



Original Contribution

Patients with cirrhosis in the ED: early predictors of infection and mortality^{☆,☆☆}



Rafael Oliveira Ximenes, MD^{a,b,*}, Alberto Queiroz Farias, PhD^a, Augusto Scalabrini Neto, PhD^b, Márcio Augusto Diniz, MS^a, Gabriel Taricani Kubota^c, Maurício Menezes Aben-Athar Ivo^c, Caroline Gracia Plena Sol Colacique^c, Luiz Augusto Carneiro D'Albuquerque, PhD^a, Roger Daglius Dias, MD, MBA^b

^a Department of Gastroenterology, University of Sao Paulo School of Medicine, 05403-010, Sao Paulo, SP, Brazil

^b Emergency Department, University of Sao Paulo School of Medicine, 05403-010, Sao Paulo, SP, Brazil

^c Undergraduate at University of Sao Paulo School of Medicine, 01246-903, Sao Paulo, SP, Brazil

ARTICLE INFO

Article history:

Received 29 July 2015

Received in revised form 2 September 2015

Accepted 6 September 2015

ABSTRACT

Background: Patients with cirrhosis have high risk of bacterial infections and cirrhosis decompensation, resulting in admission to emergency department (ED). However, there are no criteria developed in the ED to identify patients with cirrhosis with bacterial infection and with high mortality risk.

Study objective: The objective of the study is to identify variables from ED arrival associated with bacterial infections and inhospital mortality.

Methods: This is a retrospective single-center study using a tertiary hospital's database to identify consecutive ED patients with decompensated cirrhosis. Clinical variables and laboratory results were obtained by chart review. Logistic regression models were built to determine variables independently associated with bacterial infection and mortality. Scores using these variables were designed.

Results: One hundred forty-nine patients were enrolled, most of them males (77.9%) with alcoholic cirrhosis (53%) and advanced liver disease (Child-Pugh C, 47.2%). Bacterial infections were diagnosed in 72 patients (48.3%), and 36 (24.2%) died during hospital stay. Variables independently associated with bacterial infection were lymphocytes less than or equal to 900/mm³ (odds ratio [OR], 3.85 [95% confidence interval {CI}, 1.47–10]; $P = .006$) and C-reactive protein greater than 59.4 mg/L (OR, 5.05 [95% CI, 1.93–13.2]; $P = .001$). Variables independently associated with mortality were creatinine greater than 1.5 mg/dL (OR, 4.35 [95% CI, 1.87–10.1]; $P = .001$) and international normalized ratio greater than 1.65 (OR, 3.71 [95% CI, 1.6–8.61]; $P = .002$). Scores designed to predict bacterial infection and mortality (Mortality in Cirrhosis Emergency Department Score) had an area under the receiver operating characteristic curve of 0.82 and 0.801, respectively. The Mortality in Cirrhosis Emergency Department Score performed better than Model for End-Stage Liver Disease score.

Conclusions: In this cohort of ED patients with decompensated cirrhosis, lymphopenia and elevated C-reactive protein were related to bacterial infections, and elevated creatinine and international normalized ratio were related to mortality. Scores built with these variables should be prospectively validated.

© 2015 Elsevier Inc. All rights reserved.

1. Introduction

1.1. Background

Bacterial infections are diagnosed in 30% to 50% of all hospital admissions for cirrhotic decompensation and are directly responsible for up to 50% of deaths in cirrhosis [1,2]. These patients are twice as likely to die of sepsis than individuals without cirrhosis [3]. Furthermore, bacterial infections carry significant morbidity, precipitating cirrhosis decompensation (hepatic encephalopathy, ascites, variceal bleeding, and/or

jaundice) and acute kidney injury (AKI) development [4]. In fact, renal failure occurs in 33% of patients with cirrhosis who have spontaneous bacterial peritonitis (SBP) and in 27% of those with sepsis unrelated to SBP, with a mortality rate of 41% to 66% [5,6]. These severe complications frequently result in admission to the emergency department (ED) [2,7].

Patients with cirrhosis require frequent visits to the ED. In a large population study performed in England, 47.3% of patients had a first diagnosis of cirrhosis during an emergency admission. The remaining 52.7% were diagnosed in an outpatient setting, but 37.8% of them had a subsequent emergency hospital admission over a 5-year period [8].

