Improving Outcomes in Critical Care of Patients With Cirrhosis and Organ Failure: Herding Runaway Horses and Securing the Barn Door

Chronic liver disease is a leading cause of death in Western countries, and represents the 12th most common cause of death in the United States. The increasing burden of chronic liver disease is mirrored by the increased utilization of health care resources for the hospital care of patients with cirrhosis. There is a pressing need to reduce morbidity and mortality in patients with cirrhosis that is borne out of the clinical duty toward individual patients and shaped by the constraints of finite health care resources.

Once decompensated, cirrhosis is associated with high rates of hospitalization, length of stay, cost, mortality, and early re-admissions. Patients frequently present with variceal bleeding, hepatic encephalopathy, or acute kidney injury, and are at increased risk of infection, which predisposes them to the development of organ failure, increased cost of care, and worse outcomes. In the largest Western intensive care unit (ICU) series, cirrhosis is associated with 30-day or in-hospital mortality rates that range from 48% to 87%, and outcomes worsen with increasing numbers of failing organs. It is for those reasons that providing critical care to patients with decompensated cirrhosis epitomizes this contrast of costs and outcomes, and challenges health care providers and systems to reconcile these by optimizing care.

This underscores the need for confident risk stratification of at least short-term outcomes in this population. Published clinical studies in this field have been largely descriptive, with modeling of mortality risk being the common focus. The models most frequently studied can be categorized as follows: liver disease–specific models (model for end-stage liver disease [MELD] and Child–Pugh classification), general ICU score such as the Acute Physiology and Chronic Health Evaluation (APACHE), and organ failure scores (most commonly the sequential organ failure assessment [SOFA], and chronic liver failure-SOFA [CLIF-SOFA]). All of these models have been shown to predict short-term mortality, with SOFA showing a slight advantage over MELD in some, but not all, studies. Comparisons of predictive performances of MELD and SOFA, as measured by the area under the receiver operator curve (AUROC) for hospital mortality, usually range from 0.75 to 0.86, but other end points have included ICU mortality, 1-month mortality, as well as 7-day and up to 1-year mortality. The variability in the performance of SOFA and MELD (typically <5% on AUROC), although seemingly limited, may speak to the heterogeneity among the published ICU-cirrhosis cohorts. Sources of heterogeneity include geographic differences that dictate health systems and economic resources on-hand, liver disease etiology, access to liver transplantation, ICU referral patterns (patients failing aggressive tertiary care vs limited pre-ICU care), and likely the willingness or ability of an ICU to accept or deny high risk transfers based on perceived utility or futility of ICU care. In addition, heterogeneity with respect to liver disease complications and infections clearly dictate outcomes, with second or late infections being associated with significantly higher hospital mortality rates. Ultimately, the common themes are that mortality risk relates to both severity of liver disease and the number of failing organs (SOFA/CLIF-SOFA), with notable overlap of common determinants (bilirubin, international normalized ratio, renal function, hepatic encephalopathy).

The impact of specific ICU management protocols in patients with cirrhosis rarely are described, but a number of recent reviews summarized best practices, and suggested some evidence base to guide intensivists and hepatologists. One therefore may expect to see improvements in outcomes over time, although such trends are difficult to discern when comparing center with center outcomes in differing eras. Longitudinal data best address this question and 2 studies spanning 1995 to 2008 and 1998 to 2012, from the United Kingdom, described incremental improvement in ICU survival rates for patients with cirrhosis admitted after 1996, 2004, and 2008. The study by McPhail et al in this month’s issue of Clinical Gastroenterology and Hepatology adds to this evidence from another large center in the United Kingdom. This decade-long study, spanning 2000 to 2010, described outcomes of a dedicated liver ICU at Kings College Hospital, with the experience of a renowned high-volume liver transplant center. It represents a large study and offers a unique vantage point to assess trends in liver disease etiology and severity, and indications and outcomes for ICU admission in patients with cirrhosis. Survival to hospital discharge improved incrementally after 2003 and 2007. The improved survival rate in patients admitted with gastrointestinal hemorrhage (after 2003 only, Supplementary Figure 3) was not surprising. Advances in the medical, endoscopic, and interventional radiology management of variceal bleeding have had a positive impact on outcomes of ICU care for that indication as previously described by the study center and others. Importantly, however, this study described improved survival for other intensive care indications over the 3 time periods (2000–2003, 2004–2007, and 2008–2010).

