



Liver, Pancreas and Biliary Tract

## Retrospective evaluation of prognostic score performances in cirrhotic patients admitted to an intermediate care unit



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### ABSTRACT

**Background:** The prognosis of cirrhotic patients in the Intensive Care Unit requires the development of predictive tools for mortality. We aimed to evaluate the ability of different prognostic scores to predict hospital mortality in these patients.

**Methods:** A single-centre retrospective analysis was conducted of 281 hospital stays of cirrhotic patients at an Intermediate Care Unit between June 2009 and December 2010. The performance of the Simplified Acute Physiology Score (SOFA), the Simplified Acute Physiology Score (SAPS) II or III, Child–Pugh, Model for End-Stage Liver Disease (MELD), MELD-Na and the Chronic Liver Failure–Consortium Acute-on-Chronic Liver Failure score (CLIF-C ACLF) in predicting hospital mortality were compared.

**Results:** Mean age was  $58.2 \pm 12.1$  years; 77% were male. The main cause of admission was acute gastrointestinal bleeding (47%). The in-hospital mortality rate was 25.3%. Receiver operating characteristic curve analyses demonstrated that SOFA (0.82) MELD-Na (0.82) or MELD (0.81) scores at admission predicted in-hospital mortality better than Child–Pugh (0.76), SAPS II (0.77), SAPS III (0.75) or CLIF-C ACLF (0.75). We then developed the cirrhosis prognostic score (Ci-Pro), which performed better (0.89) than SOFA.

**Conclusion:** SOFA, MELD and especially the Ci-Pro score show the best performance in predicting hospital mortality of cirrhotic patients admitted to an Intermediate Care Unit.

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## 1. Introduction

Despite the improvement of treatments and management, the mortality of cirrhotic patients in the Intensive Care Unit (ICU) remains higher than that of other patients: around 50% according to the most recent studies [1–10]. Identifying patients who will benefit from hospitalisation in the ICU is a major challenge.

To better identify patients at a high risk of death and thus to discriminate which would be the best candidates for hospitalisation in the ICU, several authors have studied the value of prognostic scores. It appears that general severity scores (the

Acute Physiology and Chronic Health Evaluation [APACHE II] or the Sequential Organ Failure Assessment [SOFA]) are more discriminating than liver-specific scores such as the Child–Pugh score and the Model for End-Stage Liver Disease (MELD) score in its various versions [7–9,11]. Among these, the SOFA is currently considered the most discriminating score for predicting the outcome of cirrhotic patients admitted to the ICU [9,11,12]. However, this score has not been validated and not necessarily adapted to another context than that of the ICU. The specific value in cirrhotic patients of other general scores such as the Simplified Acute Physiology Score currently used in the ICU [13], is debated (SAPS II) [1,7–9] or unknown (SAPS III). Among the specific scores used in patients with cirrhosis, the MELD seems more discriminating than the Child–Pugh score [11,14]. Its variants (iMELD or MELD-Na) do not seem to perform better in this indication [9]. Recently, the new CLIF consortium ACLF score (CLIF-C ACLF) demonstrated its superiority over the MELD and MELD-Na at predicting the risk of mortality in patients with acute-on-chronic liver failure [15]. Its performance is apparently independent of the hospitalisation setting.

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Usually, these prognostic scores are calculated at admission into the ICU to predict in-hospital mortality. To our knowledge, none of these scores has been assessed specifically in an Intermediate Care Unit (InCU), upstream of the ICU. The challenge would be to predict the prognosis of a patient before his transfer to the ICU to help intensivists and hepatologists choose whether or not to propose the transfer.

The aim of our study was to evaluate the ability of general scores (SOFA, SAPS II or SAPS III) and liver-specific scores (Child–Pugh, MELD, MELD-Na and CLIF-C ACLF) to predict in-hospital mortality of cirrhotic patients admitted to an Intermediate Care Unit. We aimed to determine whether calculating the scores on admission rather than at the time of the transfer to the ICU might help physicians to better estimate the prognosis of cirrhotic patients with acute complications.

## 2. Materials and methods

### 2.1. Population

A retrospective study was conducted including all patients with cirrhosis who were admitted to the Intermediate Care Unit (InCU) of the department of Hepato-Gastroenterology of Caen University Hospital between June 1st, 2009 and December 31st, 2010. The diagnosis of cirrhosis was based on histological criteria after performing a liver biopsy, or on an array of clinical, laboratory, endoscopic and imaging tests. The InCU of the Department of Hepato-Gastroenterology in Caen University Hospital is staffed by hepatologists. At our centre, cirrhotic patients are hospitalised in this unit when they have an acute complication such as acute variceal bleeding, severe decompensation of cirrhosis or infections. Patients admitted to this unit can benefit from cardiopulmonary monitoring. However, patients who require mechanical ventilation, amines or dialysis sessions must be transferred to the ICU.