Early recognition and treatment of severe complications are generally related to better clinical outcomes. In patients with SBP, the most common bacterial infection in cirrhosis, treatment with suitable antibiotics and large volume albumin infusion in the first 6 hours from diagnosis have reduced mortality rates from 80% to 20% in the last 3 decades, in addition to reducing renal failure development in almost 70% [5,9].

[☆] Grants: This study received no grants or other financial supports from any institution.

^{☆☆} Conflicts of interest: The authors declare that they have no potential conflicts of interest.

* Corresponding author at: Instituto Goiano de Medicina—Professor Alfredo de Castro Avenue, 377, Setor Oeste, 74110-030, Goiania, GO, Brazil. Tel.: +55 62 9965 4454.

E-mail address: rximenes@gmail.com (R.O. Ximenes).

However, the benefit of such treatment may be restricted to high-risk patients (serum creatinine >1 mg/dL and/or serum bilirubin >4 mg/dL), who should be recognized as early as possible [10–12].

1.2. Importance

Despite the great importance of identifying high-risk patients among cirrhotic decompensated individuals, there are no current criteria developed or validated in the emergency setting, although this is the place where most patients with decompensated cirrhosis will be evaluated and would benefit from early detection and treatment of bacterial infections and other severe complications.

1.3. Goals of this investigation

In this article, we evaluated patients with decompensated cirrhosis who visited the ED and were admitted to the hospital. Our aim was to evaluate the early predictors, on the arrival to the ED, of the presence of bacterial infection and in-hospital mortality.

2. Materials and methods

2.1. Study design and setting

This was a retrospective single-center study performed in the ED of a Brazilian university hospital. The Hospital das Clínicas, which belongs to the University of São Paulo's Medical School (HCFMUSP), is a tertiary university hospital with more than 180,000 annual ED visits, of which 14,000 result in hospital admission. In this hospital, the hepatology service includes a 24-hour endoscopy unit, interventional radiology, a hepatology intensive care unit, and a liver transplantation service. The study was approved by the ethical review board of HCFMUSP (CAPPesq).

2.2. Selection of participants

From January 1, 2009, to June 30, 2011, consecutive patients seen in the ED of HCFMUSP with decompensated cirrhosis were identified in the hospital database. Medical records of patients with ED diagnosis of cirrhosis (*International Statistical Classification of Diseases, 10th Revision* [ICD-10], code K74) or correlated conditions (viral hepatitis [ICD-10 code B18], alcoholic liver disease [ICD-10 code K70], autoimmune hepatitis [ICD-10 code K75.4], hemochromatosis [ICD-10 code E83.1], Wilson disease [ICD-10 code E83.0], other liver diseases [ICD-10 code K76], ascites [ICD-10 code R18], esophageal varices [ICD-10 code I85], and peritonitis [ICD-10 code K65]) were screened for inclusion by 2 independent researchers. For patients with more than 1 hospital admission during the study period, only data from the first admission were considered.

Inclusion criteria were (a) patients aged 18 years or older; (b) cirrhosis diagnosis by liver biopsy or a combination of clinical, laboratory, radiological, and endoscopic data; and (c) admission to the ED related to cirrhosis decompensation (hepatic encephalopathy, ascites, variceal bleeding, and/or jaundice).

Exclusion criteria were (a) patients with terminal illness (metastatic neoplasia or severe cardiopulmonary or neurologic disease); (b) hospital discharge in less than 24 hours after admission; and (c) patients with previous solid organ transplantation.

The medical record review was performed by 3 fifth year medical students and 2 members of the medical staff (1 emergency physician and 1 hepatologist). Medical students were trained on the first 20 charts and could then contact the staff at any time to clarify doubts.

Data from ED admission were inserted into standardized electronic spreadsheets (software Excel, Microsoft Office 2007), which included age, sex, cirrhosis etiology, cirrhosis complications (ascites, encephalopathy, variceal bleeding, hepatorenal syndrome, and spontaneous bacterial peritonitis), comorbidities, clinical variables

(heart rate, blood pressure, temperature, and Glasgow Coma Scale), laboratory results (C-reactive protein [CRP], leukocytes, neutrophils, lymphocytes, neutrophil/lymphocyte relationship, creatinine, urea, sodium, international normalized ratio [INR], bilirubin, and albumin), culture results, Child-Pugh classification, Model for End-Stage Liver Disease (MELD) score, MELD-Na score, site of infection, and infection classification according to International Sepsis Definitions Conference (ISDC) 2001 (absent, possible, probable, or definite and sepsis, severe sepsis, or septic shock) [13]. Standardized electronic spreadsheets also included all creatinine values measured during the first 48 hours from hospital admission, length of hospital stay, and cause of death in nonsurvivors.

