Cirrhotic patients in the medical intensive care unit: Early prognosis and long-term survival*

Vincent Das, MD, PhD; Pierre-Yves Boelle, PhD; Arnaud Galbois, MD; Bertrand Guidet, MD, PhD; Eric Maury, MD, PhD; Nicolas Carbonell, MD; Richard Moreau, MD, PhD; Georges Offenstadt, MD

LEARNING OBJECTIVES
After participating in this educational activity, the participant should be better able to:

1. Evaluate the usefulness of factors that influence outcome when triaging cirrhotic patients.
2. Analyze factors that influence outcome when triaging cirrhotic patients.

Unless otherwise noted, the faculty’s, staff’s, and authors’ spouse(s)/life partner(s) (if any) have nothing to disclose.

The authors have disclosed that they have no financial relationships with, or financial interests in, any commercial companies pertaining to this educational activity.

All faculty and staff in a position to control the content of this CME activity have disclosed that they have no financial relationship with, or financial interests in, any commercial companies pertaining to this educational activity.

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Objectives: To reassess the prognosis of patients with cirrhosis admitted to the intensive care unit.

Design: A retrospective study in a medical intensive care unit in a teaching hospital in France.

Patients: All patients with cirrhosis without previous liver transplantation admitted in the period from 2005 to 2008.

Interventions: None.

Main Results: One hundred thirty-eight patients were studied. Survival rates in the intensive care unit, in hospital, and at 6 months were 59% (95% confidence interval, 50%–67%), 46% (95% confidence interval, 38%–54%), and 38% (95% confidence interval, 30%–47%), respectively. In-hospital survival rates for patients requiring vasopressors, mechanical ventilation, or renal replacement therapy were 20%, 33%, and 31%, respectively. On day 1, independent risk factors for in-hospital mortality were age, albuminemia, international normalized ratio, and the Sequential Organ Failure Assessment score computed after discarding points for hematologic failure (modified Sequential Organ Failure Assessment score). Liver disease severity, assessed using a clinical classification, did not correlate with in-hospital mortality. In patients still alive after 3 days, the only prognostic factor was the modified Sequential Organ Failure Assessment score computed after 3 days. To predict in-hospital mortality, the modified Sequential Organ Failure Assessment score on day 1 had a greater area under the receiver operating characteristic curve (0.84) than the Simplified Acute Physiology Score II (0.78), the Child-Pugh score (0.76), the model for end-stage liver disease score (0.77), or the model for end-stage liver disease–natremia score (0.75). The in-hospital mortality rate with three or four nonhematologic organ failures on day 1 was not >70%, whereas it was 89% with three nonhematologic organ failures after 3 days spent in the intensive care unit.

Conclusion: In-hospital survival rate of intensive care unit-admitted cirrhotic patients seemed acceptable, even in patients requiring life-sustaining treatments and/or with multiple organ failure on admission. The most important risk factor for in-hospital mortality was the severity of nonhematologic organ failure, as best assessed after 3 days. A trial of unrestricted intensive care for a few days could be proposed for select critically ill cirrhotic patients. (Crit Care Med 2010; 38:2108–2116)

Key Words: liver cirrhosis; prognosis; critical care; critical illness; intensive care units; mechanical ventilation

*See also p. 2259.

Medical Doctor (VD), Service de Réanimation Médicale, Paris, France; Physical Doctor (VD), Service de Réanimation Médicale, Paris, France; Associate Professor (P-YB), INSERM, Université Pierre et Marie Curie, Paris, France; Doctor (AG), Service de Réanimation Médicale, Hôpital Saint-Antoine (AP-HP), Paris, France; Professor of Intensive Care Medicine (BG), Service de Réanimation Médicale, Paris, France; Head Department (BG), Service de Réanimation Médicale, Paris, France; Professor of Intensive Care (EM), Service de Réanimation Médicale, Hôpital Saint-Antoine, Assistance Publique, Complications of Cirrhosis, INSERM U773, Centre de Recherche Bichat-Beaujon CRB3 and Liver Unit, Hôpital Beaujon, Clichy, France; Director (GO), Medical ICU, Hôpital Saint-Antoine, Paris, France; and Professor (GO), Université Pierre et Marie Curie, Paris, France. Unité de Recherche en Épidémiologie Systèmes d’Information et Modélisation (U707), Paris, France.

