and colleagues².

Even though our cohort is relatively small, our survival discrimination for MELD and CTP scores, as pointed out by Reverter et al, were almost identical (AUC 0.79 and 0.75, respectively¹) to those reported in their study (AUC 0.79 and 0.74, respectively²).

We recognize that comparing our CTP model (internally validated) and Reverter’s recalibrated MELD model is not fair and that our model requires external validation. However, we were unable to validate the recalibrated MELD model even after further analysis of our data using quintiles as suggested by Reverter et al, that is, the recalibrated MELD still had a significant disagreement between observed and predicted mortality ($p=0.017$ per Hosmer-Lemeshow Goodness-of-Fit test) (Figure). When analyzing the data using MELD score ranges, the data were reasonably aligned with Reverter’s predicted survival rates (0%, 21% and 45% for MELD scores <11, 11–19 and >19, respectively) but it is highly probable that their mortality rates for each CTP class would also be aligned with our suggested survival rates (CTP-A <10%, CTP-B 10–30%, CTP-C >33%).

Beyond statistical issues, the purported disadvantages of using subjective variables in the CTP score are probably exaggerated. Recently, these “subjective” variables could be

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successfully obtained retrospectively using a large administrative database that showed an excellent survival discrimination among the 3 different CTP classes and, in fact, showed a better prognostic value than MELD which only discriminated 1–5-year outcomes accurately in patients with a CTP score >11 ³. Not including decompensating events (mainly ascites) in a model, does not allow for proper stratification of patients into the two main prognostic stages of cirrhosis, compensated and decompensated. In fact, stages with ascites were the most important in predicting mortality in patients with MELD >15 but <20 who died on the transplant list⁴. Importantly, in the setting of variceal hemorrhage, co-authors of the letter-to-the-editor showed that MELD scores were not as useful as CTP class in identifying patients at risk for infection⁵, an important determinant of mortality.

Furthermore, while we agree that MELD score is more of an objective assessment than the CTP classification, it is still subject to misclassification and manipulation depending on laboratory variability or medication use^{6,7}.

Unlike the MELD score, CTP class provides an overall clinical assessment of the prognostic clinical stages of cirrhosis. The presence or not of other complications of cirrhosis (ascites, encephalopathy) has been deemed to be of major relevance in defining primary endpoints in patients after variceal hemorrhage⁸. Therefore, in conditions such as variceal hemorrhage that can occur in otherwise compensated or in decompensated patients, the clinical stage of cirrhosis should be considered in prognostic models.

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Figure.

Calibration plot for Reverter-MELD Model on 6-week Mortality. P-value determined by the Hosmer-Lemeshow Goodness-of-Fit test. The Reverter-MELD model had a significant disagreement between predicted and observed risk of death