The presence of AKI was defined according to Acute Kidney Injury Network criteria [14]. For AKI determination, we considered serum creatinine measures during the first 48 hours from hospital admission. *Acute kidney injury* was defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dL or a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline). In this study, data on urine output were not available [15].

All collected data were assessed by another investigator (AQF) for the identification of disagreements and obvious problems.

2.3. Interventions

Emergency physicians managed patients with cirrhosis at their discretion. At HCFMUSP, most physicians follow American Association for Study of Liver Disease or European Association for Study of the Liver guidelines for cirrhosis complications management. Physicians were not aware of this study.

2.4. Outcome measures

Patients' infection status was defined according to the ISDC 2001 [13]. Patients classified with definite, probable, or possible infection were considered to be patients with bacterial infection.

The severity of their infection was then classified in sepsis, severe sepsis, or septic shock, according to standard definitions [13].

Mortality was determined during hospital stay. Patients who were discharged from hospital were considered survivors. There was no follow-up after hospital discharge.

2.5. Statistical analysis

Statistical analysis was performed with the software R 3.0.1 (The R Foundation for Statistical Computing, 2013). Discrete variables were reported as percentages. Continuous variables were presented as medians with interquartile ranges.

Using area under the receiver operating characteristic (ROC) curve (AUROC) and maximum Youden Index, the continuous variables' effectiveness and best cutoff values to identify patients with bacterial infection and to identify survivors were determined. Continuous variables were categorized according to these cutoff values.

Simple binary logistic regression models were built, and variables with $P \leq .1$ were inserted in multiple binary logistic regression models to determine variables independently associated with bacterial infection and to determine variables independently associated with mortality according to the Akaike Information Criterion.

Scores using variables associated with bacterial infection and mortality were built from the resized regression coefficients giving a range of scores from 0 to 100 points. Receiver operating characteristic curve analysis was performed to evaluate the scores' discrimination effectiveness using AUROC and maximum Youden Index. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were calculated at maximum Youden Index cutoffs.

Bootstrap analysis was used for scores validation (1000 random bootstrap samples of patients drawn with replacement from the original sample) to calculate the optimism on the effectiveness measures.

Sampling unit was disregarded when there was at least 1 variable involved in the analysis with missing data.

3. Results

3.1. Characteristics of study subjects

During the study period, there were 277 ED admissions from 159 patients with cirrhosis. Ten patients were excluded: 7 for hospital discharge in less than 24 hours after admission, 2 with terminal illness (metastatic cancer), and 1 with previous liver transplantation. The remaining 149 patients were considered in our analysis. Baseline characteristics of eligible patients are shown in Table 1.

The cirrhosis decompensations that caused ED admission were ascites in 113 (75.8%) patients, hepatic encephalopathy in 88 (59.1%), jaundice in 43 (29.0%), and variceal bleeding in 12 (10.1%).

Acute kidney injury according to Acute Kidney Injury Network criteria occurred in 61 patients (40.9%) during the first 48 hours after admission. Median length of hospital stay was 5 days (2–9 days).

3.2. Outcomes

Seventy-two patients (48.3%) were diagnosed with bacterial infection: 27 (37.5%) with spontaneous bacterial peritonitis, 20 (27.8%) with urinary tract infection, 11 (15.3%) with pneumonia, 9 (12.5%) with skin and soft tissue infection, and 5 (6.9%) with other sites of infection. The classification of severity of infection was sepsis in 9 patients (12.5%), severe sepsis in 14 (19.4%), and septic shock in 4 (5.6%). The other 45 patients (62.5%) did not meet criteria for sepsis.

Ninety-nine cultures were performed, of which 30 (30.3%) were positive. Isolated microorganisms were *Escherichia coli* in 12 (40.0%) cultures, *Klebsiella pneumoniae* in 10 (33.3%), *Staphylococcus aureus* in 3 (10.0%), other gram negatives in 3 (10.0%), and other gram positives in 2 (6.7%).

