Research Article

Comparative Research of the Value of Some Scoring Systems for Prognosis of Re-Bleeding and In-Hospital Mortality in Liver Cirrhosis with Acute Variceal Bleeding

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Abstract

Background: Upper gastrointestinal hemorrage due to acute esophageal varices bleeding is a common complication and a leading cause of death in patients with cirrhosis. Therefore, predicting the risk to have an active management to prevent re-bleeding and death is crucial. Currently, there are many prognostic scoring systems have been proposed, but research is needed to find a valid score to apply in clinical practice in each country and population.

Aim: To compare the value of ALBI (Albumin-Bilirubin), PALBI (Platelet-Albumin-Bilirubin), AIMS65, MELD, Child-Pugh scores in predicting early rebleeding and in-hospital mortality of acute variceal bleeding in patients with cirrhosis.

Subjects and methods: A cross-sectional descriptive study on cirrhotic patients with acute variceal bleeding treated at the Department of Gastroenterology, Intensive care unit - Military Hospital 103 and Institute for Treatment of Digestive Diseases - 108 Military Central Hospital from September 2020 to May 2022. Calculate ALBI, PALBI AIMS65, MELD, Child-Pugh and compare with rates of early rebleeding and in-hospital mortality, then determine and compare the prognostic value through analysis of the Area under the Curve (AUC).

Results: Two hundred twenty two patients with acute esophageal bleeding were eligible for inclusion in the study. The rates of rebleeding and in-hospital mortality were 9.0% and 6.8%, respectively. Regarding the prognosis of early rebleeding, the ALBI and PALBI scores have good prognostic value (AUROC 0.74; 95% CI: 0.63-0.85 and AUROC 0.7; 95% CI: 0.59-0.81; p=0.004 respectively), while the Child Pugh, MELD, AIMS65 scores have little prognostic value with AUROC < 0.70. Regarding prognosis of in-hospital mortality: the ALBI, PALBI, MELD and AIMS65 all have good value in predicting in-hospital mortality with AUROC of 0.81 (95% CI: 0.68-0.93, respectively; p<0.001); 0.8 (95% CI: 0.69-0.91; p<0.001); 0.83 (95% CI: 0.72-0.93; p<0.001), 0.82 (95% CI: 0.76-0.87, p<0.001), while Child Pugh score only has medium prognosis value with AUROC 0.79 (95% CI: 0.66-0.92; p<0.05). However, there was no significant difference between these prognostic scores.

Conclusion: The ALBI, PALBI, MELD and AIMS65 scores all have similar good predictive value of in-hospital mortality, but with early rebleeding prognosis, only ALBI and PALBI have good value. The Child-Pugh score did not show prognostic value like other scores both in predicting early rebleeding and in-hospital mortality.

Keywords: ALBI; PALBI; AIMS65; MELD; Child-pugh score; Acute variceal bleeding; Cirrhosis

Introduction

Upper gastrointestinal hemorrhage due to acute variceal bleeding in portal hypertension syndrome is one of the serious complications in patients with cirrhosis, although much progress has been made in diagnosis and treatment. However, the mortality rate remains high, ranging from 10%-20%, mainly due to failure to control bleeding in the first days [1,2]. Prognosis of acute variceal bleeding is often difficult not only because of the severity of bleeding but also depending on the underlying cirrhosis. Some scoring systems have been studied for prognosis such as Child-Pugh score, Model of End-stage Liver Disease (MELD), AIMS65, etc. However, the values of these scores are not high with the area under the ROC curve < 0.7 in prognosis of rebleeding risk and the prognosis of 6-week mortality rate reached the highest at only 0.74 [3].

ALBI score was developed by author Johnson et al. [4], then Roayaie et al. [5] proposed the PALBI score by adding platelet index as an index in portal hypertension syndrome in order to stratify the prognosis for HCC patients which is better than the Child-Pugh score. In recent years, there are a few studies that apply these two scoring systems to the prognosis of patients with acute variceal bleeding, initially achieving some remarkable results [6,7]. With the advantage of using conventional tests reflecting liver function and portal hypertension, it is objective and has wide applicability.

