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Comparative evaluation of ALBI, MELD, and Child-Pugh scores in prognosis of cirrhosis: is ALBI the new alternative?

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Abstract

Background The existence of reliable prognostic indices is of paramount importance in the management of cirrhosis. Both the model for end-stage liver disease (MELD) score and the older Child-Pugh (CP) scores are widely used. The albumin-bilirubin (ALBI) score, initially used in hepatocellular carcinoma, has not been thoroughly investigated in cirrhosis. The aim of this study was to compare the prognostic accuracy of ALBI, MELD, MELD with sodium (MELD-Na), CP, and the corrected for creatinine CP scores in a genetically homogeneous Cretan cirrhotic population.

Methods One hundred ninety-five outpatients or hospitalized cirrhotics (127 male, median age 66 years) were studied over a period of 2 years and ALBI, platelet-albumin-bilirubin, MELD, MELD-Na, CP score, and 2 types of modified CP score (CP-I and CP-II) with serum creatinine were calculated and correlated with survival.

Results ALBI had an optimum balance between sensitivity and specificity (area under the curve 0.704, 95% confidence interval [CI] 0.630-0.778) compared to the other scores. In the multivariate analysis, the only factors independently associated with death were the ALBI score (hazard ratio [HR] 2.51, 95%CI 1.69-3.73; P<0.001), the MELD-Na score (HR 1.04, 95%CI 1.00-1.09; P=0.045), and age (HR 1.05, 95%CI 1.03-1.07; P<0.001). When only decompensated cirrhosis was evaluated, the multivariate analysis showed that the ALBI score (HR 3.03; 95%CI 1.92-4.78; P<0.001), and age (HR 1.05, 95%CI 1.03-1.07; P<0.001) were independently associated with death.

Conclusion ALBI score might be a better prognostic indicator of mortality in cirrhosis and given its simplicity could substitute for the CP, MELD, and MELD-Na scores.

Keywords Cirrhosis, model for end-stage liver disease, Child-Pugh, albumin-bilirubin score

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Introduction

The existence of reliable prognostic indices is of paramount importance in the management of cirrhosis. The Child-Pugh (CP) score has been used for more than 40 years. It was initially proposed to assess the outcomes of cirrhotic patients after surgery for portal hypertension and gradually gained wider acceptance [1-3]. Two modified types of CP score encompassing serum creatinine have also been evaluated [4]. The model for end-stage liver disease (MELD) score was first applied to patients undergoing transjugular intrahepatic portosystemic shunts [5], but since 2002 it has been used for assessing candidates for liver transplantation [6]. MELD-Na, a modified MELD score incorporating serum sodium, has been used for survival prediction, taking account of the significance of hyponatremia in early mortality from cirrhosis [7-9].

The albumin-bilirubin (ALBI) score is a recently proposed and very simple score that evaluates only 2 objective parameters that are readily available for every cirrhotic patient. The ALBI score has been reported to assess liver dysfunction and prognosis in patients with hepatocellular carcinoma [10,11], in patients with primary biliary cholangitis [12], in cirrhotic patients with upper gastrointestinal bleeding [13], and in various hepatitis-B virus-related liver diseases [14,15]. However, its usefulness in assessing a cirrhotic cohort of patients has not been adequately evaluated.

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Conflict of Interest: None

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The aim of this study was to compare the prognostic accuracy of ALBI, platelet-albumin-bilirubin (PALBI), MELD, MELD-Na, CP, and CP corrected for creatinine scores in a genetically homogeneous Cretan cirrhotic population.

Patients and methods

Data on 195 consecutive cirrhotic patients either attending the liver outpatient clinic or hospitalized in the gastroenterology wards within a 2-year period were retrospectively analyzed. The study was approved by the Institutional Ethics Review Board of the Hospital and written consent was provided by all patients. Cirrhosis was determined either by liver biopsy (52%) or by compatible imaging and clinical and endoscopic findings (esophageal varices, ascites). Cirrhosis was classified as decompensated when ascites, variceal hemorrhage or hepatic encephalopathy were recorded.