During hospital stay, 36 patients (24.2%) died. Cause of death was sepsis in 23 patients (63.9%), variceal bleeding in 5 (13.9%), AKI in 3 (8.3%), and other causes in 5 (13.9%). Among patients with AKI, 31.1% died,

Table 1

Baseline characteristics of eligible patients, n = 149

| | |
|---------------------------------|--------------------|
| Age, y | 59 (52–66) |
| Sex (masculine) | 77.9% |
| Cirrhosis etiology | |
| Alcohol | 53.0% |
| Hepatitis C | 16.8% |
| Cryptogenic | 10.1% |
| Alcohol + hepatitis C | 8.7% |
| Other | 11.4% |
| Ascites | 75.8% |
| Heart rate, beat/min | 86 (74–99) |
| Systolic blood pressure, mm Hg | 111.5 (99.7–130) |
| Diastolic blood pressure, mm Hg | 70 (55–80) |
| CRP, mg/L | 36.7 (11.0–76.1) |
| Leukocytes, per mm ³ | 7850 (5560–11 050) |
| Creatinine, mg/dL | 1.2 (0.9–2.3) |
| Sodium, mEq/L | 136 (131–140) |
| INR | 1.5 (1.3–1.8) |
| Bilirubin, mg/dL | 2.2 (1.3–5.0) |
| Albumin, g/dL | 2.8 (2.4–3.3) |
| Child–Pugh | |
| A | 3.5% |
| B | 49.3% |
| C | 47.2% |
| MELD | 18 (13–25) |
| MELD–Na | 21 (16–29) |

Table 2

Variables with $P \leq .1$ in the simple binary logistic regression model for bacterial infection

| Variable | OR (95% CI) | P |
|----------------------------------|-------------------|-------|
| Ascites | 1.93 (0.89–4.19) | .095 |
| No hepatic encephalopathy | 2.33 (1.19–4.55) | .013 |
| HR >90 beat/min | 2.04 (0.99–4.2) | .055 |
| SBP <90 mm Hg | 2.33 (0.93–5.88) | .071 |
| DBP <60 mm Hg | 2.17 (1.05–4.55) | .037 |
| Leukocytes >9470/mm ³ | 3.05 (1.53–6.11) | .002 |
| Neutrophil >5400/mm ³ | 2.93 (1.5–5.7) | .002 |
| Lymphocytes ≤900/mm ³ | 3.23 (1.56–6.67) | .001 |
| N/L >4.85 | 4.7 (2.35–9.38) | <.001 |
| INR >1.66 | 2.05 (0.99–4.23) | .052 |
| CRP >59.4 mg/L | 5.25 (2.09–13.16) | <.001 |

Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; N/L, neutrophil/lymphocyte relationship.

compared to 17.6% among those without. Mortality rate in patients with bacterial infection was 31.9% compared to 18.1% in those without.

3.3. Variables associated with bacterial infection

In the simple binary logistic regression model, variables associated with bacterial infection that were subsequently inserted into the multiple binary logistic regression model are shown in Table 2.

After the multiple binary logistic regression, variables independently associated with bacterial infection were lymphocytes less than or equal to 900/mm³ (odds ratio [OR], 3.85 [95% confidence interval [CI], 1.47–10]; $P = .006$) and CRP greater than 59.4 mg/L (OR, 5.05 [95% CI, 1.93–13.2]; $P = .001$). In the ROC curve analysis, lymphocytes had an AUROC of 0.60 (0.516–0.701); and CRP, an AUROC of 0.72 (0.622–0.817).

3.4. Variables associated with mortality

In the simple binary logistic regression model, variables associated with mortality that were subsequently inserted into the multiple binary logistic regression model are shown in Table 3.

After the multiple binary logistic regression, variables independently associated with mortality were creatinine greater than 1.5 mg/dL (OR, 4.35 [95% CI, 1.87–10.1]; $P = .001$) and INR greater than 1.65 (OR, 3.71 [95% CI, 1.6–8.61]; $P = .002$). In ROC curve analysis, creatinine had an AUROC of 0.756 (0.657–0.855) and INR an AUROC of 0.701 (0.598–0.803).