For information regarding this article, E-mail: vincent.das@chi-andre-gregoire.fr

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Liver cirrhosis is responsible for approximately 8,000 deaths annually in France (1). Whatever the reasons for intensive care unit (ICU) admission may be (related to cirrhosis or not), cirrhosis independently worsens the prognosis of ICU-admitted patients (2, 3). The prognosis of ICU-admitted cirrhotic patients has been assessed in several studies, but questions remain unanswered (4–26). First, reported inhospital mortality rates varied from 50% to 100%, so the utility or futility of life-sustaining treatments in these patients has been questioned (5, 9, 12, 15, 17, 18). Second, if organ failure-specific scores performed better than the Child-Pugh score to predict inhospital death in ICU-admitted cirrhotic patients, then the performances of more recently developed liver disease-specific scores (model for end-stage liver disease [MELD], and MELD–natremia [Na]) are underdocumented in these patients (27). Of note is that these liver disease-specific scores, initially designed to predict operative risk (Child-Pugh score) or mortality for cirrhotic patients on the waiting list for liver transplantation (MELD and MELD-Na scores), have never been designed to predict mortality in the setting of ICU admission (27). Third, the impact of liver disease severity on the prognosis of ICU-admitted cirrhotic patients remains questioned (9, 14, 19, 23, 25). Finally, because most studies were performed >10 years ago, the current prognosis of these patients needs to be updated. Because intensivists require objective measurements of prognosis when making decisions, such as triage or treatment limitations, we performed a retrospective study over a period of 3 years to reassess the prognosis of ICU-admitted cirrhotic patients and to identify prognostic factors in this population. At the conclusion of this CME activity, participants should be able to evaluate factors that influence outcome when triaging cirrhotic patients, analyze factors that influence outcome when triaging cirrhotic patients and assess risk factors for inhospital mortality in patients with cirrhosis.

PATIENTS AND METHODS

We conducted an observational retrospective study in the medical ICU (MICU) of the Saint-Antoine Hospital, Paris, France, which is a 776-bed teaching hospital with a closed 14-bed general MICU and a 44-bed liver unit with eight beds dedicated to intensive care for patients with liver disease (liver ICU). The hospital is also a liver transplant center. Two different medical and nurse teams are in charge of the liver ICU and the MICU, which are located in separate buildings. Hepatologists are in charge of the liver ICU. Intensivists are in charge of the MICU. Cirrhotic patients requiring intensive care without hepatic organ failure (for example, severe alcoholic hepatitis or gastrointestinal bleeding without shock, aspiration, or encephalopathy) are primarily admitted to the liver ICU. Cirrhotic patients with hepatic organ failure, except the hepatorenal syndrome, are proposed for admission to the MICU. Admission decisions are made by the attending physician and intensivists. Bedridden patients (those patients unable to walk and fully dependent for daily support at a time point before the acute disease that requires admission to the ICU) are usually denied MICU admission. Patients with the hepatorenal syndrome also are usually denied MICU admission and are treated in the liver ICU, because they probably would not benefit from renal replacement therapy (RRT) (28). Once patients have been admitted to the ICU, decisions to limit or withdraw life-sustaining treatments usually are not made before the fourth day after ICU admission.

All patients admitted to the MICU between May 2005 and March 2008 with histologic or clinical diagnosis of cirrhosis were included. These patients were identified from computerized ICU discharge reports. Patients with previous liver transplantation were excluded.

The following data were collected: demographic characteristics; reason for admission; Charlson comorbidity index (excluding points for liver disease); cause of cirrhosis; clinical and biological data required for calculation of severity scores, including the degree of ascites (defined following the classification outlined by the Child-Pugh score); need for vasopressors, mechanical ventilation, or RRT cause of death in the MICU; and decisions to limit or withdraw life-sustaining treatments in the MICU. Preadmission functional status was assessed using the Knaus scale (A, prior good health, no functional limitation; B, mild to moderate limitation of activity because of a chronic disease; C, serious but not incapacitating restriction of activity; and D, severe restriction of activity, including persons bedridden or institutionalized) (29).