Age, sex, cause of cirrhosis, compensation status, age at diagnosis of cirrhosis, first complications of decompensated cirrhosis, existence or appearance of hepatocellular cancer, as well as biochemical variables (creatinine, total bilirubin, albumin, international normalized ratio, prothrombin time, sodium, potassium, alkaline phosphatase, γ-glutamyl transferase, transaminases) were recorded for all patients.

Patients were followed-up for a median of 27.2 months (interquartile range [IQR] 46.9, 95% confidence interval [CI] 0-105.6). Three patients were lost to follow up. Every cirrhotic patient was followed-up in our screening program for hepatocellular carcinoma, which involves undergoing an ultrasound examination every 6 months with α-fetoprotein levels and contrast-enhanced ultrasound with SonoVue every year. The CP, MELD, MELD-Na, ALBI, and PALBI scores were assessed for every patient at first examination [1,2,11,16]. The PALBI score was calculated as:

$$PALBI = (2.02\times\log_{10}\ \text{bilirubin})+(-0.37\times(\log_{10}\ \text{bilirubin})^2)+(-0.04\times\text{albumin})+(-3.48\times\log_{10}\ \text{platelets})+(1.01\times(\log_{10}\ \text{platelets})^2)$$ [17].

In addition, 2 types of modified CP score (CP-I and CP-II) with serum creatinine as the sixth variable were also calculated:

Table 1 Baseline clinical and laboratory characteristics in 195 cirrhotic patients

Characteristics	Value
Age (years), median (IQR, range)	66 (18, 31-95)
Male sex, n (%)	127 (65.1)
Etiology of cirrhosis, n (%)	
Alcohol	71 (36.4)
Viral	56 (28.7)
Alcohol & viral	16 (8.2)
NAFLD	21 (10.8)
PBC	18 (9.2)
Cryptogenic	4 (2.1)
Decompensated cirrhosis, n (%)	142 (72.8)
Laboratory results (mean±SD)	
Creatinine (mg/dL)	1.09 (0.27)
Serum albumin (g/dL)	3.3 (0.72)
Total serum bilirubin (mg/dL)	2.8 (3.49)
International normalized ratio	1.39 (0.38)
Ascites, n (%)	99 (50.8)
Hepatic encephalopathy, n (%)	33 (16.9)
MELD score, median (IQR, range)	12 (9, 6-30)
MELD-Na score, median (IQR, range)	15 (11, 3-33)
CP score, median (IQR, range)	7 (4, 5-13)
CP score I, median (IQR, range)	8 (5, 5-17)
CP score II, median (IQR, range)	7 (5, 5-15)
ALBI, median (IQR, range)	-2.68 (1.23, -4.25 to -0.64)
PALBI, median (IQR, range)	-2.55 (0.91, -3,17 to -0.21)

NAFLD, non-alcoholic fatty liver disease; PBC, primary biliary cholangitis; IQR, interquartile range; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with sodium; CP Child-Pugh; ALBI, albumin-bilirubin score; PALBI, platelet-albumin-bilirubin score

Table 2 Comparisons of the areas under the ROC curve for CP, CP-I, CP-II, MELD, MELD-Na, ALBI and PALBI scores in relation to 1-, 6-, 12-, and 24-month survival