3.5. Score of infection prediction

The score designed to predict bacterial infection (Bacterial Infection in Cirrhosis Score [BIC Score]) can be calculated using the following formula:

$$\text{BIC Score} = -22.0770 + 0.2715 \times \text{HR} + 0.0058 \times \text{Leukocytes} + \text{N/L} \\ \times (1.7918 - 0.0067 \times \text{Lymphocytes}) + 0.2099 \times \text{CRP}$$

Receiver operating characteristic curve analysis showed an AUROC of 0.82 (0.734–0.905), with the best cutoff value of 33.55. Patients

Table 3

Variables with $P \leq .1$ in the simple binary logistic regression model for mortality

| Variable | OR (95% CI) | P |
|------------------------------------|-------------------|-------|
| AKI | 2.98 (1.37–6.46) | .006 |
| SBP ≤100 mm Hg | 2.56 (1.08–5.88) | .034 |
| DBP ≤68 mm Hg | 2.5 (1.05–5.88) | .038 |
| Leukocytes >11 420/mm ³ | 3.96 (1.74–9) | .001 |
| Neutrophil >7100/mm ³ | 3.8 (1.73–8.31) | .001 |
| N/L >6 | 3.1 (1.43–6.74) | .004 |
| Na ≤135 mEq/L | 1.92 (0.9–4.17) | .089 |
| Creatinine >1.5 mg/dL | 4.85 (2.17–10.83) | <.001 |
| Albumin ≤2.7 g/dL | 2.13 (0.97–4.54) | .06 |
| Bilirubin >2.77 mg/dL | 2.09 (0.97–4.47) | .059 |
| INR >1.65 | 4.25 (1.92–9.4) | <.001 |

Table 4
Characteristics of BIC Score performance

| | Value (95% CI) | Validation values (95% CI) |
|-------------|------------------|----------------------------|
| Sensitivity | 0.69 (0.54–0.81) | 0.64 (0.48–0.78) |
| Specificity | 0.83 (0.69–0.92) | 0.80 (0.63–0.9) |
| PPV | 0.8 (0.65–0.89) | 0.77 (0.60–0.85) |
| NPV | 0.72 (0.57–0.86) | 0.67 (0.54–0.82) |
| PLR | 3.95 (2.05–7.63) | – |
| NLR | 0.38 (0.24–0.59) | – |

with a BIC Score above this value had an 80% chance of bacterial infection, compared to a 28% chance in patients with a BIC Score less than 33.55. Sensitivity, specificity, PPV, NPV, PLR, and NLR are shown in Table 4 as well as sensitivity, specificity, PPV, and NPV calculated after correction for optimism in the bootstrap validation setting.

3.6. Score of mortality prediction

The score designed to predict mortality (Mortality in Cirrhosis Emergency Department Score [MED Score]) can be calculated using the following formula:

$$\text{MED Score} = -21.4074 + 8.8879 \times \text{Creatinine} + 17.1078 \times \text{INR}$$

Receiver operating characteristic curve analysis showed an AUROC of 0.801 (0.714–0.889), with the best cutoff value of 27.37. Patients with a MED Score above this value had a mortality rate of 60%, compared to a mortality rate of 11% in patients with a MED Score less than 27.37. Sensitivity, specificity, PPV, NPV, PLR, and NLR are shown in Table 5 as well as sensitivity, specificity, PPV, and NPV calculated after correction for optimism in the bootstrap validation setting.

The AUROCs for MELD and MELD Na scores were 0.766 and 0.779, respectively. The Figure shows the ROC curve of MED Score.

4. Discussion

This series of 149 consecutive patients with cirrhosis admitted to the ED included patients with advanced liver failure (47.2% Child-Pugh C; median MELD at admission, 18), mainly due to alcoholic cirrhosis (53%). These patients had a high incidence of AKI during the first 48 hours after admission (40.9%) and a high in-hospital mortality rate (24.2%).

As with all retrospective studies, ours has some limitations. Medical records frequently have missing data. In this study, heart rate was not recorded in 20 charts (13.4%) and blood pressure in 25 (16.8%). Some laboratory tests were not performed in all patients, especially CRP, which was not measured in 43 patients (28.9%) at admission. These missing data reduce the study strength but do not invalidate our results, as complete data from ED admission were available in more than a hundred patients, which is a considerable sample number compared to most studies in cirrhotic patients [4–6].