Vietnam is a country endemic for hepatitis B virus (HBV) with a high infection rate of 10.7% and alcohol abuse is quite common, so chronic liver diseases and cirrhosis with complications is increasing (especially gastrointestinal bleeding due to rupture of esophageal

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varices). However, studies on the prognostic factors of acute variceal bleeding are limited; especially there is no study on the value of the ALBI and PALBI scores. Therefore, we conducted the study with the objective: "Comparative research of the value of some scoring systems for prognosis of re-bleeding and in-hospital mortality in liver cirrhosis with acute variceal bleeding".

Materials and Methods

Subjects

A cross-sectional descriptive study, follow-up in 222 patients diagnosed with acute variceal bleeding on the background of cirrhosis, treated at 2 major university hospitals in Vietnam, the Department of Gastroenterology, and Intensive care unit- Military Medical Hospital 103 - Military Medical University and Institute of Digestive Diseases-108 Military Central Hospital, from September 2020 to May 2022.

Inclusion criteria: Patients admitted to the hospital in the state of hematemesis and/or melena, undergo gastro-oesophageal endoscopy to confirm the source of bleeding due to ruptured varices (with blood spurting or oozing from the veins (active bleeding); or blood clots, platelet plugs on the walls of the varices (bleeding stops)); or varices with blood in the esophagus or stomach but without any other possible cause of bleeding [2].

Simultaneously, the patient has the syndromes of liver failure, portal hypertension and changes in liver morphology, blood tests and imaging to confirm the diagnosis of cirrhosis.

Exclusion criteria: Patients with no endoscopic finding of acute variceal bleeding or other causes such as Mallory-Wiess syndrome, esophageal ulcer, peptic ulcer; liver cancer (primary or secondary), taking or have recently taken antithrombotic agents.

Methods

All patients enrolled in the study had their history taken (history of GI bleeding, liver disease, other comorbidities); Clinical examination to assess hemodynamics (pulse, blood pressure), symptoms of hematemesis, melena, signs of blood loss and perform convential tests (total blood count, blood biochemistry, coagulation) in order to diagnosis and treatment.

*ALBI score formula:

ALBI $= -0.085 \times$ Albumin (g/L) $+0.66$ x $\log_{10}$ Bilirubin (μmol/L)

The score is divided into 3 levels: ALBI-1 ($\leq$ -2.60), ALBI-2 (-2.60 to -1.39) and ALBI-3 (>-1.39) [4].

*PALBI score formula:

PALBI $=2.02 \times \log_{10}$ Bilirubin $-0.37 \times (\log_{10}$ Bilirubin$)^2$ $-0.04 \times$ Albumin $-3.48 \times \log_{10}$ Platelete $+1.01 \times (\log_{10}$ Platelete$)^2$

The score is divided into 3 levels: PALBI-1 ($\leq$ -2.53), PALBI-2 (>-2.53 and $\leq$ -2.09), and PALBI-3 (>-2.09) [5].

*MELD score

MELD is based on the patient's serum creatinine, Bilirubin, and INR values calculated by the following formula:

MELD$=3.78 \times$ Ln [Bilirubin (mg/dL)]$+11.2 \times$ Ln [INR]$+9.57 \times$ Ln [Creatinine (mg/dL)]$+6.43$

Note: If the patient is on hemodialysis twice in the past 7 days, the serum creatinine is 4.0 mg/dL [8,9].

*AIMS65 score: 5 AIMS65 scoring factors including serum albumin <3g/dL, INR>1.5, mental disorder, systolic blood pressure $\leq$ 90 mmHg and age >65. Score spectrum 0-5 and divided into two levels of risk, low risk (score 0-1) and high risk (score 2-5) [10].

