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Prediction of esophageal varices in patients with HCV-related cirrhosis using albumin-bilirubin, platelets-albumin-bilirubin score, albumin-bilirubin-platelets grade, and GAR

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Abstract

Background: Development of esophageal varices (EVs) is the main complication of portal hypertension. Early detection prevents variceal bleeding. Baveno VI consensus recommended endoscopy if transient elastography (TE) > 20 kPa and platelets below 150,000/mm³.

Aim: Assessment of the reliability of the albumin-bilirubin (ALBI), platelets-albumin-bilirubin (PALBI), albumin-bilirubin-platelets (ALBI-PLT) score, and gamma-glutamyl transferase-platelets (GAR) ratio as non-invasive models for prediction of EVs presence and the need for endoscopy in patients with HCV-related cirrhosis.

Methods: HCV-related F4 fibrosis by TE or cirrhosis patients were included ($n = 661$). Full metabolic profile, CBC, ultrasonography, and endoscopy were done.

Results: The average age was 42.89 years mainly males. Patients with EVs had statistically significant ($p < 0.05$) higher TE values, ALBI, ALBI-PLT, and PALBI than those without EVs. Both groups were comparable for GAR. Large varices were statistically ($p < 0.05$) associated with higher ALBI, ALBI-PLT, and PALBI. Both small and large varices had comparable TE and GAR. EVs detection cutoffs (sensitivity, specificity): TE > 20 kPa (83.64%, 91.62%), ALBI > -2.43 (81.28%, 74.89%), ALBI-PLT > 3 (77.34%, 72.93%), and PALBI > -2.28 (62.1%, 76.4%). On comparison of the ROCs, TE was better than ALBI ($p < 0.05$), ALBI-PLT, and PALBI. ALBI was better than ALBI-PLT and PALBI. Both ALBI-PLT and PALBI are comparable ($p > 0.05$). Positive indirect hemagglutination of schistosomiasis, portal vein diameter, splenic vein diameter, TE, ALBI, ALBI-PLT, and PALBI were independent predictors of EVs existence. On multivariate analysis, portal vein diameter, TE, and ALBI score were significant.

Conclusion: The ALBI, ALBI-PLT, and PALBI are useful predictors of EVs presence and the need of diagnostic endoscopy especially in centers that lack FibroScan.

Keywords: HCV, Esophageal varices, Cirrhosis, Transient elastography, ALBI, PALBI, ALBI-PLT

Background

Portal hypertension (PHTN) is a pathological increased portal vein pressure. It is defined as hepatic venous pressure gradient (HVPG) > 5 mmHg [1]. Anatomically, the etiology may be prehepatic, e.g., portal vein thrombosis, intrahepatic, e.g., cirrhosis and post-hepatic, e.g., congestive

hepatopathy. The intrahepatic causes can be classified into presinusoidal as schistosomiasis, sinusoidal as viral-related cirrhosis, and postsinusoidal as Budd-Chiari syndrome [2].

Liver cirrhosis is the most important cause of portal hypertension. There are several factors associated with pathogenesis of portal hypertension. There is increased intrahepatic vascular resistance to the portal flow due to sinusoidal capillarization as well as fibrosis-induced distortion of the vasculature. Dynamically, there is contraction

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of the smooth muscles of the blood vessels, hepatic stellate cells around the sinusoids, and the myofibroblasts in the fibrous septae, in response to increased vasoconstrictors, e.g., endothelins, norepinephrine, angiotensin II, cysteinyl leukotrienes and decreased intrahepatic vasodilators as nitrous oxide. Splanchnic vasodilation in response to glucagon, nitrous oxide, prostacyclin, bacterial translocation, and carbon monoxide is a major cause of increased portal venous flow [1, 3].

Esophageal varices (EVs), a major complication of portal hypertension, may rupture and bleed with increased mortality rate. EVs are dilated tortuous submucosal veins usually in the distal esophagus. They develop when HVPG > 10 mmHg but bleed when HVPG > 12 mmHg [1]. Endoscopy is the gold standard for the detection and diagnosis for the follow-up of EVs.

By doing endoscopy, we can classify variceal size, detect gastric varices and portal hypertensive gastropathy. Moreover, endoscopy is a therapeutic tool that allows variceal eradication, for example, band ligation and glue obturation of gastric varices [4].

Endoscopy is costly, bothersome for the patients especially if done without conscious sedation. So, non-invasive methods for variceal detection are warranted. Clinically, splenomegaly, platelet count, and platelet to spleen ratio > 909 are suggestive of portal hypertension. Radiologically, Doppler, CT, and MRI can detect varices. Furthermore, liver stiffness measured by transient elastography (TE) as with FibroScan can predict EVs. Recently, endoscopic video capsule can diagnose EVs but cannot assess the size [5].