Isolated encephalopathy was defined as flapping tremor, confusion, or coma with exclusion of other causes and no aggravating factor (gastrointestinal bleeding, infection, drug or metabolic disorder). Infection on admission was diagnosed by the attending physician using standard criteria (clinical symptoms, imaging techniques, biological and microbiological examinations). In microbiologically undocumented cases, infection could be clinically documented (spontaneous peritonitis: polymorphonuclear cells count >250 per cubic millimeter in ascites with negative culture; pneumonia using standard criteria). Of note is that in our ICU, bronchoalveolar lavage is systematically performed when pneumonia is suspected.

Liver disease severity was assessed on ICU admission not only with liver disease-specific scores (Child-Pugh, MELD, and MELD-Na), according to the previously published formula, but also with the clinical classification proposed by D’Amico et al (30), based on a clinical history of cirrhosis complications.

The Child-Pugh score was calculated from five parameters (degree of ascites, degree of encephalopathy, prothrombin time, serum bilirubin, and albumin) (31). The MELD score was calculated as follows:

\[
\text{MELD} = 9.57 \times \ln(\text{serum creatinine} [\text{mg/dL}]) + 3.78 \times \ln(\text{serum bilirubin} [\text{mg/dL}]) + 11.2 \times \ln(\text{international normalized ratio (INR)}) + 6.43 (22) \]

The MELD-Na score was calculated as follows:

\[
\text{MELD-Na} = \text{MELD} - \text{serum sodium} - [0.25 \times \text{MELD} \times (140 - \text{serum sodium})] + 40, \text{with serum sodium values varying from 125 to 140 mmol/L (33)}.\]

The D’Amico classification (30) is as follows: stage 1, no history of ascites, no known esophageal varices; stage 2, no history of ascites, known esophageal varices without a history of bleeding; stage 3, history of ascites; and stage 4, history of variceal bleeding.

The general ICU-specific score (Simplified Acute Physiology Score II) was calculated on day 1 (34). Organ failure-specific scores (Sequential Organ Failure Assessment [SOFA] and the number of organ failures) were calculated on day 1 and at 3 days after MICU admission (35). An organ failure was defined as SOFA score of ≥3 points for the concerned organ (need for vasopressor, mechanical ventilation with PaO₂/Fio₂ ratio of <200, Glasgow Coma Scale score of <9, serum bilirubin of >100 μmol/L, serum creatinine of >300 μmol/L or oliguria lasting for >24 hrs or need for RRT, or platelet count of <50,000/mm³) (23).

Therapeutic limitation was related to treatment withholding or withdrawal. Decision to forego cardiopulmonary resuscitation was not considered as withholding of treatment. Only the limitation decisions written in the medical chart were collected. Survival was determined in the MICU, in the hospital, and 6 months after MICU admission.

Statistical Analysis

Data are shown as mean values ± SD or as percentages when necessary. Survival was calculated using the Kaplan-Meier method on day 180 after MICU admission and is shown as value and 95% confidence interval (CI).

Risk factors for inhospital death were determined by logistic regression. Analyses were also performed in patients still alive on day 3. The factors associated with inhospital mortality in the univariate analysis (p < 0.20) were included in a multivariate analysis. Backward elimination of variables was performed until all remaining variables were significant at the p < .05 level. Only the variables that had a strong theoretical basis were included in the analyses: demo-
The results of the univariate analysis are presented in Table 3. Of note is that the liver disease severity staged according to D’Amico’s classification did not correlate with inhospital mortality.

Because hematologic failure was not associated with mortality, a modified SOFA score, excluding points for hematologic failure, was computed. The following factors were included in multivariate analysis: age, infection, secondary admission from a unit different from the emergency department, serum albumin, degree of ascites, INR, and modified SOFA score. After backward elimination, age older than 50 yrs, lower serum albumin, higher INR, and higher modified SOFA score remained independently associated with inhospital mortality (Table 4).

