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EDITORIAL

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Is LiFe worth living? It all depends on the liver

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The title is derived from a bon mot by the American philosopher William James (1842—1910).

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Regardless of the initial cause, critical illness almost invariably involves serious derangement of function across multiple organs and body systems. While much attention has rightly been directed towards the development of predictive models which seek to measure illness severity and forecast outcome in severe multiple organ failure [1], severe respiratory failure [2] and renal injury [3], less work has been undertaken to elucidate the specific impact of acute hepatic dysfunction in the context of chronic liver disease—despite recognition that liver injury in critically ill patients is associated with poor outcome [4]. The complex care needs and high mortality of patients with severe acute liver failure is well-described [5], and approaches for predicting outcomes for patients with chronic liver disease [6], decompensated cirrhosis [7] and cirrhotic patients in the intensive care unit (ICU) [8] are established. Regardless of these advances, however, the importance of evolving hepatic dysfunction as part of an overall non-liver specific critical illness may still be underappreciated [9], even in patients with known chronic liver problems. In their work to develop a laboratory-based liver injury failure evaluation (LiFe) score, Edmark et al. [10] outline an interesting approach to the development, validation and potential application of a simple tool that may assist intensivists in the evaluation and management of patients with known chronic liver disease admitted to the ICU.

In developing the LiFe score, Edmark and colleagues first conducted an online survey of European Society of Intensive Care Medicine members and received over 150 responses, mainly from European clinicians. Over one-third of respondents indicated that they worked in academic centers with specific hepatobiliary expertise. From the survey results, the three most highly ranked markers of liver injury were identified: the international normalised ratio (INR), total bilirubin and arterial lactate—considered to be representative of liver synthetic capacity, excretory function and metabolic properties, respectively. A research registry holding records from two large academic medical centres in Boston was then accessed to obtain de-identified records of patients admitted to the ICU during an 18-year period ending in 2007. Over 90,000 records were evaluated, of which more than 85,000 were excluded from the analysis because the patients did not have chronic liver disease and more than 6000 were excluded because laboratory test results for the three aforementioned parameters were not available. The Boston-based derivation cohort was therefore ultimately based on 945 patients. Records from a major liver transplant centre in London were then accessed to obtain the validation cohort of 971 patients. A clinical prediction tool was then created using a logistic regression model describing the risk of 30-day mortality as a function of lactate, INR and total bilirubin data collected from the derivation cohort at admission to ICU. Further statistical refinement and validation of the model was then undertaken prior to the application of the resulting model to the validation cohort.

Derivation cohort patients were mainly white, mainly medical and mainly older, and half were male. Nearly one-third of all patients died in hospital, and 43 % had sepsis. Patients were classified as low, intermediate, high and very high risk according to their LiFe score distribution, which ranged from 0 to >8. Patients in the validation cohort were also mainly male, but slightly younger and over one-half died in hospital. Outcomes in the validation cohort were similar to those predicted by the LiFe score, with good calibration and moderate discrimination for hospital mortality across each of the four defined categories. The LiFe score had a similar predictive value as the APACHE II and SAPS II scores in the validation cohort, but was somewhat more discriminating than the SOFA and CLIF-SOFA scores.

The LiFe score has several strengths. It is derived from a reasonably large cohort of patients and has undergone validation in a separate cohort from a distant jurisdiction. It utilises commonly collected laboratory values and as such is quite easy to apply in bed-side clinical practice. It also performs moderately well in terms of meaningful outcome predictions, approaching the capability of more complex physiologically based scoring systems in this regard. There are, however, a range of important limitations to the approach undertaken in developing the LiFe score and its subsequent application. First, the method for identifying the three laboratory parameters on which the model is based is somewhat informal and novel in nature and may be influenced by a range of factors that are difficult to identify or predict. Second, in only a small proportion of the original cohort of ICU admissions were data available on all of the three variables collected at admission to ICU, resulting in the inclusion of only this small proportion in the study and thereby introducing a considerable potential for bias. Third, the values measured are more likely to be abnormal (and therefore more likely to be measured by treating clinicians) in the more severely ill and, as a result, the cohort may have a disproportionate number of patients with more extreme critical illness, such as severe sepsis. Finally, the INR [11], total bilirubin concentration [12] and lactate [13] levels are not specific to liver injury and are often elevated by a range of process which have little or no direct or specific impact on the liver. In critical illness these parameters reflect general organ dysfunction and illness severity markers rather than liver-specific measures [14]. Even for patients for whom liver dysfunction is a primary driver of critical illness, outcomes vary markedly between acute on chronic liver failure and decompensated chronic liver disease patients. Perhaps it is unrealistic to expect that any simple scoring system based only on a small number of laboratory parameters could reliably predict outcomes across the heterogenous group of patients with known chronic liver disease who become critically ill.

Edmark et al. [10] have provided useful insights into the potential for a relatively simple scoring system using routinely measured laboratory parameters to predict mortality outcomes in critically ill patients with chronic liver disease. The use of web-based survey polling clinicians for their views on useful parameters to measure is an interesting approach that might be increasingly useful to rapidly access the collective clinical wisdom across a broad cross-section of experts [15]. While the LiFe score is less powerful than the SOFA and CLIF-SOFA scores, the use of routinely collected pathology test results confers several advantages, including ease of use and the ready application to large intensive care datasets. The development of such predictive tools based on parameters routinely collected and available for complex, yet automated analysis may prove to be very powerful. This approach may have increasing utility as integrated clinical decision support technologies become commonplace to assist clinicians at the bedside [16]. The challenges for future research in this domain include the identification of appropriate parameters to measure, the ability to generalise applicability beyond the study cohort and the practical implementation into clinical practice in a manner that meaningfully impacts on patient care and improves outcomes.

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