# Disease-specific scoring or generic scoring in ICU?

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Scoring systems are largely used in critically ill patients. Various scores have been developed over the last 30 years (1) to predict outcome at the early stage of ICU admission (within the first 24 hours), mainly in-hospital mortality but some are designed also to predict length of stay in ICU. Most of them use the disease severity rather independently of the primary reason for ICU admission, and are so called generic ICU scores, like Acute Physiology and Chronic Health Evaluation (APACHE I through IV), Simplified Acute Physiology Score (SAPS), or Mortality Probability Model (MPM) (2-7). Other scoring systems were developed for sequentially assessment of the severity of organ failure during the ICU stay like Multiple Organ Dysfunction Score (MODS), or Sequential Organ Failure Assessment (SOFA) (8-10). Though not designed for that purpose, these scores can be also used to predict mortality in various clinical conditions (1). All these scores are based on a large number of physiological and general health data, up to 129 items have to be collected, and computer-assisted calculation is often possible.

Scores specific of organ dysfunction, or disease-specific, exist as such like the Glasgow Coma Scale (GCS) for neurologic dysfunction, but are also included into the generic score. Indeed, APACHE, SAPS or SOFA scores include a GCS in the multiple parameters taken into account for the risk calculation (2,6,8). Other organ dysfunctions incorporated in generic scoring systems are defined by outstanding biomarkers like creatinine for renal failure, or bilirubin for liver dysfunction. However, authors have considered that bilirubin alone is not enough for adequately evaluating acute hepatic dysfunction in case of previous liver disease. Therefore, recently, several adaptations have been proposed to customize pre-existing generic scores for patients who experience acute-on-chronic liver failure, like SOFA-L or CLIF-SOFA scores (11-13).

In a recent issue of Intensive Care Medicine, Christin Edmark and coworkers went further and have proposed a new, very simple scoring system for this specific subset of ICU patients (14). The Life score is a disease-specific score, i.e., a liver-injury score, proposed to predict outcome in critically ill patients who were admitted in ICU for acute-on-chronic liver disease. The study population was extracted from a large cohort of patients admitted in ICU in two academic medical centers. From 92,886 patients admitted over 4 years, 7,048 were suffering from chronic liver disease (7.5%), out of which 945 were included in the derivation cohort to build the Life Score. Predictors included in the scoring system were determined by 157 experts working mainly in ICU (72%), most of them in Europe (76%). The experts were asked to select useful, practical and easy to obtain factors for discriminating between those with acute liver failure and those without. They retained three factors, bilirubin, INR and arterial lactate, which were then used in an univariate logistic regression to determine the association between in-hospital mortality and the predictors in the derivation cohort. A clinical prediction model was created as a function of the predictors, each being classified in four gravity levels at ICU admission (arterial lactate 0–1.9, C2.0–3.9, C4.0–5.9, C6.0 mg/dL; total bilirubin 0–1.9, C2.0–3.9, C4.0–5.9, C6.0 mg/dL; INR 0–1.9, C2.0–3.9, C4.0–5.9, C6.0). A risk score was then calculated for each patient, and the population was divided into four categories: patients at low risk, patients at intermediate risk, patients at high risk and patients at very high risk for death. The scoring system was tested afterwards in a validation cohort (n=971), and compared to other current scoring systems

APACHE II, SAPS II, SOFA and CLIF-SOFA.

The Life score showed good calibration and discrimination for in-hospital mortality in critically ill patients with chronic liver disease and approaches the performance of physiological-based scoring systems when using C-Statistic [C-Statistic was 0.771 (95% CI: 0.74–0.80) versus 0.799 (95% CI: 0.77–0.83) for SOFA, or 0.813 (95% CI: 0.79–0.84) for CLIF-SOFA, 0.768 (95% CI: 0.74–0.80) for APACHE II, and 0.781 (95% CI: 0.75–0.81) for SAPS II].

Therefore a simple risk scoring which includes only three biomarkers is as good as more sophisticated scores that include many other predictors, outside the liver function itself, such as cardiac, respiratory, renal and hematologic functions. These results clearly suggest first that acute-on-chronic liver failure patients are a specific subset of ICU patients, and second, the pivotal role of liver failure in critical care with life-threatening consequences on organs and function (15). Indeed, if liver dysfunction is not uncommon in ICU, especially during sepsis, liver failure incidence is less than 10% but no doubt it contributes to aggravate the prognosis (16).

The three markers retained by the experts, INR, total bilirubin, and lactate were considered as specific of liver function, reflecting the synthetic, excretory and metabolic properties, respectively. They are very close to the predictors used in the modern score to assess chronic liver disease (MELD score) which includes bilirubin, INR and creatinine (17).

Serum bilirubin concentration is a well established marker of the hepatic synthetic function, although it represents excretory function. Of the three MELD variables, serum total bilirubin is the most important. It has a linear relationship with 90-day mortality in patients waiting for liver transplantation (17). It is a strong prognosis predictor of short-term mortality in acute-on-chronic liver failure (18). Interestingly, the only generic score that does not include any biomarker of liver function, APACHE II, was the less performing test in Christin Edmark and coworkers' study (2). Conversely, bilirubin is part of SAPS and SOFA scoring systems, and improves the C-Statistic, which is higher than that of Life score.

INR is practically useful and correlates with mortality risk in patients with end-stage liver disease (17). However, INR has at least two major limitations: (I) interlaboratory variation in INR may approximate 25%; (II) INR was designed to standardize the anticoagulation effect of warfarin and not to evaluate the severity of liver disease. As a result, INR may not be valid to assess liver impairment (17). Yet, adding INR in the scoring system, instead of platelet count in the SOFA score, confers to the CLIF-SOFA score the highest C-Statistic, suggesting better prediction ability.

Contrary to the two previous biomarkers, lactate may not be considered as specific of liver failure. It is a biological signal of a general imbalance between oxygen delivery and oxygen demand, therefore by itself a strong independent predictor of ICU mortality, whatever the primary reason for ICU admission (19,20). As the liver contributes to lactate clearance, which is a predictive marker of mortality from all-cause in ICU (21), high level of lactate may be even more predictive in case of acute-on-chronic liver failure. Christin Edmark and coworkers' study was not designed to assess the respective role of each biomarker, but it is likely that lactate and bilirubin both play a major role in determining the prognosis of these patients.

Nevertheless, a score able to assess significantly the prognosis with very few variables is very attractive. The selection of these variables is then crucial. It may be puzzling that an arbitrary choice, although inspired by experts, is as effective as score based on a selection of variables through a sophisticated statistical method. However, many scoring systems use variables selected by experts like APACHE II or SOFA (2,8). That means selection is then based, of course, on basic knowledge of the pathology but also on expert's intuition and subjectivity. However, a well conducted study includes a test in a validation cohort and appropriate statistical testing objectively confirms the appropriateness of the scoring system to discriminate patients. In this respect, Christin Edmark and coworkers' study was quite well done, and authors' assumption that the Life Score can be quickly, easily and conveniently utilized at the bedside for early risk prediction in patients with chronic liver disease, though the performance does not match that of SOFA or CLIF-SOFA, sounds quite good.

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## Footnote

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