*Child-Pugh score: Based on 5 parameters as ascites, hepatic encephalopathy, albumin concentration, serum total bilirubin and Prothrombin time (INR). The spectrum ranges from 5 to 15 and is divided into 3 levels: Child-Pugh A with a score of 5-6, Child-Pugh B with a score of 7-9 and Child-Pugh C with a score of 10-15 [11].

Perform emergency endoscopy as soon as hemodynamic status allows, grade I, II, III varices according to the Japan Society of Endoscopy in 2010, bleeding status (blood is bleeding from the varicose veins) or has stopped bleeding (blood clot, platelet plug); perform interventional ligation with rubber bands for cases of bleeding or have stopped but high dilatation (grade II, III).

The patients were treated according to a uniform regimen based on their disease status, including blood volume resuscitation, hemostasis (immobilization, endoscopic intervention, hemostatic drugs, portal hypertension pressure lowering drugs...), blood transfusion as indicated, prevention of hepatic encephalopathy and infection. Monitor early rebleeding and mortality during hospital treatment.

Re-bleeding: assessed according to the Baveno VI consensus (2015) when at least 1 of the following criteria is present: (1) Hematemesis at 2 hours or more after drug therapy or specific endoscopic hemostasis. If the patient has a nasogastric tube, recurrent bleeding is defined as >100 mL of red blood aspirated after hemostasis. (2) Decrease in Hemoglobin of 30 g/L or more (approximately 9% Hemotocrit) in patients who have not received blood transfusion within 24 hours. Early rebleeding was counted within the first 5 days of admission [1,2].

Data collection and statistical analysis

Using the statistical software SPSS 25.0 to draw charts on Excel 2016. Qualitative variables calculate frequency and percentage. For quantitative variables: mean, standard deviation, median, min, max. Assess the ROC (Receiver Operating Characteristic) curve and determine the Area Under the Curve (AUC) to find a reasonable cut-off point with corresponding specificity and sensitivity (the cut-off point is the point at which maximum J value with J=sensitivity+specificity- 1). With the cut-off found, use the 2 × 2 table to redefine the Sensitivity (Se), Specificity (Sp). p<0.05 was considered to be statistically significant.

Results

Baseline characteristic of the included patients

The mean age in the study was 54.7 ± 10.4 with males was the majority (94.1%). 90.5% of patients had a history of cirrhosis, 64.4% had ever had GI bleeding due to rupture of esophageal varices, mainly due to alcohol (71.2%). Common hospital admission symptoms were hematemesis and melena (54.1%), 44.1% of patients had ascites of varying degrees (Table 1).

Gastro-oesophageal endoscopy results: Grade III esophageal varices were found in 80.6% of patients, with 12.6% finding active bleeding from varices. 20 patients (9.0%) early rebleeding and 15 cases (6.8%) died in hospital.

Characteristics of scoring systems

Cirrhotic patients with acute variceal bleeding often have severe liver failure; most patients are at Child-Pugh B and C (81.1%), ALBI-2 and ALBI-3 (98.1%), PALBI-2 and PALBI-3 (96.4%). The rate of patients at high risk of death when AIMS65 ≥ 2 is 50.5% (Table 2).

Table 1: Baseline characteristic of the included patients (n=222).

Variables		X ± SD or n (%)
Mean age		54,7 ± 10,4
Gender	Male	209 (94.1)
	Female	13 (5.9)
Clinical manifestation at admission	Hematemesis	48 (21.6)
	Melena	54 (24.3)
	Hematemesis and melena	120 (54.1)
Cirrhosis history	Yes	201 (90.5)
	No	21 (9.5)
Esophageal varices rupture history	Yes	143 (64.4)
	No	79 (35.6)
Cirrhosis origin	Alcohol	158 (71.2)
	HBV	29 (13.1)
	HCV	5 (2.2)
	Alcohol plus hepatic virus	28 (12.6)
	N/A	2 (0.9)
Ascites degree	None	124 (55.9)
	Mild/Moderate	75 (33.8)
	Severe	23 (10.3)
Esophageal varices degree	I	6 (2.7)
	II	37 (16.7)
	III	179 (80.6)
Bleeding status	Active bleeding	28 (12.6)
	Stable	194 (87.4)
Clinical process	Early rebleeding	20 (9.0)
	In-hospital mortality	15 (6.8)

Table 2: Characteristics of scoring systems (n=222).

