Turk J Gastroenterol *2016; 27: 180-6*

Albumin-bilirubin score for predicting the in-hospital mortality of acute upper gastrointestinal bleeding in liver cirrhosis: A retrospective study

LIVER

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ABSTRACT

Background/Aims: The albumin-bilirubin (ALBI) score is a new model for assessing the severity of liver dysfunction. In the present study, we aimed to retrospectively compare the performance of ALBI with Child-Pugh and the model for end-stage liver disease (MELD) scores for predicting the in-hospital mortality of acute gastrointestinal bleeding (AUGIB) in liver cirrhosis.

Materials and Methods: All cirrhotic patients with AUGIB were eligible, provided they had the data needed to determine the ALBI score. Areas under the receiving-operator characteristics curve (AUC) are reported.

Results: Overall, 631 patients were included. In all the included patients, the AUC of the ALBI, Child-Pugh, and MELD scores were 0.808, 0.785 (p=0.5831), and 0.787 (p=0.7033), respectively. In patients with only hepatitis B virus-related liver cirrhosis, the AUC of the ALBI, Child-Pugh, and MELD scores were 0.865, 0.836 (p=0.6064), and 0.818 (p=0.6399), respectively. In patients with only alcohol-related liver cirrhosis, the AUC of the ALBI, Child-Pugh, and MELD scores were 0.869, 0.860 (p=0.9003), and 0.801 (p=0.5548), respectively. In patients treated with endoscopic therapy for AUGIB, the AUC of the ALBI, Child-Pugh, and MELD scores were 0.873, 0.884 (p=0.7898), and 0.834 (p=0.5531), respectively.

Conclusion: The prognostic performance of the ALBI score was comparable with that of the Child-Pugh and MELD scores for predicting the in-hospital mortality of AUGIB in liver cirrhosis.

Keywords: Liver cirrhosis, bleeding, prognosis, survival, albumin-bilirubin score

INTRODUCTION

Recently, the albumin-bilirubin (ALBI) score has been established as a more convenient and evidence-based model to assess the severity of liver dysfunction in patients with hepatocellular carcinoma (HCC) (1,2). The major advantage is that the prognostic value is comparable between the ALBI and Child-Pugh scores, but two subjective variables [i.e., ascites and hepatic encephalopathy [HE]] included in the Child-Pugh score are excluded from the ALBI score. The benefit of the ALBI score for assessing liver function has also been confirmed in advanced HCC patients treated with sorafenib (3). An ALBI score of >– 2.118 may be inappropriate for the use of sorafenib. More recently, a retrospective study also compared the prognostic performance of ALBI versus Child-Pugh, the model for end-stage liver disease (MELD), Mayo risk, Yale, European, and Newcastle scores in patients with primary biliary cirrhosis (4). Compared with other scores, the ALBI score had the highest prognostic performance in such patients. Furthermore, in the multivariate analysis, the ALBI score was the only independent prognostic factor.

Acute upper gastrointestinal bleeding (AUGIB) is a lethal complication of liver cirrhosis. Child-Pugh and MELD scores are two of the most important models for predicting the survival of AUGIB in such patients (5,6). Several studies by our team and others have also suggested a similar prognostic performance between them (7,8). However, the role of the ALBI score for the

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Received: December 03, 2015 **Accepted:** January 12, 2016

assessment of prognosis of AUGIB in liver cirrhosis remains unclear. Herein, we conducted a retrospective study to compare the prognostic performance of the ALBI score with two traditional models in a large cohort of cirrhotic patients with AUGIB.

MATERIALS AND METHODS

Study design

In this retrospective study, all patients with a diagnosis of liver cirrhosis and AUGIB who were admitted to the General Hospital of Shenyang Military Area hospital between January 2011 and June 2014 were potentially eligible. The exclusion criteria were as follows: 1) malignancy, especially HCC and 2) absence of data to calculate the ALBI and Child-Pugh scores. Notably, repeated admission was not excluded. The primary end point was the in-hospital mortality. This study was approved by the Medical Ethical Committee of the General Hospital of Shenyang Military Area. The approval number was No. k (2015) 7. The patient's informed written consent was waived because of the retrospective nature.

