

Machine Learning for Mortality Prediction in Cirrhotic Sepsis: Moving Beyond MELD, SOFA, and CLIF-SOFA

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BACKGROUND AND AIMS

Sepsis in patients with cirrhosis carries an in-hospital mortality exceeding 40%, reflecting a pathophysiology distinct from sepsis in non-cirrhotic hosts. Cirrhosis-associated immune dysfunction, gut bacterial translocation, splanchnic vasodilatation, and impaired hepatic clearance together amplify septic organ failure.^{1,2} Despite this, prognostication continues to rely on scores developed for unrelated purposes: Model for End-Stage Liver Disease (MELD) and MELD-Na for transplant allocation,^{3,4} Sequential Organ Failure Assessment (SOFA) for general critical illness,⁵ and Chronic Liver Failure-SOFA (CLIF-SOFA) for acute-on-chronic liver failure.⁶ Each captures only part of the relevant biology. The authors therefore developed machine learning (ML) models that simultaneously integrate hepatic, renal, haemodynamic, and inflammatory variables, and benchmarked them against established scores.⁷

MATERIALS AND METHODS

Using the MIMIC-IV v3.1 database,⁸ the authors identified 1,612 adults (≥ 18 years) with cirrhosis and concurrent sepsis admitted to the ICU between 2008–2022, defined by validated International Classification of Diseases (ICD)-9/10 codes. Variables collected within the first 24 hours encompassed demographics, liver function tests, renal indices, sepsis markers (lactate, pH, white cell count, anion gap), haemodynamics, Glasgow Coma Scale (GCS), cirrhosis complications, and use of vasopressors or mechanical ventilation. Four algorithms such as logistic regression, random forest, XGBoost, and gradient boosting were trained on an 80/20 stratified split with five-fold cross-validation. Performance was assessed by area under the receiver operating characteristic curve (AUC), area under the precision-recall curve, and Brier score, with 1,000-iteration bootstrap 95% CIs.

RESULTS

In-hospital mortality was 45.7% (737/1,612), vasopressors were used in 48.4%, and mechanical ventilation in 46.1%. Random forest and logistic regression achieved the highest discrimination (AUC: 0.787; 95% CI: 0.740–0.834 and 0.737–0.832, respectively), outperforming CLIF-SOFA (0.710), SOFA (0.710), MELD (0.708), and MELD-Na (0.708) by an approximately 11% relative AUC gain. The random forest model yielded a sensitivity of 65.3%, a specificity of 77.8%, a positive predictive value of 71.1%, and a negative predictive value of 72.9%. The most influential predictors were maximum lactate, bilirubin, international normalised ratio, creatinine, and minimum pH, integrating sepsis-driven tissue hypoperfusion with hepatic synthetic and excretory failure.

DISCUSSION

The ceiling on prognostic performance in cirrhotic sepsis appears to be set not by the available data, but by the rigidity of legacy scoring systems. ML models capture non-linear interactions, for example, the disproportionate risk conferred by elevated lactate in patients already exhibiting coagulopathy that linear, equally-weighted scores cannot. The dominance of variables straddling both pathologies supports the concept that ICU mortality in this population is governed by the intersection, rather than the sum, of sepsis and hepatic failure.⁹ Translation to bedside use will require external validation in geographically and ethnically diverse cohorts, prospective recalibration, and integration into electronic health record workflows that preserve clinician interpretability.

CONCLUSION

Machine learning offers clinically meaningful gains over MELD-, SOFA- and CLIF-SOFA-based prognostication in patients with cirrhosis with sepsis. A cirrhosis-specific, sepsis-aware ML risk tool, once externally validated, could refine triage, resource allocation and goals-of-care discussions in this high-mortality population.

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