Survival (months)	Score	Area under ROC curve	95%CI	P-value
1	CP score	0.889	0.82-0.95	<0.001
	CP-I	0.874	0.80-0.94	<0.001
	CP-II	0.889	0.82-0.95	<0.001
	MELD	0.874	0.79-0.95	<0.001
	MELD-Na score	0.874	0.80-0.94	<0.001
	ALBI	0.912	0.84-0.98	<0.001
	PALBI	0.823	0.71-0.92	<0.001
6	CP score	0.786	0.71-0.85	<0.001
	CP-I	0.796	0.72-0.86	<0.001
	CP-II	0.793	0.72-0.86	<0.001
	MELD	0.767	0.69-0.84	<0.001
	MELD-Na score	0.795	0.724-0.86	<0.001
	ALBI	0.785	0.70-0.86	<0.001
	PALBI	0.737	0.65-0.82	<0.001
12	CP score	0.763	0.69-0.83	<0.001
	CP-I	0.770	0.69-0.84	<0.001
	CP-II	0.769	0.69-0.84	<0.001
	MELD	0.748	0.67-0.81	<0.001
	MELD-Na score	0.780	0.71-0.84	<0.001
	ALBI	0.781	0.71-0.85	<0.001
	PALBI	0.717	0.64-0.79	<0.001
24	CP score	0.751	0.68-0.82	<0.001
	CP-I	0.753	0.68-0.82	<0.001
	CP-II	0.754	0.68-0.82	<0.001
	MELD	0.732	0.66-0.80	<0.001
	MELD-Na score	0.755	0.68-0.82	<0.001
	ALBI	0.780	0.71-0.84	<0.001
	PALBI	0.694	0.62-0.77	<0.001

ROC, receiver operating characteristic; CI, confidence interval; CP, Child-Pugh; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with sodium; ALBI, albumin-bilirubin score; PALBI, platelet-albumin-bilirubin score

CP-I (range: 5-19) was derived from the original CP score by adding 0 points for creatinine <1.3 mg/dL and 4 points for creatinine ≥1.3 mg/dL, according to Angermayr *et al* [4], while CP-II (range: 5-19) was derived from the original CP score by adding 0 points for creatinine <1.3 mg/dL, 2 points for creatinine 1.3-1.8 mg/dL, and 4 points for creatinine >1.8 mg/dL. According to the proposed cutoff points for ALBI and PALBI scores, we stratified our patients into 3 groups. For ALBI score: grade 1 (score -2.60), grade 2 (>-2.60 to -1.39), and grade 3 (>-1.39) [11]. For PALBI score: grade 1 (score ≤-2.53), grade 2 (>-2.52 to -2.09), and grade 3 (>-2.09) [17,18].

Statistical analysis

Analysis was performed using the IBM SPSS 14.0 software, with statistical significance defined at a=0.05. All variables were checked for normality of distributions by the Kolmogorov-Smirnov test and the binomial test. Data were reported as mean ± standard deviation and median, IQR. Continuous variables were compared using Student's *t*-test, the Mann-Whitney *U*-test or one-way analysis of variance, as appropriate. Furthermore, receiver operating characteristic (ROC) analysis was performed and the area under the curve (AUC) was calculated to assess the 6 scoring systems. Survival analysis was conducted by performing a Kaplan-Meier estimate, testing for several selected parameters. Cox proportional hazard regression was performed to test the effect of other independent variables on survival times (1, 6, 12, 24 months) of different groups of patients, controlling for confounders and interaction terms.

Results

The baseline clinical and laboratory characteristics of the 195 cirrhotic patients included in the study are summarized in Table 1: 127 patients (65.1%) were male; the median age was 66 years. The most common cause of cirrhosis was alcohol (36.4%), followed by viral hepatitis (28.7%). One hundred forty-two patients (72.8%) presented with decompensated cirrhosis. Median MELD, MELD-Na, CP, CP-I, CP-II, ALBI, and PALBI scores were 12 (IQR 9, range 6-30), 15 (IQR 11, range 3-33), 7 (IQR 4, range 5-13), 8 (IQR 5, range 5-17), 7 (IQR 5, range 5-15), -2.68 (IQR 1.23, range -4.25 to -0.64), and -2.55 (IQR 0.91, range -3.17 to -0.21), respectively.