Data collection

All data were collected from the patients' medical charts by our study group. Some patients had been included in previous studies (7,9-13) because our study group has continuously collected the data of cirrhotic patients admitted to our hospital. The primary data collected were as follows: age, sex, etiology of liver diseases, ascites, HE, red blood cell, hemoglobin, white blood cell, platelet count, total bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, blood urea nitrogen, creatinine, sodium, potassium, prothrombin time, activated partial thromboplastin time, and international normalized ratio. Treatment modalities for AUGIB included endoscopic therapy (i.e., band ligation, sclerotherapy, and/or tissue glue injection), Sengstaken-Blackmore tube, somatostatin or octreotide, and blood transfusion.

Definitions

The definitions of AUGIB were reviewed according to the following considerations. First, upper gastrointestinal bleeding was considered if the patients presented with hematemesis and/or melena. Second, fecal occult blood tests were also reviewed. Upper gastrointestinal bleeding was considered if the fecal occult blood test at admission was positive. Third, AUGIB was defined as an acute episode of upper gastrointestinal bleeding within 5 days before admission (14). AUGIB was not considered if the interval between a recent episode of upper gastrointestinal bleeding and admission was unclear. Because not all patients underwent endoscopy, the source of bleeding was not restricted in our study. AUGIB was independently evaluated by two investigators, and finally validated by another investigator. A consensus was reached after discussion among them. Grades of HE and ascites were evaluated according to the relevant guidelines (15,16). The ALBI, Child-Pugh, and MELD scores were calculated according to the relevant formula (1,5,6).

ALBI score=($\log_{10}$ bilirubin×0.66)+(albumin×−0.085).
In this equation, the unit of bilirubin is umol/L and that of albumin is g/L.

Statistical analysis

All statistical analyses were performed using the MedCalc software version 11.4.2.0. (Microsoft partner program, MedCalc Software bvba, Ostend, Belgium). Continuous data were expressed as the mean±standard deviation (SD) and the median with minimum and maximum. Categorical data were expressed as the frequency (percentage). Receiving-operator characteristics curve analyses were performed to identify the discriminative capacity of the ALBI, Child-Pugh, and MELD scores in predicting the in-hospital mortality. Areas under the receiving-operator characteristics curves (AUC) with 95% confidence intervals (CIs) were calculated and compared among using the DeLong tests. A best cut-off value was selected as the sum of sensitivity and specificity was maximal. Then, sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), positive predictive value (PPV), and negative predictive value (NPV) with 95% CIs were reported. Subgroup analyses were performed in patients with only hepatitis B or C virus-related liver cirrhosis and in those treated with endoscopic therapy for AUGIB. $P<0.05$ was considered statistically significant.

RESULTS

Patients

During this period, a total of 713 cirrhotic patients with AUGIB were admitted to our hospital. Among them, 631 patients, in whom the ALBI and Child-Pugh scores could be calculated according to the adequate data, were finally included in this study. The patients' characteristics are shown in Table 1. A majority of patients were male and had hepatitis B or C virus infection and alcohol abuse. Among the 381 patients treated with endoscopic therapy for AUGIB, 160 underwent band ligation alone, 7 underwent band ligation in combination with sclerotherapy, 47 underwent band ligation in combination with tissue glue injection, 2 underwent band ligation in combination with sclerotherapy and tissue glue injection, 35 underwent sclerotherapy alone, 3 underwent sclerotherapy in combination with tissue glue injection, 124 underwent tissue glue injection alone, and 1 underwent endoclip hemostasis. In the remaining two patients, endoscopic treatment modalities were unclear because the relevant data were unavailable from medical charts.

Comparison of in-hospital mortality among the ALBI, Child-Pugh, and MELD scores in all the patients

The in-hospital mortality was 4.4% (28/631). The AUC of the ALBI score for predicting the in-hospital mortality was 0.808 (95% CI: 0.775–0.838, $p<0.0001$) (Figure 1a). The best cut-off value of

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Table 1. Patients' characteristics