### Risk Factors for Inhospital Mortality Assessed on Day 1

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### Outcome and Causes of Death

Survival rates in the MICU, in the hospital, and 6 months after MICU admission were 59% (95% CI, 50%–67%), 46% (95% CI, 38%–54%), and 38% (95% CI, 30%–47%), respectively (Fig. 1). Most deaths occurred in hospital, and the 6-month survival of the patients discharged alive from the hospital was 86%.

Death in the MICU was attributable to the persistence or aggravation of the initial disease in 79% of cases (multiple organ failure, 60%; brain lesions, 10%; refractory shock, 9%) or to a secondary complication in 21% of cases (bleeding, 11%; nosocomial infection, 5%; other, 5%). Death in the MICU was preceded by a written decision to limit or withdraw life-sustaining treatments in 65% of cases.

### Risk Factors for Inhospital Mortality Assessed on Day 1

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When we forced the hematologic failure into the model of Table 4, the strength of association of hematologic failure with death was much reduced compared with the univariable case (odds ratio [OR] for death, 0.6; 95% CI, 0.2 to 1.9; \( p = .4 \)), and the ORs for the other variables were not altered (data not shown).

**Risk Factors for Inhospital Mortality in Patients Still Alive After 3 Days**

In patients still alive after 3 days, in univariate analysis, secondary admission, infection on admission, and lower serum albumin were no longer associated with inhospital mortality whereas other risk factors remained associated (data not shown). Hemodynamic, hepatic, renal, neurologic, or respiratory failure after 3 days (data not shown) and SOFA score computed after 3 days (data not shown). The change in modified SOFA score over the first 3 days, adjusted for the baseline value, was not more significantly associated with in-hospital death than the modified SOFA score computed after 3 days (data not shown).

**Comparison of Discrimination Ability of Different Scores to Predict Inhospital Mortality**

All the following scores, computed on day 1, were correlated with in-hospital mortality: modified SOFA score and the number of nonhematologic organ failures (see Table 3), Child-Pugh score (OR, 1.5; 95% CI, 1.3 to 1.8, for 1 additional unit; \( p = 0.01 \)), MELD score (OR, 1.9; 95% CI, 1.5 to 2.4; \( p = 0.001 \)), MELD-Na score (OR, 1.7; 95% CI, 1.4 to 2.3; \( p = 0.001 \)), and Simplified Acute Physiology Score II (OR, 1.7; 95% CI, 1.4 to 2.0; \( p < 0.001 \)). Receiver operating characteristic curves were constructed for these scores, calculated on day 1 in all patients, to predict in-hospital death (Fig. 2). The AUROCs were as follows: modified SOFA score, 0.84; number of nonhematologic organ failures, 0.78; Simplified Acute Physiology Score II, 0.78; MELD, 0.77; Child-Pugh score, 0.76; and MELD-Na, 0.75. The AUROC of the modified SOFA score was significantly greater than the AUROC of each of the other scores (\( p < 0.05 \) for all other scores).

The AUROC of the linear predictor derived from the multivariate logistic regression on day 1 (0.65 \times \text{INR} + 0.25 \times \text{modified SOFA score} − 0.07 \times \text{serum albumin} + 1.88 \text{if age is older than 50 yrs}) was 0.89, which was not significantly higher than the AUROC of the modified SOFA score.