The ROC curves of all 7 scoring systems for 1-, 6-, 12-, and 24-month survival are shown in Fig. 1. All scoring systems were found to have diagnostic accuracy in predicting survival (P<0.001). ALBI had the optimum balance between sensitivity and specificity (AUC 0.704, 95%CI 0.630-0.778) compared with

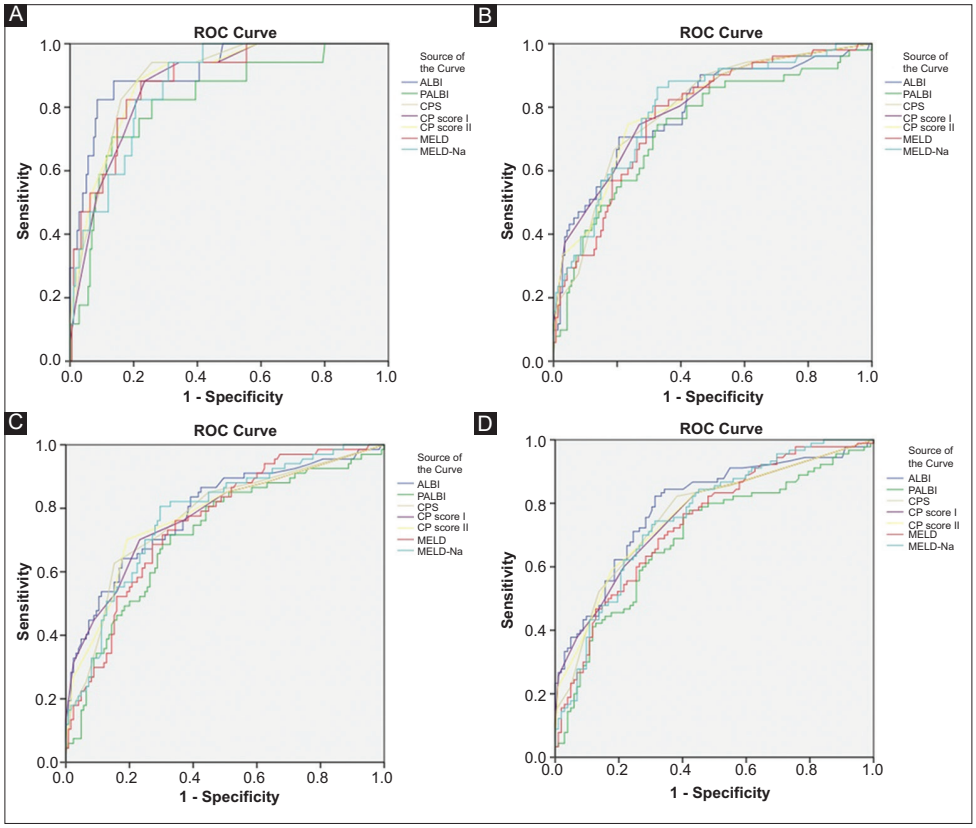

Figure 1 ROC curves CP, modified CP-I, modified CPS-II, MELD, MELD-Na, PALBI and ALBI scores for 1- (A), 6-(B), 12-(C), and 24-(D) months
ROC, receiver operating characteristic; CI, confidence interval; CP, Child-Pugh; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with sodium; ALBI, albumin-bilirubin score; PALBI, platelet-albumin-bilirubin score

the other scores. All scoring systems appeared to have excellent prognostic accuracy (AUC>0.80) for 1-month survival. The ALBI score appeared to have an advantage in predicting 1-, 12-, and 24-month survival (AUC 0.912, 0.781, 0.780, respectively) (Table 2). CP-I and MELD-Na were slightly better in predicting 6-month survival (AUC 0.796 and 0.795, respectively).

When compensated and decompensated cirrhotics were evaluated, none of the scores was satisfactory for survival prognosis; however, the number of compensated cirrhotics at first examination was relatively small and that might have influenced the results. In decompensated cirrhosis the ALBI score was at least similar to, or even better than all the other scores in predicting 1-, 6-, 12- and 24-month survival, as shown in Table 3.

In the univariate analysis, the ALBI, PALBI and MELD-Na scores and age were found to be significantly associated with mortality. Similarly, ALBI and PALBI grade 3 presented at least 14.83 and 2.89 times higher risk, respectively. In the multivariate analysis, the only factors independently associated with death were the ALBI score (hazard ratio [HR] 2.51, 95% CI 1.69-3.73; P<0.001), the MELD-Na score (HR 1.04, 95% CI 1.00-1.09; P=0.045), and age (HR 1.05; 95%CI 1.03-1.07; P<0.001) (Table 4).