	N	Mean or Frequency	SD	Median	Minimum	Maximum
Age (years)	631	55.91	12.0622	54.92	6.28	95.13
Sex (Male/Female) - n	631	423/208				
Etiology - n	631					
HBV alone		183				
HCV alone		40				
HBV+HCV		2				
Alcohol		158				
HBV+Alcohol		31				
HCV+Alcohol		9				
HBV+HCV+Alcohol		2				
Others or unknown		206				
Ascites (No/Mild/Moderate-Large) - n	631	330/65/236				
HE (No/Grade I-II/Grade III-IV) - n	631	590/35/6				
WBC (10^9/L)	630	6.198	5.1559	4.6	0.9	46.1
RBC (10^{12}/L)	630	2.617	0.6767	2.55	0.93	5.1
Hb (g/L)	630	73.994	21.9035	72	23	150
PLT (10^9/L)	630	100.716	92.6186	75	13	842
TBIL (umol/L)	631	28.552	36.7006	19.8	2.1	553.6
ALB (g/L)	631	30.372	6.6167	30.5	10	48
ALP (U/L)	631	93.697	84.1331	71.9	17	889
GGT (U/L)	631	80.146	132.9675	33	5	1168
ALT (U/L)	631	32.623	51.7378	23	5	1064
AST (U/L)	631	50.311	105.2471	30	7	1487
BUN (umol/L)	618	8.957	5.859	7.71	1.63	48
Cr (umol/L)	618	69.827	60.7157	60	20	919
Na (mmol/L)	624	138.513	4.3934	138.9	116.4	153.9
K (mmol/L)	624	4.125	0.5548	4.09	2.78	7.87
PT (s)	631	17.178	4.945	16.1	10.8	62.8
INR	631	1.435	0.5985	1.29	0.77	7.96
APTT (s)	628	41.651	9.7612	40.15	25.7	168
ALBI score	631	−1.71	0.6331	−1.726	−3.403	0.219
Child-Pugh score	631	7.567	1.8977	7	5	15
MELD score	618	6.949	6.5028	5.844	−11.501	37.649
Treatment - n						
Somatostatin or octreotide	631	582				
Blood transfusion	631	403				
Sengstaken Blakemore tube	631	19				
Endoscopic therapy	631	381				

HBV: hepatitis B virus; HCV: hepatitis C virus; HE: hepatic encephalopathy; WBC: white blood cell; RBC: red blood cell; Hb: hemoglobin; PLT: platelet; TBIL: total bilirubin; ALB: albumin; ALP: alkaline phosphatase; GGT: gamma-glutamyl transpeptidase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; Cr: creatinine; PT: prothrombin time; INR: international normalized ratio; APTT: activated partial thromboplastin time; ALBI: albumin-bilirubin, MELD: model for end-stage liver disease.

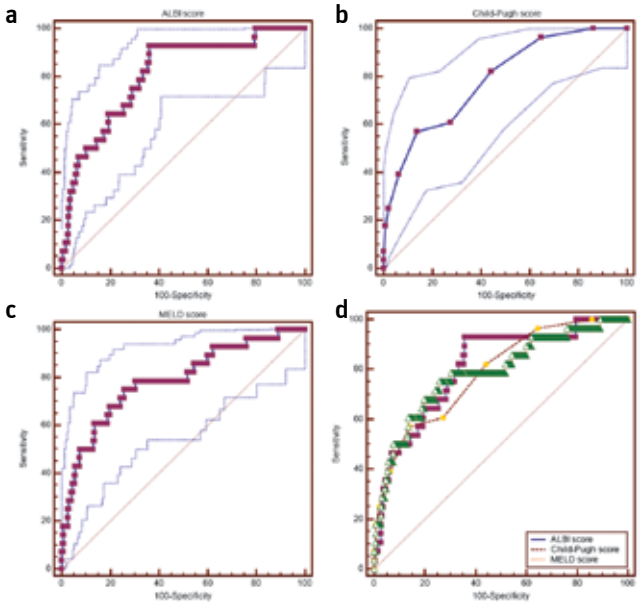

Figure 1. a-d. ROC of the ALBI, Child-Pugh, and MELD scores for predicting the in-hospital mortality of AUGIB in all the included patients. Panel A: ALBI score. Panel B: Child-Pugh score. Panel C: MELD score. Panel D: comparison of the three scores.