Scales		Value
CTP	X ± SD	8.2 ± 2.2
	Min-Max	41760
	A/B/C n (%)	42 (18.9)/ 104 (46.8)/ 76 (34.3)
MELD	X ± SD	15.4 ± 5.7
	Min-Max	15523
AIMS65	X ± SD	1.62 ± 1.15
	Min – Max	0-5
ALBI	X ± SD	-1.26 ± 0.63
	Min - Max	-2.75 - 0.58
	ALBI-1/ALBI-2/ALBI-3 n (%)	2 (0.9)/ 92 (41.4)/ 128 (57.7)
PALBI	X ± SD	-1.78 ± 0.42
	Min-Max	-3.0-(-0.76)
	PALBI-1/PALBI-2/PALBI-3 n (%)	8 (3.6)/ 45 (10.3)/ 169 (76.1)

Values of predictive scores for early rebleeding and mortality

In the prognosis of early rebleeding, only the ALBI and PALBI scores had good predictive value with AUROC of 0.74 (95% CI: 0.63-0.85) and 0.70 (0.59-0.81). However, when predicting mortality, only Child-Pugh score has medium prognostic value (AUROC 0.79, 95% CI: 0.66-0.92), the remaining 4 scores all have good prognostic value (AUROC ≥ 0.80), of which the highest is the MELD score (AUROC 0.83, 95% CI: 0.72-0.93) (Table 3).

Comparison of the area under the ROC curve in the prognosis of early rebleeding

In the prognosis of early rebleeding ALBI score has AUROC greater than Child-Pugh, MELD, AIMS65 by 0.1; 0.1; 0.05,

respectively. However, this difference was not statistically significant (p>0.05; z<1.96) (Table 4) (Figure 1).

The PALBI scale with AUROC is higher than the Child-Pugh, MELD, AIMS65 scale by 0.06; 0.06; 0.01, respectively. However, this difference was not statistically significant (p>0.05; z<1.96).

Comparison of the area under the ROC curve in the prognosis of early mortality

The ALBI score has a greater AUROC than the Child-Pugh score of 0.02; smaller than MELD score of 0.02, smaller than AIMS65 score of 0.01. However, this difference was not statistically significant (p>0.05; z<1.96).

The PALBI score has an AUROC greater than the Child Pugh score of 0.01; smaller than MELD score of 0.03, smaller than AIMS65 score of 0.02. However, this difference was not statistically significant (p>0.05; z<1.96) (Table 5) (Figure 2).

Discussion

Some clinical and endoscopic characteristics of the included patients

The 222 patients had an average age of 54.7 ± 10.4 years; male accounted for the majority of 94.1%; 90.5% had a history of previous cirrhosis and 143 patients (64.4%) had acute variceal bleeding. The results of our study are consistent with the results of many studies showings that cirrhosis is more common in middle age, more men are affected than women and often have to be hospitalized many times due to complications, especially GI bleeding. Common hospital admission symptoms were hematemesis and melena (54.1%), 48 patients only have hematemesis (21.6%) and 54 patients only have melena (24.3%). Research by Elsafty et al. [12] also noted that patients with acute variceal bleeding were often hospitalized with 2 spontaneous symptoms of hematemesis and melena (64%), while only 21% of hematemesis alone and 15% of melena alone.