In decompensated cirrhotic patients, the multivariate analysis showed that the ALBI score (HR 3.03, 95%CI 1.92-4.78; P<0.001), and age (HR 1.05, 95%CI 1.03-1.07; P<0.001) were independently associated with death (Table 5).

During the follow-up period 124 patients died. All deaths were liver related. The Kaplan-Meier survival curve indicated a worse prognosis for patients with decompensated cirrhosis (P=0.03) and for patients with cirrhosis due to alcohol abuse or viral hepatitis (P=0.04) (Fig. 2).

Discussion

This study suggests that the ALBI score has a prognostic accuracy similar to that of other established scores for mortality prediction in cirrhosis. These data, if validated in larger studies, may be of significant clinical importance in view of the simplicity of this score.

Table 3 Comparisons of the areas under the ROC curve of CP, CP-I, CP-II, MELD, MELD-Na, ALBI, and PALBI scores for 1-, 6-, 12-, and 24-month survival based on the compensation status

Survival (months)	Score	Area under ROC curve		95%CI		P-value	
		Compensated	Decompensated	Compensated	Decompensated	Compensated	Decompensated
1	CP score	-	0.846	-	0.76-0.93	-	<0.001
	CP-I	-	0.827	-	0.73-0.92	-	<0.001
	CP-II	-	0.851	-	0.76-0.94	-	<0.001
	MELD	-	0.32	-	0.73-0.93	-	<0.001
	MELD-Na	-	0.26	-	0.73-0.91	-	<0.001
	score	-	0.879		0.78-0.97	-	<0.001
	ALBI	-	0.780		0.66-0.89	-	<0.001
	PALBI						
6	CP score	0.536	0.755	0.23-0.83	0.67-0.83	0.81	<0.001
	CP-I	0.495	0.784	0.21-0.77	0.70-0.86	0.97	<0.001
	CP-II	0.495	0.780	0.21-0.77	0.70-0.85	0.97	<0.001
	MELD	0.566	0.730	0.24-0.89	0.64-0.81	0.66	<0.001
	MELD-Na	0.561	0.770	0.28-0.83	0.69-0.84	0.68	<0.001
	score	0.393	0.769	0.06-0.71	0.68-0.85	0.48	<0.001
	ALBI	0.449	0.712	0.04-0.85	0.62-0.80	0.73	<0.001
	PALBI						
12	CP score	0.469	0.764	0.26-0.67	0.68-0.84	0.78	<0.001
	CP-I	0.431	0.792	0.23-0.62	0.71-0.86	0.53	<0.001
	CP-II	0.431	0.791	0.23-0.62	0.71-0.86	0.53	<0.001
	MELD	0.683	0.716	0.48-0.88	0.63-0.80	0.10	<0.001
	MELD-Na	0.617	0.772	0.44-0.79	0.69-0.84	0.29	<0.001
	ALBI	0.517	0.782	0.27-0.75	0.70-0.85	0.88	<0.001
	PALBI	0.494	0.702	0.22-0.76	0.61-0.78	0.96	<0.001
24	CP score	0.441	0.749	0.26-0.61	0.66-0.83	0.53	<0.001
	CP-I	0.458	0.760	0.27-0.63	0.68-0.83	0.66	<0.001
	CP-II	0.455	0.768	0.27-0.63	0.69-0.84	0.64	<0.001
	MELD	0.636	0.698	0.45-0.81	0.61-0.78	0.15	<0.001
	MELD-Na	0.608	0.735	0.45-0.76	0.65-0.81	0.26	<0.001
	ALBI	0.477	0.786	0.27-0.67	0.71-0.86	0.80	<0.001
	PALBI	0.374	0.697	0.16-0.58	0.61-0.78	0.18	<0.001