Although this good news is most welcome, the investigators noted some important caveats. First, improved survival could not be attributed to any specific
ICU measures, limiting systematic impact on other ICU practices. Second, disease severity as assessed by APACHE II scores decreased over time, as did MELD scores (although this was attributed solely to less renal dysfunction). On this point, the investigators attributed improved survival to a policy of early and aggressive ICU care, when interventions may be more effective in reversing the acute disease process, as suggested by others. As encouraging as that is, one cannot objectively assess an ICU’s receptiveness to admissions without clearly defined admission criteria and data on patients denied admission for any perceived futility. These admittedly are difficult data to collect, however, the potential for selection bias to contribute to trends of improved survival with lower disease severity cannot be summarily ruled out. Despite these concerns, McPhail et al described improved hospital survival even in patients admitted with high APACHE II scores (>20), and in patients with 3 organ failures by SOFA/CLIF-SOFA, an undoubtedly severely ill group.

The mortality rates in recent years in the United Kingdom, per this study and others with median admission MELD scores of 26 to 29, differ from recent (2005–2010) US data. The latter described 30-day mortality rates (which approximated hospital mortality) at 2 high-volume transplant centers that ranged from 54% to 87%, with a median ICU admission MELD score of 30 to 33, and greater risk noted in patients with renal or respiratory failure. The willingness to admit a high-risk cirrhotic patient to the ICU is likely to be influenced by multiple factors, including listing for liver transplantation or the potential for it. Higher liver transplantation rates in the United States at higher MELD scores, and possibly the molding of referral patterns by economic and medicolegal factors, may result in Transatlantic differences in ICU admission criteria, disease severity, and outcomes. Therefore, comparisons and applicability of data on outcomes may be limited by geographic and health system factors, even in Western countries.

With respect to model performance for the prediction of hospital mortality, CLIF-SOFA performed marginally better than SOFA, but both scores performed well on ICU admission and during the subsequent week. How SOFA or CLIF-SOFA perform compared with MELD may be influenced by patient mix, given that better performance of MELD compared with SOFA was reported previously by the same center in patients with variceal bleeding. Perhaps more importantly though is how such predictive models may be put to practical use. Futility of ICU care is undefined in this population, and prediction of early time point–defined mortality, such as 1-week mortality, is limited by lower AUROC. The low sensitivity and wide 95% confidence intervals of the positive predictive values, even at thresholds with high specificity, suggest that even in this large study, futility would be difficult to define on a case-by-case basis. Improvement in SOFA over the first 3 days in the ICU was a favorable indicator, and makes the case for a 3-day trial of aggressive care for critically ill cirrhotic patients. That said, the poor outcomes in patients with 4 or more organ failures are conveyed with a note of warning. Although these data may be useful for counseling patients and families within the study centers themselves, broader application would be facilitated by multicenter validation with defined admission criteria and management protocols.

In summary, this was a large, single-center study on ICU outcomes in patients with cirrhosis, describing improving outcomes in recent years across the spectrum of liver disease severity and indication for ICU admission (gastrointestinal bleeding vs other). That outcomes could be optimized for this population in an experienced high-volume transplant center is cause for some optimism. Frequently, critical illness in patients with cirrhosis is pessimistically perceived as the horse has already left the barn. This study suggests that with the right expertise and application of resources, some runaway horses can be herded back, and that with early aggressive care the barn door can be better secured.

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References


Conflicts of interest
The authors disclose no conflicts.

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