For the patients still alive after 3 days, the AUROCs were as follows: modified SOFA score computed after 3 days, 0.84; number of nonhematologic organ failures computed after 3 days, 0.78; modified SOFA score on day 1, 0.70; number of nonhematologic organ failures on day 1, 0.60; Simplified Acute Physiology Score II, 0.63; Child-Pugh score, 0.69; MELD score, 0.67; and MELD-Na score, 0.66. The AUROC of the modified SOFA score computed after 3 days was significantly greater than the AUROC of scores calculated on day 1, but it was not statistically
3. As displayed, even in the presence of nonhematologic organ failures and in-hospital mortality is illustrated in Figure of nonhematologic organ failures and in-hospital mortality: Results of multivariate analysis Table 4.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;50 yrs</td>
<td>2.7 (1.3–5.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Male</td>
<td>0.7 (0.3–1.4)</td>
<td>.26</td>
</tr>
<tr>
<td>Charlson score</td>
<td>0.95 (0.7–1.2)</td>
<td>.66</td>
</tr>
<tr>
<td>Knaus autonomy scale</td>
<td>1.3 (0.8–2.1)</td>
<td>.45</td>
</tr>
<tr>
<td>Secondary admission from nonemergency ward</td>
<td>2.5 (1.3–5.0)</td>
<td>.01</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>0.6 (0.3–1.4)</td>
<td>.50</td>
</tr>
<tr>
<td>Liver disease severity stage (D’Amico’s classification)</td>
<td>1</td>
<td>.96</td>
</tr>
<tr>
<td>Stage 1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Stage 2 (compared with stage 1)</td>
<td>0.8 (0.3–2.2)</td>
<td></td>
</tr>
<tr>
<td>Stage 3 (compared with stage 1)</td>
<td>0.9 (0.4–2.2)</td>
<td></td>
</tr>
<tr>
<td>Stage 4 (compared with stage 1)</td>
<td>0.9 (0.3–2.1)</td>
<td></td>
</tr>
<tr>
<td>Infection on admission</td>
<td>2.6 (1.3–5.3)</td>
<td>.01</td>
</tr>
<tr>
<td>Direct complication of cirrhosis as final diagnosis</td>
<td>1.3 (0.7–2.6)</td>
<td>.41</td>
</tr>
<tr>
<td>Severity of ascites (per grade of the ascites component of the Child-Pugh score)</td>
<td>3.3 (1.6–10)</td>
<td>.002</td>
</tr>
<tr>
<td>Hyponatremia (per 10-mmol/L decrease)</td>
<td>1.1 (0.8–2)</td>
<td>.55</td>
</tr>
<tr>
<td>Hypoalbuminemia (per 5-g/L decrease)</td>
<td>1.3 (1.1–1.7)</td>
<td>.02</td>
</tr>
<tr>
<td>International normalized ratio (per 0.1 additional unit)</td>
<td>1.2 (1.1–1.3)</td>
<td>.0003</td>
</tr>
<tr>
<td>Cardiovascular failure</td>
<td>7.9 (3.7–18.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>2.8 (1.3–6.0)</td>
<td>.009</td>
</tr>
<tr>
<td>Neurologic failure</td>
<td>2.6 (1.3–5.4)</td>
<td>.007</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4.5 (2.1–9.7)</td>
<td>.0001</td>
</tr>
<tr>
<td>Liver failure</td>
<td>3.2 (1.6–6.7)</td>
<td>.002</td>
</tr>
<tr>
<td>Hematologic failure</td>
<td>1.8 (0.8–4.0)</td>
<td>.19</td>
</tr>
<tr>
<td>Number of nonhematologic organ failures</td>
<td>1</td>
<td>.001</td>
</tr>
<tr>
<td>No organ failure</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1 organ failure (compared with no organ failure)</td>
<td>4.4 (1.3–17.8)</td>
<td></td>
</tr>
<tr>
<td>2 organ failures (compared with no organ failure)</td>
<td>7.9 (2.1–35.7)</td>
<td></td>
</tr>
<tr>
<td>3 organ failures (compared with no organ failure)</td>
<td>18 (5.9–69.3)</td>
<td></td>
</tr>
<tr>
<td>Sequential Organ Failure Assessment score (per 1 additional unit)</td>
<td>1.3 (1.2–1.5)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Correlation Between the Number of Organ Failures and Inhospital Mortality

The relationship between the number of nonhematologic organ failures and inhospital mortality is illustrated in Figure 3. As displayed, even in the presence of three or four nonhematologic organ failures on day 1, the inhospital mortality was <70%. The presence of three organ failures or more after 3 days indicated a mortality of 89%.

Identification of Patients With Very High Inhospital Mortality Rates

The mortality rates in patients requiring vasopressors, mechanical ventilation, or RRT and in patients in class C of the Child-Pugh score were 80%, 67%, 69%, and 67%, respectively.

Cutoff values predicting inhospital death with a specificity of >90% have been determined for organ-failure specific scores computed on day 1 and after 3 days and are shown in Table 5.