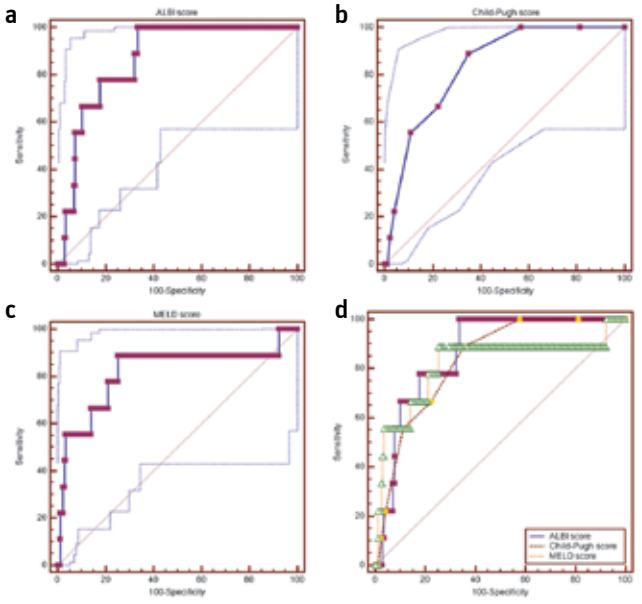

Figure 2. a-d. ROC of the ALBI, Child-Pugh, and MELD scores for predicting the in-hospital mortality of AUGIB in patients with only hepatitis B virus-related liver cirrhosis. Panel A: ALBI score. Panel B: Child-Pugh score. Panel C: MELD score. Panel D: comparison of the three scores.

the ALBI score was −1.5237, with a sensitivity of 92.86% (95% CI: 76.5–99.1), a specificity of 64.01% (95% CI: 60.0–67.9), a PLR of 2.58 (95% CI: 2.3–2.9), an NLR of 0.11 (95% CI: 0.03–0.4), a PPV of 10.7 (95% CI: 7.1–15.3), and an NPV of 99.5 (95% CI: 98.1–99.9).

The AUC of the Child-Pugh score for predicting the in-hospital mortality was 0.785 (95% CI: 0.751–0.817, p<0.0001) (Figure 1b). The best cut-off value of the Child-Pugh score was 9, with a sensitivity of 57.14% (95% CI: 37.2–75.5), a specificity of 86.24% (95% CI: 83.2–88.9), a PLR of 4.15 (95% CI: 3.0–5.7), an NLR of 0.50 (95% CI: 0.3–0.8), a PPV of 16.2 (95% CI: 9.5–24.9), and an NPV of 97.7 (95% CI: 96.1–98.8).

The AUC of the MELD score for predicting the in-hospital mortality was 0.787 (95% CI: 0.752–0.818, P<0.0001) (Figure 1c). The best cut-off value of the MELD score was 9.5801, with a sensitivity of 75.00% (95% CI: 55.1–89.3), a specificity of 74.24% (95% CI: 70.5–77.7), a PLR of 2.91 (95% CI: 2.3–3.6), an NLR of 0.34 (95% CI: 0.2–0.6), a PPV of 12.1 (95% CI: 7.7–18.0), and an NPV of 98.4 (95% CI: 96.8–99.4).

The AUC for predicting the in-hospital mortality was not significantly different between the ALBI versus Child-Pugh (p=0.5831) or MELD scores (p=0.7033) (Figure 1d).

Comparison of in-hospital mortality among the ALBI, Child-Pugh, and MELD scores in patients with only hepatitis B virus-related liver cirrhosis

The in-hospital mortality in patients with only hepatitis B virus-related liver cirrhosis was 3.2% (5/158). The AUC of the ALBI score for predicting the in-hospital mortality was 0.865 (95% CI: 0.806–0.911, p<0.0001) (Figure 2a). The best cut-off value of the ALBI score was −1.5179, with a sensitivity of 100.00% (95% CI: 66.4–100.0), a specificity of 66.67% (95% CI: 59.1–73.6), a PLR of 3.00 (95% CI: 2.7–3.3), an NLR of 0.00, a PPV of 13.4 (95% CI: 6.3–24.0), and an NPV of 100.0 (95% CI: 96.8–100.0).

The AUC of the Child-Pugh score for predicting the in-hospital mortality was 0.836 (95% CI: 0.774–0.887, P<0.0001) (Figure 2b). The best cut-off value of the Child-Pugh score was 7, with a sensitivity of 88.89% (95% CI: 51.8–99.7), a specificity of 64.94% (95% CI: 57.4–72.0), a PLR of 2.54 (95% CI: 2.0–3.3), an NLR of 0.17 (95% CI: 0.03–1.1), a PPV of 11.6 (95% CI: 5.1–21.6), and an NPV of 99.1 (95% CI: 95.2–100.0).

