Predictors of Mortality in the Critically Ill Cirrhotic Patient: Is the Model for End-Stage Liver Disease Enough?

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BACKGROUND: Critically ill cirrhotics require liver transplantation urgently, but are at high risk for perioperative mortality. The Model for End-stage Liver Disease (MELD) score, recently updated to incorporate serum sodium, estimates survival probability in patients with cirrhosis, but needs additional evaluation in the critically ill. The purpose of this study was to evaluate the predictive power of ICU admission MELD scores and identify clinical risk factors associated with increased mortality.

STUDY DESIGN: This was a retrospective review of cirrhotic patients admitted to the ICU between January 2011 and December 2014. Patients who were discharged or underwent transplantation (survivors) were compared with those who died (nonsurvivors). Demographic characteristics, admission MELD scores, and clinical risk factors were recorded. Multivariate regression was used to identify independent predictors of mortality, and measures of model performance were assessed to determine predictive accuracy.

RESULTS: Of 276 patients who met inclusion criteria, 153 were considered survivors and 123 were nonsurvivors. Survivor and nonsurvivor cohorts had similar demographic characteristics. Nonsurvivors had increased MELD, gastrointestinal bleeding, infection, mechanical ventilation, encephalopathy, vasopressors, dialysis, renal replacement therapy, requirement of blood products, and ICU length of stay. The MELD demonstrated low predictive power (c-statistic 0.73). Multivariate analysis identified MELD score (adjusted odds ratio [AOR] = 1.05), mechanical ventilation (AOR = 4.55), vasopressors (AOR = 3.87), and continuous renal replacement therapy (AOR = 2.43) as independent predictors of mortality, with stronger predictive accuracy (c-statistic 0.87).

CONCLUSIONS: The MELD demonstrated relatively poor predictive accuracy in critically ill patients with cirrhosis and might not be the best indicator for prognosis in the ICU population. Prognostic accuracy is significantly improved when variables indicating organ support (mechanical ventilation, vasopressors, and continuous renal replacement therapy) are included in the model. (J Am Coll Surg 2017; 224:276–282. © 2016 Published by Elsevier Inc. on behalf of the American College of Surgeons.)

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Patients with decompensated liver cirrhosis frequently require critical care management, accounting for approximately 26,000 ICU admissions each year in the US.[1] In the ICU, liver disease is often accompanied by sepsis and multiple organ dysfunction,[2] resulting in mortality rates between 43% and 87%.[3-7] Due to high resource use and high mortality,[1,8] accurate prognostic indicators for use in the ICU are important for guiding treatment decisions, talking with patients and families, and identifying patients who might benefit most from continued ICU care.

The Model for End-stage Liver Disease (MELD) is currently used to predict 90-day mortality in patients

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Abbreviations and Acronyms

AOR = adjusted odds ratio
CRRT = continuous renal replacement therapy
FFP = fresh frozen plasma
LOS = length of stay
MELD = Model for End-stage Liver Disease
MELD-Na = Model for End-stage Liver Disease including serum sodium
PRBC = packed RBC

with cirrhosis and provides an objective, continuous scale of liver disease severity. Although MELD was originally developed for patients undergoing a transjugular intrahepatic portosystemic shunt procedure, it has been examined as a prognostic indicator across a range of liver diseases and populations,[9-11] and is now the key factor in assigning priority for liver transplantation. The initial MELD score implemented in 2002 incorporated laboratory values of creatinine, bilirubin, and international normalized ratio for prothrombin time, but did not include any surrogate for portal hypertension. In 2016, the Organ Procurement and Transplantation Network updated the model to include serum sodium (MELD-Na), as several studies have found sodium to be an important predictor of survival among liver transplantation candidates.[12,13]

Although MELD and the new MELD-Na have high prognostic value in the cirrhotic population as a whole,[12,14] these models were not designed to predict survival in critically ill patients.[15] The use of MELD and MELD-Na as prognostic indicators in the ICU, where liver-specific complications are often compounded by extrahepatic organ dysfunction, needs additional investigation. The purpose of this study was to determine whether adding clinical factors indicative of organ dysfunction to MELD and to MELD-Na improves the predictive accuracy for survival of these models in a subset of patients whose severity of illness is significantly higher than that of traditionally studied cirrhotic populations.

METHODS

This is a single-center retrospective review of all adult patients (18 years of age and older) who were admitted to the ICU with a diagnosis of liver cirrhosis between January 1, 2011 and December 31, 2014. Demographic characteristics and clinical data, including age, sex, number of pretransplantation ICU admissions during the hospital stay, first ICU admission MELD and MELD-Na scores and incidence of gastrointestinal bleeding, infection, hepatic encephalopathy, ascites, mechanical ventilation requirement, vasopressor requirement, dialysis requirement, continuous renal replacement therapy (CRRT) requirement, and transfusion data (packed RBCs [PRBCs]), platelets, and fresh frozen plasma (FFP) during pretransplantation ICU stays were collected via chart review.

The MELD and MELD-Na scores were calculated according to current Organ Procurement and Transplantation Network guidelines.[16] The MELD was calculated using the following equation:

$$9.57 \times \ln(\text{creatinine mg/dL}) + 3.78 \times \ln(\text{bilirubin mg/dL}) + 11.2 \times \ln(\text{international normalized ratio}) + 6.43,$$

rounded to the nearest tenth decimal place and multiplied by 10. When calculating MELD, laboratory values <1.0 were set to 1.0 and creatinine values were adjusted for dialysis with a limit of 4.0 mg/dL. For patients with a MELD score >11, MELD-Na was calculated using the following equation:

$$\text{MELD-Na} = \text{MELD} + 1.32 \times (137 - \text{sodium mmol/L}) - [0.033 \times \text{MELD} \times (137 - \text{sodium mmol/L})].$$

Sodium values <125 mmol/L were set to 125 and sodium values >137 mmol/L were set to 137, per Organ Procurement and Transplantation Network policy. An upper limit of 40 was not applied for MELD and MELD-Na scores.

If MELD and MELD-Na scores were not available on the date of admission, the earliest available scores within 7 days of admission were used for analysis. When more than one laboratory result for the same test was recorded within a 24-hour period, the earliest test value was used in MELD and MELD-Na calculations. Gastrointestinal bleeding was demonstrated on esophagogastroduodenoscopy or noted on the medical record during the ICU stay. Infection was defined by any positive culture, including blood, sputum, urine, and paracentesis fluid cultures. Hepatic encephalopathy and ascites were defined by a noted diagnosis on the medical record. Vasopressor requirement was defined by any vasopressor (norepinephrine, epinephrine, vasopressin, dobutamine, dopamine, and ephedrine) or combination of vasopressors administered in the ICU. Outcomes included mortality, hospital length of stay (LOS), and total ICU LOS.

Patients were followed until transplantation, discharge, or death and were categorized by disposition status; patients who were discharged or underwent transplantation were considered survivors, and those who died or were discharged to hospice after withdrawal of care were