Undergoing gastro-oesophageal endoscopy, we encountered the majority of patients with grade III varices (80.6%), while there were 2.7% patients with grade I. At the same time, we found 12.6% patients has active bleeding from the varices requires immediate emergency intervention to stop the bleeding. Our results are consistent with those of Elsafty et al. [12] over 250 patients with acute variceal bleeding, 4% also had grade I dilated varices and 17% needed emergency band ligation of bleeding varicose veins.

Rates of early rebleeding and in-hospital mortality

Monitoring the clinical progress during the patient's hospital stay was treated with a uniform regimen recommended by professional associations; we found that 9.0% of patients had early rebleeding and 6.8% in-hospital deaths. A study by Aluizio et al. [3] on 222 patients with acute variceal bleeding showed that the rate of early rebleeding within the first 5 days of hospital admission was 4.5%, the mortality rate was 5.0%. Follow-up up to 6 weeks, the rate of rebleeding and mortality both increased to 18.5%. The study on 631 patients by Zou et al. [7] also recorded the in-hospital mortality rate of patients with variceal bleeding in the first 5 days is 4.4%. Thus, esophageal varices bleeding are a serious complication in cirrhotic patients with high in-hospital mortality, requiring early prognosis of high-risk groups to have active treatment methods.

Characteristics of scoring systems

The ALBI score was developed by author Johnson et al. [4], on

Table 3: Values of predictive scores for early rebleeding and mortality.

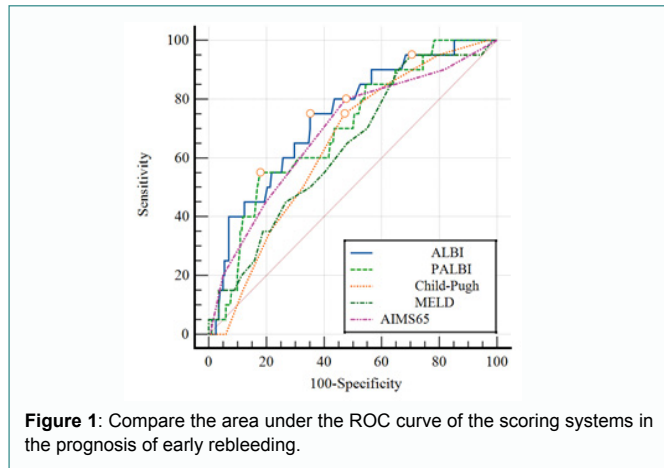| Scales	Clinical process	Cut off value	AUROC (95%CI)	Se (%)	Sp (%)	PPV (%)	NPV (%)	p
CTP	Early rebleeding	9	0.64 (0.54-0.75)	75	53	13.6	95.5	<0.05
	Mortility	11	0.79 (0.66-0.92)	73.3	81.2	22	97.7	<0.05
MELD	Early rebleeding	12	0.64 (0.52-0.76)	95	29.7	11.8	98.4	<0.05
	Mortility	18	0.83 (0.72-0.93)	80	75.4	19	98.1	<0.001
AIMS65	Early rebleeding	2	0.69 (0.63-0.75)	80.0	52.5	14.3	96.4	<0.001
	Mortility	3	0.82 (0.76-0.87)	73.3	81.6	22.4	97.7	<0.001
ALBI	Early rebleeding	-1,16	0.74 (0.63-0.85)	75.0	65.0	17.4	96.3	<0.001
	Mortility	-0,97	0.81 (0.68-0.93)	80.0	75.0	18.8	98.1	<0.001
PALBI	Early rebleeding	-1,45	0.70 (0.59-0.81)	55.0	82.2	23.4	94.9	0.004
	Mortility	-1,63	0.80 (0.69-0.91)	86.7	63.3	14.6	98.5	<0.001

Figure 1: Compare the area under the ROC curve of the scoring systems in the prognosis of early rebleeding.

Table 4: Comparison of AUROC ALBI, PALBI scores with Child-Pugh, MELD, AIMS65 in the prognosis of early rebleeding.