The AUC of the MELD score for predicting the in-hospital mortality was 0.818 (95% CI: 0.753–0.871, P=0.0013) (Figure 2c). The best cut-off value of the MELD score was 9.6615, with a sensitivity of 88.89% (95% CI: 51.8–99.7), a specificity of 74.71% (95% CI: 67.5–81.0), a PLR of 3.51 (95% CI: 2.7–4.5), an NLR of 0.15 (95% CI: 0.02–1.0), a PPV of 15.7 (95% CI: 7.0–28.6), and an NPV of 99.2 (95% CI: 95.7–100.0).

The AUC for predicting the in-hospital mortality was not significantly different between the ALBI versus Child-Pugh (P=0.6064) or MELD scores (p=0.6399) (Figure 2d).

Comparison of in-hospital mortality among the ALBI, Child-Pugh, and MELD scores in patients with alcohol alone related liver cirrhosis

The in-hospital mortality in patients with only alcohol-related liver cirrhosis was 4.9% (9/183). The AUC of the ALBI score for predicting the in-hospital mortality was 0.869 (95% CI: 0.807–0.918, p<0.0001) (Figure 3a). The best cut-off value of the ALBI

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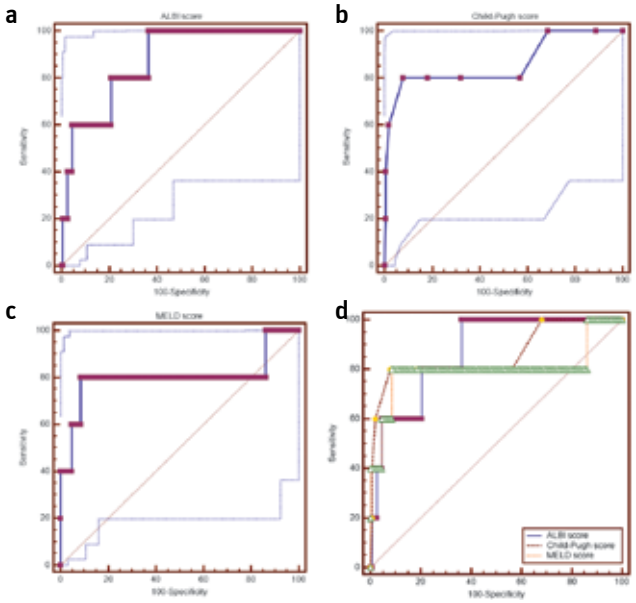

Figure 3. a-d. ROC of the ALBI, Child-Pugh, and MELD scores for predicting the in-hospital mortality of AUGIB in patients with only alcohol-related liver cirrhosis. Panel A: ALBI score. Panel B: Child-Pugh score. Panel C: MELD score. Panel D: comparison of the three scores.

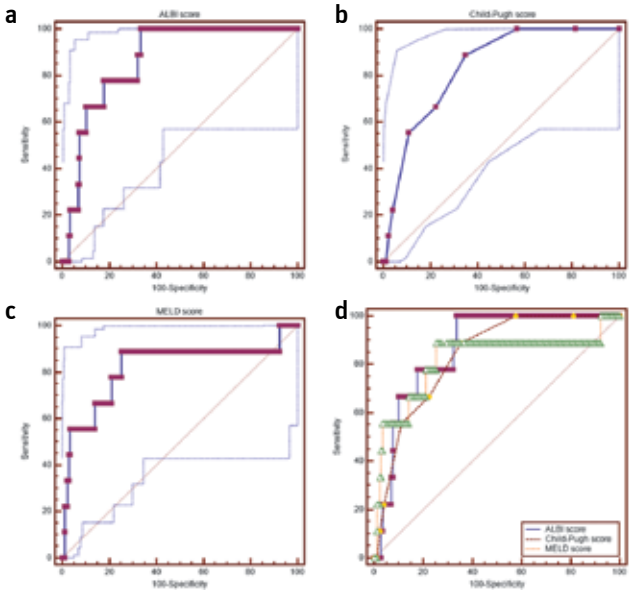

Figure 4. a-d. ROC of the ALBI, Child-Pugh, and MELD scores for predicting the in-hospital mortality of patients treated with endoscopic therapy for AUGIB. Panel A: ALBI score. Panel B: Child-Pugh score. Panel C: MELD score. Panel D: comparison of the three scores.