Using the coding system of our centre, 367 hospital stays of cirrhotic patients admitted to the InCU during the study period were identified. If a patient was admitted a second time to the InCU during the study period this second stay was included in the study, but if a patient was transferred to ICU and then re-admitted to the InCU during the same hospital stay he was not included a second time in the cohort. Similarly, the stays of patients without complication hospitalised for logistical reasons that did not warrant hospitalisation in the InCU (work-up before listing for liver transplantation, paracentesis, etc.) were excluded. The medical records with missing data were not included in the analysis. In total, 281 hospital stays representing 223 patients were analysed because 43 patients were hospitalised several times during the inclusion period.

### 2.2. Data

Age, gender, date of diagnosis of cirrhosis (cirrhosis known or discovered during hospitalisation) and aetiology of cirrhosis, the cause of hospitalisation, ICU transfers and the reason for the transfer, liver transplantation, death, length of InCU stay, and length of hospital stay were collected. The clinical and laboratory parameters necessary to calculate the SOFA, SAPS II and SAPS III, Child–Pugh, MELD, MELD-Na and CLIF-C ACLF scores were collected at admission and at 48 h [13,15–17].

Organ failures (cardiovascular, respiratory, liver, renal, neurological and coagulation) were listed at admission into the InCU and at 48 h. For each vital component, organ failure was defined by a SOFA sub-score of 3 or 4 for the organ concerned.

### 2.3. Statistical analysis

The group of patients who survived to discharge from the hospital was compared with the group of non-survivors. Continuous variables were compared using Student's *t* tests and categorical variables were compared using Chi-squared tests or Fisher's test. Variables associated with death with a  $p < 0.1$  were included in a multivariate logistic regression model using a stepwise selection of variables. A logarithmic transformation was used for laboratory variables with skewed distribution: bilirubin, INR, blood urea nitrogen, creatinine, platelets and leucocytes. Goodness of fit of the model was verified using a Hosmer–Lemeshow test. To identify which score had the best discrimination capacity for predicting ICU mortality, Areas Under Receiver–Operating Characteristics curve (AUROC) were compared. Sensitivity, specificity, and positive and negative predictive values were determined for each score. Cut-off values were identified using the highest Youden index (sensitivity + specificity – 1) [18]. The validity of each chosen cut-off was studied by comparing the subgroups of patients with regard to mortality.

The *p* value was considered significant when it was less than 0.05. Statistical analyses were performed using SAS 9.2 (Cary, NY, USA).

The protocol was approved by the local Ethics Committee (Comité de Protection des Personnes [CPP] Nord-Ouest III, Caen, France).

## 3. Results

### 3.1. Patients

Two hundred and eighty one hospital stays of cirrhotic patients were studied. Characteristics of the patients are described in Table 1. The mean age was  $58.2 \pm 12.1$  years; 77% were male. Alcohol abuse was the main cause of cirrhosis (88%). Cirrhosis was diagnosed before hospitalisation in 80% of cases (225/281). The leading causes of hospitalisation in the InCU were acute gastrointestinal bleeding (47%) and infection, established on bacteriological analyses or suspected based on clinical or laboratory tests (23%).

The majority of patients were Child–Pugh class C (62%). The number of organ failures was  $0.6 \pm 0.8$  (Table 1). The most common organ failure was liver failure (28.5%), followed by renal failure (13.5%) and coagulation failure (12.5%).

The mean length of hospital stay in the InCU was  $13 \pm 17$  days, for a mean total duration of hospitalisation of  $14 \pm 15$  days. Thirty-six patients (12.8%) were transferred to the ICU. The two main reasons for ICU transfer were respiratory distress ( $n = 8$ ; 22.9%) and septic shock ( $n = 7$ ; 20%). Five of these patients had liver transplantation during their stay in the ICU.

The cumulative incidence of hospital mortality was 25.3% (71 patients). For the purpose of the study, the entire study population was divided into the group of patients who died during hospitalisation, referred to as the “non-survivors group”, and the group of patients who survived hospitalisation: the “survivors group”.

### 3.2. Comparison of survivors versus non-survivors

Demographic variables (age, gender), as well as the cause of cirrhosis were not significantly associated with an increased risk of death (Table 1).

The diagnosis on admission differed between the two groups. Acute gastrointestinal bleeding was the most frequent (58% of admissions) cause of admission in the survivors group, while infections or acute alcoholic hepatitis and jaundice were the most

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