Predictors of Outcome in Decompensated Liver Disease: Validation of the SOFA-L Score

Abstract:
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A growing number of patients with liver disease are being referred for critical care support. We have recently shown that a combination of lactate and SOFA score (SOFA-L score) may provide an accurate, objective measurement of prognosis in a group of patients admitted to ICU with alcoholic liver disease. This score has not been validated in an independent patient cohort. A retrospective study was performed where patients admitted to our ICU with decompensated liver disease (any cause) were included. The SOFA-L score accurately predicted in-hospital mortality in this group of patients. Furthermore, a SOFA-L score >12 at any time point during ICU admission correlated with a mortality rate greater than 80%. Given the highly accurate predictive ability of this score we investigated its ability to predict mortality in an independent cohort of patients with a high mortality.

Introduction
The outcome of patients with liver cirrhosis who are admitted to an Intensive Care Unit is generally poor, with prognostic tools developed for this population. Predictors that best underlines the need for appropriate triage of patients. Both liver specific and acute physiological scoring systems can assist in predicting prognosis and thus aid in decisions regarding triage and treatment limitations. Liver specific scoring systems used commonly in clinical practice in this cohort of patients include the Child Pugh score, the Model for End Stage Liver Disease (MELD) score and the MELD-Na score (MELD score with inclusion of sodium). Acute physiological scoring systems commonly used in the ICU cohort include the Acute Physiology and Chronic Health Evaluation (APACHE) score and Sequential Organ Failure Assessment (SOFA) score. It is unclear which scoring system best predicts outcome in this cohort of patients. Das et al showed that the SOFA scores on day 1 of ICU admission (excluding points for haematological failure) was the score that best predicted in-hospital mortality in a cohort of patients with liver cirrhosis. However the validation group used in this study comprised all-comers with cirrhotic liver disease. Previous evidence suggested that mortality rate and predictors of death may be different for patients with alcoholic liver disease admitted to ICU than in a heterogeneous group of all cause liver failure, due to the main to a younger mean age and increased prevalence of alcohol abuse. We postulate that by adapting the commonly used physiological and laboratory parameters that would provide an optimal outcome prediction model in this group of patients. We found that a combination of lactate and SOFA score, measured on day of admission may provide an accurate, objective measurement of prognosis. This model had an area under the receiver operating characteristic curve of 0.93 on day 1, with 88.7% of predictions correct. Moreover, a SOFA-L score >12 at any time point during ICU admission correlated with a mortality rate greater than 80%. Given the highly accurate predictive ability of this score we investigated its ability to predict mortality in an independent cohort of patients admitted to ICU with all-cause liver disease.

Methods
This retrospective observational study was carried out in the Intensive Care Unit of St Vincents University Hospital. St Vincents is the National Liver Transplant Centre and a tertiary referral centre for patients with liver cirrhosis. Inclusion criteria for the study included admission to ICU with a diagnosis of decompensated cirrhosis, acute liver failure or GI bleed secondary to liver failure. Exclusion criteria included those patients on a liver transplant waiting list, or those with an elective post-operative indication for ICU admission. Patient data was collected retrospectively from July 2012 to June 2013. Demographic details, cause of liver disease, and relevant physiological and laboratory data were collected as well as number of organ failures and requirement for organ support. From this data MELD, MELD Na, SOFA and SOFA-L scores were calculated. In calculation of the scores, the poorest parameters during the first 24 hours of their admission were used. Patients with multiple admissions were categorised as new admissions when >72 hours elapsed between admissions. Outcomes recorded were survival to ICU discharge, hospital discharge or six months. Scores were correlated with mortality rates and predictors of death may be different for patients with alcoholic liver disease admitted to ICU than in a heterogeneous group of all cause liver failure, due to the main to a younger mean age and increased prevalence of alcohol abuse.