score was −1.4851, with a sensitivity of 100.0% (95% CI: 47.8–100.0), a specificity of 63.40% (95% CI: 55.2–71.0), a PLR of 2.73 (95% CI: 2.4–3.1), an NLR of 0.00, a PPV of 8.2 (95% CI: 2.7–18.1), and an NPV of 100 (95% CI: 96.2–100.0).

The AUC of the Child-Pugh score for predicting the in-hospital mortality was 0.860 (95% CI: 0.796–0.910, P=0.0033) (Figure 3b). The best cut-off value of the Child-Pugh score was 10, with a sensitivity of 80.0% (95% CI: 28.4–99.5), a specificity of 92.16% (95% CI: 86.7–95.9), a PLR of 10.2 (95% CI: 6.6–15.8), an NLR of 0.22 (95% CI: 0.03–1.4), a PPV of 25.0 (95% CI: 7.3–52.4), and an NPV of 99.3 (95% CI: 96.1–100.0).

The AUC of the MELD score for predicting the in-hospital mortality was 0.801 (95% CI: 0.730–0.861, P=0.0706) (Figure 3c). The best cut-off value of the MELD score was 15.2704, with a sensitivity of 80.0 % (95% CI: 28.4–99.5), a specificity of 91.39% (95% CI: 85.7–95.3), a PLR of 9.29 (95% CI: 6.0–14.4), an NLR of 0.22 (95% CI: 0.04–1.4), a PPV of 23.5 (95% CI: 6.8–49.9), and an NPV of 99.3 (95% CI: 96.0–100.0).

The AUC for predicting the in-hospital mortality was not significantly different between the ALBI versus Child-Pugh (p=0.9003) or MELD scores (p=0.5548) (Figure 3d).

Comparison of in-hospital mortality among the ALBI, Child-Pugh, and MELD scores in patients treated with endoscopic therapy for AUGIB

The in-hospital mortality in patients treated with endoscopic therapy for AUGIB was 2.4% (9/381). The AUC of the ALBI score for predicting the in-hospital mortality was 0.873 (95% CI: 0.836–0.905, p<0.0001) (Figure 4a). The best cut-off value of the ALBI score was −1.492, with a sensitivity of 100.0% (95% CI: 66.4–100), a specificity of 69.62% (95% CI: 64.7–74.3), a PLR of 3.29 (95% CI: 3.1–3.5), an NLR of 0.0, a PPV of 7.4 (95% CI: 3.4–13.6), and an NPV of 100.0 (95% CI: 98.6–100.0).

The AUC of the Child-Pugh score for predicting the in-hospital mortality was 0.884 (95% CI: 0.848–0.915, p<0.0001) (Figure 4b). The best cut-off value of the Child-Pugh score was 9, with a sensitivity of 77.78% (95% CI: 40.0–97.2), a specificity of 88.98% (95% CI: 85.3–92.0), a PLR of 7.06 (95% CI: 5.0–10.0), an NLR of 0.25 (95% CI: 0.07–0.9), a PPV of 14.6 (95% CI: 6.1–27.8), and an NPV of 99.4 (95% CI: 97.8–99.9).

The AUC of the MELD score for predicting the in-hospital mortality was 0.834 (95% CI: 0.793–0.871, p<0.0001) (Figure 4c). The best cut-off value of the MELD score was 8.3613, with a sensitivity of 88.89% (95% CI: 51.8–99.7), a specificity of 75.0% (95% CI: 70.2–79.4), a PLR of 3.56 (95% CI: 2.8–4.5), an NLR of 0.15 (95% CI: 0.02–0.9), a PPV of 8.1 (95% CI: 3.5–15.3), and an NPV of 99.6 (95% CI: 98.0–100.0).

The AUC for predicting the in-hospital mortality was not significantly different between ALBI versus Child-Pugh (P=0.7898) or MELD scores (p=0.5531) (Figure 4d).