ROC, receiver operating characteristic; CI, confidence interval; CP, Child-Pugh; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with sodium; ALBI, albumin-bilirubin score; PALBI, platelet-albumin-bilirubin score

Table 4 Crude and adjusted HR for death and 95%CI for ALBI, PALBI and MELD-Na scores

Covariates	Unadjusted			Adjusted[a]		
	HR (95%CI)	c-statistics HR	P-value	HR (95%CI)	c-statistics HR	P-value
ALBI	2.78 (2.11-3.67)	0.704	<0.001	2.51 (1.69-3.73)	0.704	<0.001
PALBI	2.16 (1.62-2.89)	0.695	<0.001	-	-	-
MELD-Na	1.11 (1.07-1.14)	0.683	<0.001	1.04 (1.00-1.09)	0.683	0.045
Age	1.03 (1.01-1.05)	0.641	<0.001	1.05 (1.03-1.07)	0.641	<0.001
ALBI grade						
1	1	-	-	-	-	-
2	2.42 (1.65-3.53)	0.701	<0.001	-	-	-
3	14.83 (7.67-28.78)	0.942	<0.001	-	-	-
PALBI grade						
1	1	-	-	-	-	-
2	1.40 (0.86-2.26)	0.686	0.16	-	-	-
3	2.89 (1.93-4.32)	0.811	<0.001	-	-	-

[a]Multivariate model adjusted for sex

HR, hazard ratio; CI, confidence interval; MELD, model for end-stage liver disease; MELD-Na, model for end-stage liver disease with sodium; ALBI, albumin-bilirubin score; PALBI, platelet-albumin-bilirubin score

Table 5 Crude and adjusted HR for death and 95%CI for ALBI score in decompensated cirrhotic patients

Covariates	Unadjusted			Adjusted[a]		
	HR (95%CI)	c-statistics HR	P-value	HR (95%CI)	c-statistics HR	P-value
ALBI	3.33 (2.32-4.77)	0.704	<0.001	3.03 (1.92-4.78)	0.704	<0.001
Age	1.04 (1.02-1.06)	0.641	<0.001	1.05 (1.03-1.07)	0.641	<0.001

[a]Multivariate model adjusted to sex

ALBI, albumin-bilirubin score; MELD-Na, model of end-stage liver disease with sodium score

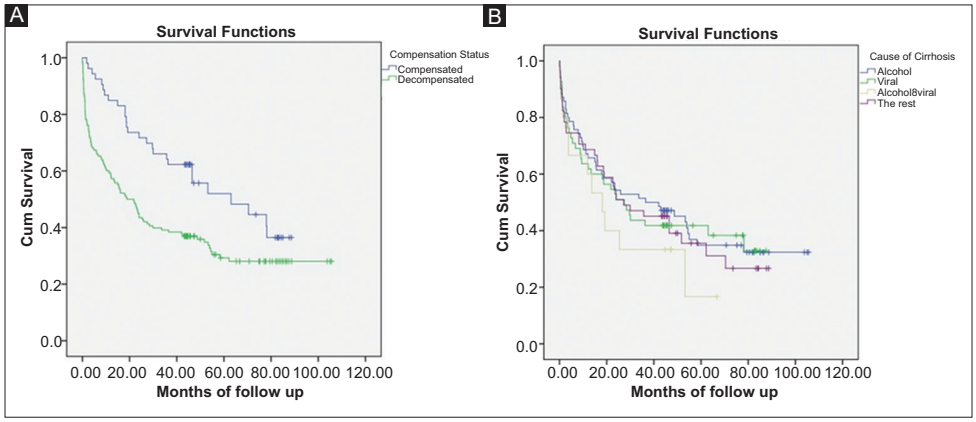

Figure 2 Kaplan-Meier survival curve for patients according to their compensation status (A) and the etiology of cirrhosis (B)

The CP score has been proposed as a reliable prognostic score in cirrhosis in many systematic reviews [19-21], but its subjective components (ascites and encephalopathy) still remain a matter of doubt. A systematic review of prognostic indicators in cirrhosis in 118 studies showed that serum albumin and bilirubin were the 2 most significant prognostic variables for survival [21].