DISCUSSION

The prognosis of ICU-admitted cirrhotic patients has been the subject of several studies, most of which were performed >10 years ago (4–27). The present study was performed to reassess the prognosis of these patients. We observed that although their overall prognosis was poor, a significant portion of ICU-admitted cirrhotic patients, including some patients requiring life-supporting treatments and/or with multiple organ failure on admission, could be discharged alive from the hospital; liver disease severity, as best assessed with clinical classification, had no impact on their prognosis once admitted to the ICU; the most important risk factor for in-hospital mortality was the severity of nonhematologic organ failure; organ failure-specific scores had a better capacity to predict inhospital mortality than liver disease-specific scores, including the newest MELD and MELD-Na scores; and patients with three nonhematologic organ failures after 3 days spent in the ICU had a very high mortality rate.

In the literature, inhospital mortality rates for ICU-admitted cirrhotic patients varied widely, from 100% in some older studies to approximately 50% in recent ones, with the latter rate being similar to the 54% mortality rate observed in the present study (4, 10, 12, 16, 23). The 6-month survival rate observed in the present study (38%) was also comparable to the 1-year survival rate of 31% reported in another recent study (11). Furthermore, whereas inhospital mortality rates for cirrhotic patients with three or more organ failures on admission or requiring vasopressors, mechanical ventilation, or RRT were close to 100% in some previous studies, 20%–40% of such patients were discharged alive from the hospital in the present study (5, 6, 9, 12, 15, 18, 20, 21, 23). Thus, as previously suggested by others (9), the prognosis of ICU-admitted cirrhotic patients seems to have improved over time. The hypotheses that may explain this observation include significant advances in medical care of cirrhotic patients and/or in general inten-
sive care, a more strict selection of cirrhotic patients by ward physicians or intensivists for ICU admission, or differences in the characteristics of studied populations (cirrhosis causes, reasons for ICU admission) (9, 38). Data on the triage process before ICU admission were not available in the present retrospective study. Our patients were critically ill, with a mean of 2.3 organ failures on admission and a rate of requirement for life-sustaining treatments as high as those in several previous studies, but they were exceptionally bedridden, which suggests that they were actually selected according to their functional status and not their acute severity (5, 9, 10, 14, 15, 18, 19, 23). Our patients often had severe liver disease—a history of ascites or variceal bleeding was present in more than half—but the hepatorenal syndrome was rare (1%). Thus, some cirrhotic patients with the most severe liver disease (refractory ascites and/or the hepatorenal syndrome, chronic encephalopathy) may have been denied admission to the MICU. Of note is that the hepatorenal syndrome indicates a severe liver failure and has a bad prognosis without liver transplantation, whereas other types of ICU-acquired acute renal failure are more often reversible (28, 39). This could explain why patients requiring RRT in the present study had a 31% survival rate, as compared with survival rates of close to 0% in previous studies (5, 15, 18). Cirrhotic patients in the present study had other particularities; most patients had alcoholic cirrhosis, as in the previous studies performed in France and Western Europe, and were still drinking, but because of the presence of the liver ICU in our hospital they were rarely admitted to the MICU for variceal bleeding, as compared with many others series (4, 10, 15, 17, 18, 21, 23). Because alcoholism has a negative impact on the prognosis of non-selected critically ill patients, and because admission for another reason than variceal bleeding is associated with a worse outcome in ICU-admitted cirrhotic patients, these observations should actually reinforce our conclusion that the prognosis of critically ill cirrhotic patients seems better in the present study than previously described (9, 10, 14, 17, 19, 21, 23, 40, 41).

In the present study, advanced age, high INR, low serum albumin, and modified SOFA score on day 1 were independent predictors for inhospital death, whereas the modified SOFA score computed after 3 days was the only prognostic factor in patients still alive after 3 days. Once select cirrhotic patients had been admitted to the ICU, liver disease severity was not correlated with inhospital mortality (14, 25). Of note is that in the present study, liver disease severity was assessed using a clinical classification.