		Child-Pugh	MELD	AIMS65
ALBI	△AUROC	0.1	0.1	0.05
	z statistic	1.73	1.83	1.08
	p	0.084	0.067	0.279
PALBI	△AUROC	0.06	0.06	0.01
	z statistic	1.00	1.54	0.129
	p	0.318	0.123	0.897

Table 5: Comparison of AUROC ALBI, PALBI score with Child-Pugh, MELD, AIMS65 in predicting early death.

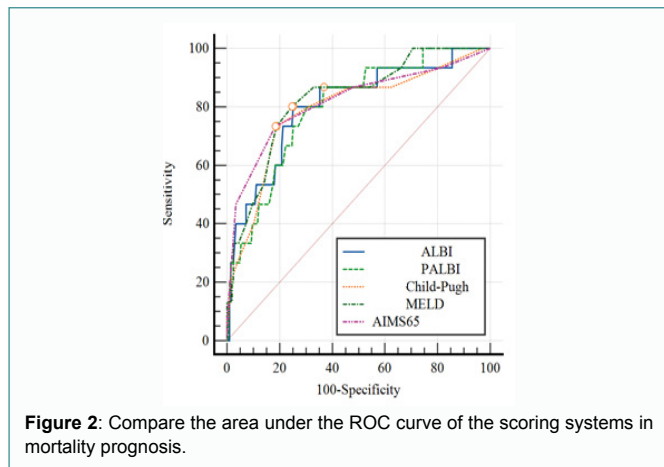|		Child-Pugh	MELD	AIMS65
ALBI	△AUROC	0.02	-0.02	-0.01
	z statistic	0.44	0.64	0.269
	p	0.658	0.524	0.788
PALBI	△AUROC	0.01	-0.03	-0.02
	z statistic	0.24	1.04	0.371
	p	0.815	0.3	0.711

Figure 2: Compare the area under the ROC curve of the scoring systems in mortality prognosis.

.which Roayaie et al. [5] proposed the PALBI score by adding platelet index- an index in portal hypertension syndrome. With the use of routine tests and ignoring some subjective factors, these scores have been applied in the prognosis of many different diseases, including patients with acute variceal bleeding and initially gave the positive results.

The results of Table 3 show that the average ALBI score in the study group was -1.26 ± 0.63, mainly in the ALBI-2 and ALBI-3 groups (41.4% and 57.7%, respectively). Our results are quite similar to those published by Elsafty et al. [12] with a mean ALBI score of -1.4 ± 0.6 and a rate of ALBI-2 of 47.2%, ALBI-3 of 52.8%. The average PALBI score in the study group was -1.78 ± 0.42, mainly in the PALBI-3 group (76.1%). This result is quite similar to that reported by Elshaarawy et al. [6] with a PALBI-3 rate of 61%, by Faisal et al. [13] also recorded the rate of PALBI-3 group as 64.3%.

Value of scores in predicting early rebleeding

Assess the ROC curve, we obtain the area under the curve of the ALBI scale is AUROC 0.74; 95% CI: 0.63-0.85; p<0.001, at the cut-off point -1.16 has a sensitivity of 75.0% and a specificity of 65.0%; of the PALBI score with AUROC 0.70; 95% CI: 0.59-0.81; p=0.004 at the cut-off point -1.45 has a sensitivity of 55.0% and a specificity of 82.2% (Table 3). While the remaining 3 scores have little value in predicting early rebleeding with AUROC <0.070. The study by Elshaarawy et al. [6] evaluated the value of some prognostic scores of patients with variceal bleeding (sample size of 1517 patients), including ALBI and PALBI scores, also showed that AUROC predicts early rebleeding (within 1 week) of ALBI, PALBI scores are 0.766; 0.794 (p<0.05). Meanwhile, research by Faisal et al. [13] on 170 patients with upper GI bleeding due to varices, the value of PALBI score in predicting rebleeding was only average with AUROC of 0.601 (95% CI: 0.502-0.699). The difference in the above study results may be due to different in sample sizes, heterogeneous assessment time for rebleeding as well as inconsistency in the selection of patients into the study.