Our study was single centered, which may compromise its external validity. The correction for optimism in the bootstrap validation helped to minimize this limitation, but an external validation of our results is warranted in the future. In fact, as our study is not a derivation of a

Table 5
Characteristics of MED Score performance

| | Value (95% CI) | Validation values (95% CI) |
|-------------|------------------|----------------------------|
| Sensitivity | 0.69 (0.52–0.84) | 0.62 (0.48–0.82) |
| Specificity | 0.85 (0.76–0.91) | 0.81 (0.74–0.89) |
| PPV | 0.6 (0.47–0.77) | 0.56 (0.43–0.72) |
| NPV | 0.89 (0.8–0.94) | 0.89 (0.79–0.93) |
| PLR | 4.49 (2.76–7.32) | – |
| NLR | 0.36 (0.22–0.60) | – |

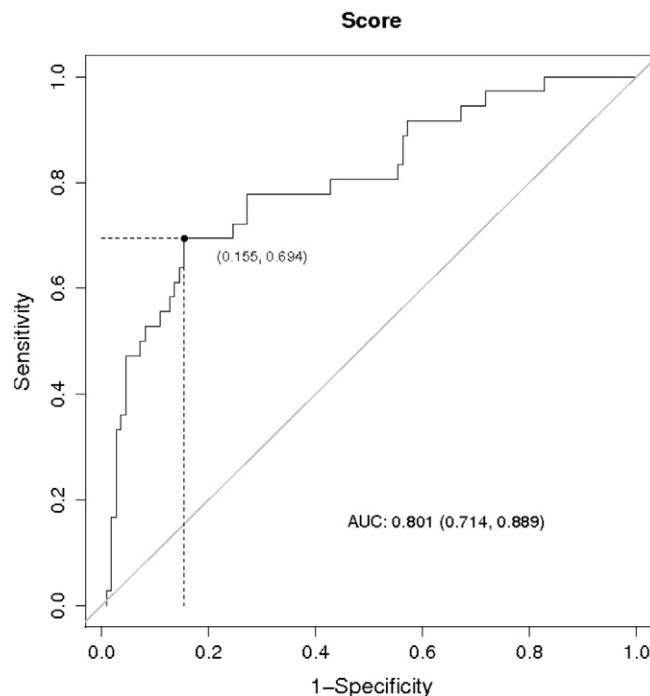


Figure. Receiver operating characteristic curve of MED Score.

clinical decision rule, a prospective validation will be necessary before our results have any applicability in clinical practice.

We found that lymphopenia and an elevated CRP are independently related to the diagnosis of bacterial infection in this population. The AUROC for CRP in the diagnosis of bacterial infection was 0.72, which is consistently lower than previously reported [16–18]. The possible explanation for this difference is the severity of liver disease in the population, which is related to a decrease in CRP accuracy in bacterial infection diagnosis [16]. Furthermore, our cohort consisted of patients admitted to the ED, who may have different characteristics to patients in other scenarios, such as a gastroenterology department or an intensive care unit. To our knowledge, the only study that evaluated CRP accuracy for bacterial infection diagnosis in patients with cirrhosis in the ED was performed by Li et al [17]. However, there are important concerns raised about the study's methodology. First of all, cirrhosis diagnosis relied on abdominal sonography, which is not an accurate method when used in isolation from other parameters such as liver biopsy, clinical, laboratory, and endoscopic data. The severity of liver disease was not evaluated, using neither Child-Pugh score nor MELD score, which is an important issue in CRP level accuracy interpretation, as previously mentioned. In addition, the study protocol does not specify the criteria used for bacterial infection and sepsis diagnosis and classification because 33.3% of patients the authors had diagnosed with sepsis did not meet Systemic Inflammatory Response Syndrome criteria, which is necessary for sepsis diagnosis according to ISDC [13].

Associating variables related to bacterial infection in a score (BIC Score) allows greater accuracy than using these variables in isolation. An advantage of BIC Score is that it uses simple and widely available parameters that can be obtained in the first hours after ED arrival, which makes it practical.

The parameters independently associated with mortality in our study were creatinine and INR, which are both part of the MELD score. Although MELD was developed to predict mortality 3 months after elective transjugular intrahepatic portosystemic shunt insertion [19], it has been validated in other clinical scenarios and is now used to prioritize patients on liver transplantation lists. In the emergency setting, MELD score performance to predict mortality was evaluated in patients with emergency surgery under general anesthesia [20] and

unstable gastrointestinal bleeding [21], with an AUROC similar from the one found in our study (0.707 and 0.736, respectively, vs 0.766). Our score, designed to predict inhospital mortality in patients with cirrhosis admitted to the ED (MED Score), performed better than MELD in this scenario, with an AUROC of 0.801.

In summary, in this cohort of ED patients with decompensated cirrhosis, lymphopenia and elevated CRP were related to bacterial infection. In this scenario, elevated creatinine and INR were related to inhospital mortality. Future areas of research resulting from this study should include a prospective validation of our scores in the emergency setting and comparison with traditional prognostic scores used in patients with cirrhosis to predict clinical outcomes in this scenario.