Results
Of the 690 patients who were admitted to ICU during the study period, 61 patients met inclusion criteria for the study. 30 of admissions were from the Medical ward, 26% from an outside hospital and 19% from the Emergency Department. Reasons for admission included gastrointestinal hemorrhage in the majority of cases, followed by hepatic encephalopathy, acute kidney injury, sepsis, respiratory failure and others unspecified. Causes for liver disease included alcoholic liver disease in 17 cases (28% cases), infective hepatitis in 19 cases (31% cases), paracetamol overdose in 5 cases (8% cases) with other causes accounting for 33%. Details of severity of illness are contained within table 2. Mean number of organ failures were 2.96 (Range 0-6). Values for the individual scoring systems are shown in Table 1. Predictive capacity of the model to predict mortality was assessed using receiver operating characteristic (ROC) curves. Predictive scores were compared using area under the receiver operating characteristic curves (AUROC). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) associated with a high probability of death (>75%) were determined from the ROC curves.

Discussion
Harmful use of alcohol is an increasing global health problem, responsible for half of all liver-related deaths in the developed world. An increasing demand is being placed on critical care services to treat these patients. Very limited and conflicting data are available on the outcome or predictors of prognosis in ICU-admitted ALO patients. Due to the paucity of available data relating to predicting outcome in this specific patient cohort, and its

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relevance to the Irish healthcare setting our group previously undertook a study to determine the optimal predictors of patient mortality in those presenting to critical care with alcohol related liver disease. We observed that the indication for hospitalization to ICU is not a predictor of patient mortality. In this cohort of patients who were less severely ill had a reasonable chance of survival. A combination of SOFA score and lactate (a score we dubbed the SOFA-L score) was a better predictor of outcome than any other general or liver-specific illness severity scores. Given the highly accurate predictive ability of this score we investigated its ability to predict mortality in an independent cohort of patients admitted to ICU with all-cause liver disease. Over a period of 1 year we reviewed all patients admitted to our Intensive Care Unit with decompensated liver disease. Of these patients, 72% had a non alcohol related cause of liver disease; a similar proportion to that in other studies. Patients with a non alcohol related cause of liver disease had a better prognosis than those with a liver cirrhosis. The study concluded that our group previously undertook a study to determine the optimal predictors of mortality among patients on the liver-transplant waiting list. N Engl J Med. 2008;359:1018-26.


11. Cholongitas E, Zenolo M, Patch D, Kwong K, Nikolopoulos V, Leandro G, Shaw S, Burroughs AK. Risk factors, sensitivity and specificity for the diagnosis of cirrhosis in patients with decompensated liver disease scored within the MELD and MELD Na. Moreover the SOFA-L score provided the optimal combination of sensitivity and specificity when compared to the other scores. A SOFA-L score of > 23 was 100% accurate in predicting mortality. These results compare favourably to our initial validation study in which the SOFA-L score was highly predictive of mortality at any time point with an area under the ROC curve for predicting in-hospital mortality of 0.93. A similar SOFA-L score (> 20) was predictive of in-hospital mortality in a validation data set. A dataset in which a scoring system is developed will tend to overestimate the predictive ability of any model developed within that group. However this independent dataset in a population of all-comers with decompensated liver cirrhosis demonstrates that our findings of a superior predictive ability of the SOFA-L score are corroborated in an independent dataset, increasing the potential usefulness in clinical practice.

An ideal predictive score needs high specificity, should be applicable at different time points, have a plausible clinical basis, and should be easy to apply at the bedside. The SOFA-L score satisfies these criteria and gives insights into the illness trajectory of critically unwell ALD patients. In our patient population, this score helped separate those patients with a reasonable medium-term survival (SOFA-L ≤21) from those with almost certain in hospital mortality (SOFA-L > 23). Those patients with SOFA-L scores between 12 and 23 inhabit a gray zone in which survival is increasingly unlikely; more information is needed about these patients, especially factors that might make them good candidates for secondary prophylaxis. This is the focus of our small study conducted in a single centre is the first step in validating the SOFA-L score in an independent cohort of patients. If it is further validated in a larger study over multiple centres, the SOFA-L score may have a role in triaging patients before ICU admission. Self-fulfilling prophecy, resulting from the use of the same parameters that will be subsequently tested for their predictive performance to make decisions on withdrawal of life-sustaining treatments, is a source of confounding common to many observational studies and may have influenced our results. However, we think it unlikely that a higher SOFA-L actually caused withdrawal of care in general, death and withdrawal of care followed a sustained period of worsening organ failure.