Using the DeLong test to compare the difference between the scores, the results in Table 2 show that: the ALBI scale has a larger AUROC than the Child-Pugh score by 0.02; 0.02 smaller than the MELD score, but this difference is not statistically significant (p>0.05; z<1.96). The PALBI score has an AUROC greater than the Child- Pugh score of 0.01; smaller than the MELD score of 0.03 but this difference was not statistically significant (p>0.05; z<1.96). Thus, in our study, the predictive value of early death of the ALBI, PALBI is equivalent to the Child-Pugh, AIMS65 and MELD scores.

Studies around the world evaluating the value of prognostic scores of variceal bleedings have shown inconsistent results. De Souza Aluizio also noted that the Child-Pugh, MELD, AIMS65 scores had no predictive value for rebleeding, while the study of Tantai et al. [14]

showed that Child-Pugh had good value in the prognosis of rebleeding with AUROC 0.717. The study of Elshaarawy et al. [6] recorded PALBI as the score with the best prognostic value, significantly higher than the value of Child-Pugh and MELD score (p<0.01), and compared with the ALBI score, the difference is close to statistical significance (p=0.052).

Values of scores in predicting in-hospital mortality

Analyzing the ROC curve predicting in-hospital mortality, we obtained all 5 scores have prognostic value, in which the PALBI, ALBI, AIMS65 and MELD scores have a good prognosis with AUROC of 0.8 (95% CI: 0.69-0.91, p<0.001); 0.81 (95% CI: 0.68-0.93, p<0.001), 0.82 (95% CI: 0.76-0.87, p<0.001) and 0.83 (95% CI: 0.69-0.91, p< 0.001), respectively, while Child-Pugh score only has medium predictive value with AUROC <0.8. The study of Zou et al. [7] also showed that the AUROC of the ALBI score in predicting in-hospital mortality in 631 patients with variceal bleeding was 0.808 (95% CI: 0.0775-0.838, p<0.001), the optimal cut-off value is -1.5273 with a sensitivity of 92.86%, a specificity of 64.01%. While research by Nagaraja et al. [15] ALBI score only has medium predictive value with AUROC of 0.743 (95% CI: 0.652-0.821). For the PALBI score, the study of Chen et al. [16] on 221 patients found that the PALBI score also has good value in predicting the risk of death in the first 30 days in cirrhotic patients with variceal bleeding with AUROC of 0.827 (almost equivalent to our results). Thus, the ALBI and PALBI scores have good value in predicting in-hospital mortality in cirrhotic patients with acute variceal bleeding.

Using the DeLong test to compare the difference between the scores, the results in Table 5 show that: the MELD score has the highest AUROC, but this difference is not statistically significant (p>0.05; z<1.96). Thus, in our study, the predictive value of early death of the ALBI and PALBI scores is equivalent to the Child-Pugh and MELD scores. The results of many studies around the world also show that with the prognosis of in-hospital mortality, the scores have prognostic value at different levels.

The study has some limitations that it has not been able to compare and evaluate the value of the scores in distance prognosis; rebleeding and in-hospital mortality is highly depending on the treatment issues (early use of positive inotropic agents, antibiotic and early endoscopic intervention...); The number of patients is not large enough.

Conclusion

The study results showed that the ALBI and PALBI scores were both valuable in predicting early rebleeding and in-hospital mortality, higher than the AIMS65, MELD and Child-Pugh scores in predicting early rebleeding but equivalent in predicting mortality. With characteristics independent of subjective factors (such as Child-Pugh, AIMS65), fairly simple calculation (can use calculation software on smartphones), ALBI, PALBI scores should be recommended to apply in clinical practice to predict cirrhotic patients with acute variceal bleeding.

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