![Figure 2. Receiver operating characteristic curves for scores, calculated on day 1, predicting inhospital mortality. SOFA, Sequential Organ Failure Assessment; SAPS, Simplified Acute Physiology Score; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with natremia.](image)

Figure 2. Receiver operating characteristic curves for scores, calculated on day 1, predicting inhospital mortality. SOFA, Sequential Organ Failure Assessment; SAPS, Simplified Acute Physiology Score; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with natremia.

![Figure 3. Correlation between inhospital mortality and the number of nonhematologic organ failures on day 1 or after 3 days spent in the intensive care unit.](image)

Figure 3. Correlation between inhospital mortality and the number of nonhematologic organ failures on day 1 or after 3 days spent in the intensive care unit.

Table 5. Cut-off values for the modified Sequential Organ Failure Assessment score and the number of nonhematologic organ failures associated with inhospital mortality rates higher than 80%

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>On day 1 (all patients, n = 138)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified SOFA score ≥17</td>
<td>19%</td>
<td>100%</td>
<td>100%</td>
<td>51%</td>
</tr>
<tr>
<td>Modified SOFA score ≥15</td>
<td>30%</td>
<td>98%</td>
<td>96%</td>
<td>44%</td>
</tr>
<tr>
<td>Modified SOFA score ≥13</td>
<td>52%</td>
<td>87%</td>
<td>83%</td>
<td>60%</td>
</tr>
<tr>
<td>Number of nonhematologic organ failures ≥5</td>
<td>16%</td>
<td>100%</td>
<td>100%</td>
<td>50%</td>
</tr>
<tr>
<td>Number of nonhematologic organ failures ≥4</td>
<td>28%</td>
<td>92%</td>
<td>81%</td>
<td>52%</td>
</tr>
<tr>
<td>After 3 days (n = 88)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified SOFA score ≥12</td>
<td>32%</td>
<td>100%</td>
<td>100%</td>
<td>57%</td>
</tr>
<tr>
<td>Modified SOFA score ≥7</td>
<td>73%</td>
<td>82%</td>
<td>82%</td>
<td>73%</td>
</tr>
<tr>
<td>Number of nonhematologic organ failures ≥4</td>
<td>2%</td>
<td>100%</td>
<td>100%</td>
<td>47%</td>
</tr>
<tr>
<td>Number of nonhematologic organ failures ≥3</td>
<td>51%</td>
<td>93%</td>
<td>89%</td>
<td>62%</td>
</tr>
</tbody>
</table>

SOFA, Sequential Organ Failure Assessment.
based on history rather than the Child-Pugh or MELD/MELD-Na scores calculated only on ICU admission. The admission values of the latter scores are likely to be altered by superimposed extrahepatic organ failure, leading to changes in biological values (9, 19, 23). Thus, hypoalbuminemia has been shown to be a frequent finding in nonselected patients on ICU admission, because it may result from hemodilution, capillary leak, or a cytokine-induced decrease in liver synthesis of albumin rather than pre-existing liver disease alone (42, 43). Similarly, INR may increase because of hypoxic hepatitis, disseminated intravascular coagulation, or bleeding-induced coagulopathy. In the present study, the absence of a prognostic impact of liver disease severity according to D'Amico’s classification, taken together with the prognostic impact of high INR or low serum albumin, suggests that INR and serum albumin might not reflect liver disease severity in the setting of ICU admission. These results could explain why Child-Pugh and MELD/MELD-Na scores on ICU admission were associated with inhospital mortality in univariate analysis, whereas the clinical classification grade was not. Thus, in the setting of ICU admission, the Child-Pugh and MELD/MELD-Na scores would behave as organ failure-specific scores rather than as liver disease-specific scores. These scores, initially designed to predict operative risk (Child-Pugh score) or mortality for cirrhotic patients on the waiting list for liver transplantation (MELD and MELD-Na scores), have never been designed to predict mortality in the setting of ICU admission. Yet, their performances to predict mortality in ICU-admitted cirrhotic patients have been extensively compared with the performances of ICU-specific or organ failure-specific scores (27). Liver disease-specific scores have even been used to exclude some cirrhotic patients from recent large randomized trials conducted in nonselected critically ill patients (44–46). Our results reinforce the conclusion that these scores, if calculated on ICU admission, should not be used in ICU-admitted cirrhotic patients.