A study by Chen *et al* [14] assessed the accuracy of ALBI in predicting 1-, 2-, and 3- year mortality in patients with hepatitis B-related cirrhosis, and ROC curves showed that the ALBI score (AUC 0.787, 0.830, and 0.833) was superior to the MELD (0.693, P=0.003; 0.717, P<0.001; 0.744, P<0.001) and CP (0.641, P<0.001; 0.649, P<0.001; 0.657, P<0.001) scores. In our study, in agreement with Chen *et al* [14], ROC analysis showed that the ALBI score was better at predicting mortality compared to MELD, MELD-Na, CP, CP-I and CP-II scores. Moreover, in the aforementioned study [14] the multivariate analysis found ALBI score and age to be independent factors associated with mortality, in accordance with our study, while in another study that included only patients with primary biliary cholangitis [12] the multivariate analysis also indicated that the ALBI score was the only independent prognostic factor, with an adjusted HR for developing a hepatic event of 27.8 (P<0.001). These findings agree with our study, where ALBI, MELD-Na score, and age were all independent variables, whereas in decompensated cirrhosis only the ALBI score was an independent prognostic factor. A study by Zou *et al* [13] evaluated the in-hospital mortality in relation to ALBI, CP, and MELD scores in 631 cirrhotic patients and found that the ALBI score had the best AUC (0.808, 0.785, 0.787, respectively). These studies suggest that ALBI is a good indicator of short-term prognosis, in agreement with our study, where 1-month survival was best assessed by ALBI (AUC 0.912).

Another study evaluated CP score, MELD, and ALBI in predicting 3-month mortality in patients with acute-on-chronic liver failure and reported that both ALBI and MELD scores were independent predictors (P<0.001); however, the ROC curves indicated that the MELD score was better than the ALBI score (AUC 0.837 and 0.784, respectively) [15]. Furthermore, a study from Taiwan in 242 patients with both compensated and decompensated cirrhosis concluded that both ALBI and MELD scores significantly predicted 3-month and 6-month mortality (AUC 0.773, 0.691 vs. 0.813, 0.740, respectively) [22].

Moreover, a recent, prospective study validated the ALBI score as a measure of liver dysfunction in patients with compensated cirrhosis and proposed a new score, ALBI-FIB4, to stratify these patients for the risk of future liver decompensation [23]. In addition, the ALBI score has been found to significantly predict portal hypertension (both clinically significant and severe) [22].

A study by Oikonomou *et al* [17] assessed the grades of both ALBI and PALBI scores in patients with decompensated cirrhosis and found that both ALBI and PALBI grade 3 patients had at least double the risk of death or transplantation. Our results are in accordance with the aforementioned study and outline the importance of ALBI grade 3, as it showed a 14 times higher risk of death compared with a 2.42 times higher risk for ALBI grade 2.

Summary Box

What is already known:

- The existence of reliable prognostic indices is of paramount importance in the management of cirrhosis
- The albumin-bilirubin (ALBI) score is a recently reported very simple score, initially used in hepatocellular carcinoma, which has not been thoroughly investigated in cirrhosis

What the new findings are:

- The ALBI score is an overall accurate and reliable score in decompensated cirrhosis, irrespective of etiology, equal to or better than the other predictive scores in predicting mortality
- Given its simplicity, the ALBI score can confidently replace the other more complex scores in addition to hepatocellular carcinoma prognosis

Our study has the limitation that it was conducted in a single tertiary institute with a relative small number of cases. Therefore, a larger cohort of well stratified cirrhotics of different etiologies should be studied in order to confirm our findings. Moreover, there was an imbalance in the compensation status of our patients, as more than 70% already had decompensated cirrhosis when they were enrolled in our study.

Nonetheless, our study has demonstrated that ALBI is an overall accurate and reliable score in decompensated cirrhosis, irrespective of etiology, equal to or better than the other predictive scores in predicting mortality. Therefore, in view of its simplicity, it can confidently replace the other more complex scores.

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