Acknowledgments

The authors declare that they did not receive help from anyone else during the research such as language or writing assistance, proofreading, or others.

References

- [1] Wong F, Bernardi M, Balk R, Christman B, Moreau R, Garcia-Tsao G, et al. Sepsis in cirrhosis: report on the 7th meeting of the International Ascites Club. *Gut* 2005; 54(5):718–25.
- [2] Navasa M, Fernández J, Rodés J. Bacterial infections in liver cirrhosis. *Ital J Gastroenterol Hepatol* 1999;31(7):616–25.
- [3] Foreman MG, Mannino DM, Moss M. Cirrhosis as a risk factor for sepsis and death: analysis of the National Hospital Discharge Survey. *Chest* 2003;124(3):1016–20.
- [4] D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006;44(1):217–31.
- [5] Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* 1999;341(6):403–9.
- [6] Terra C, Guevara M, Torre A, Gilabert R, Fernández J, Martín-Llahí M, et al. Renal failure in patients with cirrhosis and sepsis unrelated to spontaneous bacterial peritonitis: value of MELD score. *Gastroenterology* 2005;129(6):1944–53.
- [7] Loo NM, Souza FF, Garcia-Tsao G. Non-hemorrhagic acute complications associated with cirrhosis and portal hypertension. *Best Pract Res Clin Gastroenterol* 2013;27(5): 665–78.
- [8] Ratib S, Fleming KM, Crooks CJ, Aithal GP, West J. 1 and 5 year survival estimates for people with cirrhosis of the liver in England, 1998–2009: a large population study. *J Hepatol* 2014;60(2):282–9.
- [9] Garcia-Tsao G. Bacterial infections in cirrhosis: treatment and prophylaxis. *J Hepatol* 2005;42(Suppl. (1)):S85–92.
- [10] Terg R, Gadano A, Cartier M, Casciato P, Lucero R, Muñoz A, et al. Serum creatinine and bilirubin predict renal failure and mortality in patients with spontaneous bacterial peritonitis: a retrospective study. *Liver Int* 2009;29(3):415–9.
- [11] Poca M, Concepción M, Casas M, Alvarez-Urturi C, Gordillo J, Hernández-Gea V, et al. Role of albumin treatment in patients with spontaneous bacterial peritonitis. *Clin Gastroenterol Hepatol* 2012;10(3):309–15.
- [12] Sigal SH, Stanca CM, Fernandez J, Arroyo V, Navasa M. Restricted use of albumin for spontaneous bacterial peritonitis. *Gut* 2007;56(4):597–9.
- [13] Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003;31(4):1250–6.
- [14] Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;11(2):R31.
- [15] de Carvalho JR, Villela-Nogueira CA, Luiz RR, Guzzo PL, da Silva Rosa JM, Rocha E, et al. Acute kidney injury network criteria as a predictor of hospital mortality in cirrhotic patients with ascites. *J Clin Gastroenterol* 2012;46(3):e21–6.
- [16] Papp M, Vitalis Z, Altörjay I, Tornai I, Udvardy M, Harsfalvi J, et al. Acute phase proteins in the diagnosis and prediction of cirrhosis associated bacterial infections. *Liver Int* 2012;32(4):603–11.
- [17] Li CH, Yang RB, Pang JH, Chang SS, Lin CC, Chen CH, et al. Procalcitonin as a biomarker for bacterial infections in patients with liver cirrhosis in the emergency department. *Acad Emerg Med* 2011;18(2):121–6.
- [18] Tsiakalos A, Karatzafiris A, Ziakas P, Hatzis G. Acute-phase proteins as indicators of bacterial infection in patients with cirrhosis. *Liver Int* 2009;29(10):1538–42.
- [19] Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology* 2000;31(4):864–71.
- [20] Kim SH, Han YD, Lee JG, Kim dY, Choi SB, Choi GH, et al. MELD-based indices as predictors of mortality in chronic liver disease patients who undergo emergency surgery with general anesthesia. *J Gastrointest Surg* 2011;15(11):2029–35.
- [21] Hsu SC, Chen CY, Weng YM, Chen SY, Lin CC, Chen JC. Comparison of 3 scoring systems to predict mortality from unstable upper gastrointestinal bleeding in cirrhotic patients. *Am J Emerg Med* 2014;32(5):417–20.