In the present study, the most important independent risk factor for in-hospital death was the severity of organ failure, as previously reported (5, 20, 21, 23). However, two results should be highlighted. First, hematologic failure had no prognostic impact, a result which has been observed by others (9, 21, 23). Second, on day 1, even in the presence of three or four nonhematologic organ failures, the inhospital mortality rate was not >70%. However, after 3 days, the presence of three nonhematologic organ failures was associated with a very high mortality rate, close to 90%. The difficulty of predicting the prognosis of ICU-admitted cirrhotic patients on day 1 has been reported by others (25, 47). Consequently, in select critically ill cirrhotic patients, intensivists may propose a trial of unrestricted intensive care for a few days, followed by withdrawal or limitation of life-sustaining treatments in the case of persistence of a high degree of organ failure after this delay. Such a policy has been advocated for patients with cancer, who seem to share common characteristics with cirrhotic patients once admitted to the ICU. Both populations were previously thought to have a bad prognosis after ICU admission, but in select patients, acceptable survival rates have been observed, even in patients requiring life-sustaining treatments on admission. Once admitted to the ICU, the prognosis does not correlate with the severity of the underlying chronic disease (cancer or cirrhosis) but rather with the severity of organ failure and is easier to assess after a few days spent in ICU rather than on ICU admission (48–50).

In clinical practice, a crucial question still unanswered is as follows: “for which critically ill cirrhotic patients should we propose a limitation or withdrawal of life-sustaining treatments?” Several authors have suggested that the use of intensive care support in cirrhotic patients requiring vasopressors, mechanical ventilation, or RRT or with three organ failures on day 1 could be futile, but our results suggest that intensivists should not systematically deny ICU admission and intensive care support to such patients, because 20%–40% of them were discharged alive from hospital in the present study (5, 9, 15, 18). In the present study, on day 1, a modified SOFA score of ≥15 or five nonhematologic organ failures and, after 3 days, a modified SOFA score of ≥12 or three nonhematologic organ failures were the criteria predicting inhospital death, with specificities close to 90%–100% and the best sensitivities, but it is difficult to specify limits beyond which treatment should be withheld when there is any chance that a life can be saved. The quantitative notion of futility is difficult to define (37).

It should be highlighted that, because the present study was monocentric, the extrapolation of our results to other populations of ICU-admitted cirrhotic patients should be performed with caution. Our results should be validated in an independent sample of patients before being applied in clinical practice. Also, self-fulfilling prophecy, a source of confounding common to observational outcome studies, may be inherent in some of our results (51). It results 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. Thus, a variable such as the number of organ failures will be a strong outcome predictor if it was already considered by intensivists as a strong argument for bad prognosis, thus influencing patient management. However, this kind of bias would have artificially worsened, not improved, the prognosis of our critically ill patients, so our conclusion of the seemingly improved outcome of cirrhotic patients requiring life-sustaining treatments or with three or four organ failures on admission would be reinforced. Other limits of the present study, such as the possibility of nonexhaustive data collection and the absence of data on the triage process before ICU admission, are related to its retrospective design and should also be highlighted.

CONCLUSION

In summary, in the present monocentric study, we observed that inhospital survival rate of select cirrhotic patients admitted to the ICU could be acceptable, even when life-sustaining treatments were required and/or multiple organ failure was present on admission, and that 6-month survival of patients discharged alive from hospital was good. The most important risk factor for inhospital mortality was the severity of nonhematologic organ failure, as best assessed after 3 days spent in ICU. Consequently, in select cirrhotic patients, intensivists may propose a trial of unrestricted intensive care for a few days, followed by withdrawal or limitation of life-sustaining treatments in the case of persistence of a high degree of organ failure after this delay.

At the conclusion of this CME activity, participants should be able to evaluate factors that influence outcome when triaging cirrhotic patients, analyze factors that influence outcome when triaging
cirrhotic patients and assess risk factors for inhospital mortality in patients with cirrhosis.

REFERENCES