DISCUSSION

To the best of our knowledge, our study is the first to explore the prognostic performance of the ALBI score for the assessment of the in-hospital mortality of AUGIB in liver cirrhosis. We found that the prognostic performance of the ALBI score was comparable with that of the Child-Pugh and MELD scores for predicting the in-hospital mortality in such patients. In detail in the overall

analysis, although the ALBI score had the largest AUC, followed by the MELD and Child-Pugh scores (0.808 versus 0.787 and 0.785), in the subgroup analysis of patients with only hepatitis B virus-related liver cirrhosis, the ALBI score still had the largest AUC, followed by the Child-Pugh and MELD scores (0.865 versus 0.836 and 0.818); in the subgroup analysis of patients with only alcohol-related liver cirrhosis, the ALBI score still had the largest AUC, followed by the Child-Pugh and MELD scores (0.869 versus 0.860 and 0.801); and in the subgroup analysis of patients treated with endoscopic therapy for AUGIB, the Child-Pugh score had the largest AUC, followed by the ALBI and MELD scores (0.884 versus 0.873 and 0.834). Taken together, the ALBI score had a moderate to high prognostic performance.

The conventional assessment of liver function is primarily based on the Child-Pugh and MELD scores in liver cirrhosis. However, they have several major drawbacks. First, a positive shifting dullness in the physical examinations readily appears when trying to define the presence of moderate to large ascites. However, at least one additional imaging modality, such as ultrasound or computed tomography scans, can be used to evaluate whether a patient has mild ascites. Second, the assessment of overt HE and its grade are more subjective. Third, INR has a substantial laboratory-to-laboratory variation because of the specific laboratory methodologies (17). Trotter et al. (18) tested the INR levels of 29 consecutive patients listed for liver transplantation in three different laboratories in the US. They found that the highest and lowest INR levels were 1.9 and 1.4, respectively, and that the percentage of difference between them was 26%. Subsequently, Trotter et al. (19) further validated a great variation of INR levels among 14 different laboratories in the US. In the 1st–5th samples, INR levels were in the ranges 1.2–2.0, 1.4–2.5, 1.7–3.4, 1.9–3.7, and 2.4–5.1. Lisman et al. (20) also confirmed such a variation of INR in seven different European laboratories. By comparison, the ALBI score, in which only blood samples need to be tested, is more convenient and objective than the Child-Pugh and MELD scores.

Limitations

First, the source of AUGIB was unclear in a number of patients. Therefore, we did not focus on patients with variceal bleeding rather than those with AUGIB. Second, a transjugular intrahepatic portosystemic shunt for the management of portal hypertension was not readily available at the General Hospital of Shenyang Military Area hospital. In current clinical practice, stratifying the risk for portal hypertension becomes more and more important (21). The Child-Pugh score has been widely used to identify a subgroup of patients at a high risk of early rebleeding and death. Cirrhotic patients with Child-Pugh class B and active bleeding on endoscopy or Child-Pugh class C will obtain more survival benefits from the early use of a transjugular intrahepatic portosystemic shunt (22-24). If the ALBI score could replace the role of the Child-Pugh score, it would be easier and more prompt to identify the candidates for an early transjugular intrahepatic portosystemic shunt for acute variceal bleeding. Third, patient selection bias and missing data should never be neglected due to the retrospective nature of the study. Fourth, long-term follow-up was unavailable; therefore, this study could not evaluate the role of ALBI for predicting the long-term prognosis.

In conclusion, the ALBI score may be a good alternative choice for the assessment of in-hospital mortality in liver cirrhosis with AUGIB. In future, prospective well-designed studies should also be conducted to further validate this issue. Also, it is more worthwhile to explore the prognostic performance of the ALBI score in other groups of chronic liver diseases.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of General Hospital of Shenyang Military Area No: k(2015)7.

Informed Consent: Written informed consent was waived for this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - X.Q.; Design - X.Q., C.Z.; Supervision - X.Q., X.G.; Funding - X.Q.; Data Collection and/or Processing - D.Z., C.Z., Z.N., F.H., J.Z., Y.P., L.J., H.D.; Analysis and/or Interpretation - X.Q., D.Z., C.Z.; Literature Review - X.Q., D.Z., C.Z.; Writer - X.Q.; Critical Review - X.G.

Conflict of interest: No conflict of interest was declared by the authors.

Financial support: The authors declared that this study has received no financial support.

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