On the one hand, the Baveno VI consensus [6] recommended screening endoscopy in patients with liver transient elastography (TE) > 20 kPa and platelets < 150,000/mm³ and vice versa. On the other hand, the TE measurement by FibroScan is not available in all hospitals.

In clinical practice, the physician needs models based on the routine investigations to alarm him about the probability of esophageal varices and need of the endoscopy.

This study aimed at assessing albumin-bilirubin (ALBI), platelets-albumin-bilirubin score (PALBI), albumin-bilirubin-platelets grade (ALBI-PLT), and gamma-glutamyl transferase-platelets (GAR) ratio as non-invasive models for prediction of EVs presence and the need for endoscopy in patients with HCV-related cirrhosis.

Methods

This study was conducted in the National Liver Institute hospitals, Menoufia University. After patient education and answering for all questions, an informed consent was signed by all patients. The study was approved by the institutional review board.

Six hundred sixty-one HCV patients with F4 fibrosis as measured by transient elastography ($n = 423$, 62.5%)

[7, 8] or clinically diagnosed as having cirrhosis. The diagnosis of liver cirrhosis was done depending on the clinical, laboratory and radiological features by abdominal ultrasonography [9].

Exclusion criteria included the following: dual or other liver disease (HBV, alcohol, etc.); portal vein thrombosis; gastric varices on endoscopy; history of previous endoscopy; previous variceal bleeding, ascites; hepatic encephalopathy; and hepatocellular carcinoma.

Thorough history taking and complete clinical examination of the patients were done. Full metabolic profile, CBC, and INR were done. Gamma-glutamyl transferase was done only in 148 cases. All investigations were done within 1 week before endoscopy.

Upper esophageo-gastroscopy was done by the same endoscopist (A) to screen for EVs presence and grade discrimination. EVs were classified into small and large varices [10].

Calculations:

$$\text{ALBI} = (\log_{10} \text{bilirubin } \mu\text{mol/L} \times 0.66) + (\text{albumin g/L} \times -0.085) \text{ [11].}$$

ALBI grades: ALBI I ≤ -2.60 , ALBI II > -2.60 to ≤ -1.39 and ALBI III > -1.39 .

$$\text{PALBI} = (2.02 \times \log_{10} \text{bilirubin}) + (-0.37 \times [\log_{10} \text{bilirubin}]^2) + (-0.04 \times \text{albumin}) + (-3.48 \times \log_{10} \text{platelets}) + (1.01 \times [\log_{10} \text{platelets}]^2) \text{ [12, 13].}$$

PALBI grades: PALBI grade 1: value ≤ -2.53 , PALBI grade 2: value from -2.53 to -2.09 , PALBI grade 3: value > -2.09

ALBI-PLT = sum of the ALBI grade (I–III) to the platelet count grade (I–II). Grade I platelet count = platelets > 150,000/mm³ and grade II platelet count = platelets $\leq 150,000/\text{mm}^3$. The ALBI PLT range is 2–5 [14].

GAR = gamma – glutamyl transferase (U/L)/platelets mm³ × 100 [15].

N.B. GAR was calculated for 77 patients without varices, 71 patients with EVs (24 small varices and 47 large varices).

Statistical analysis

Data were statistically analyzed using IBM® SPSS® Statistics® version 21 for Windows (IBM Corporation, North Castle Drive, Armonk, NY, USA) and MedCalc® version 18.2.1 (Seoul, Republic of Korea). Data were expressed as mean ± standard deviation, median (interquartile range) for data that are not normally distributed and column percentage for nominal data. All p values are 2 tailed, with values < 0.05 considered statistically significant, $p = 0.01$ is highly significant and $p = 0.001$ is very highly significant. Comparisons between two groups were performed using Student's t test for parametric data, and Mann-Whitney test for non-parametric data. Chi-squared test (χ^2) and Fisher exact test for categorical data analysis. The receiver operating characteristic

Table 1 Baseline characteristics, investigations, and scores

		No EVs N = 458	EVs N = 203	p
Age (years)		40.48 ± 11.38 40 (17)	51.16 ± 8.55 51 (9)	0.001 [#]
Sex	Female	131 (28.6%)	65 (32.0%)	0.406
	Male	327 (71.4%)	138 (68.0%)	
IHA Sch.	Negative	320 (89.4%)	43 (78.2%)	0.025
	Positive	38 (10.6%)	12 (21.8%)	
Total bilirubin (mg/dL)		1.26 ± 1.74 0.85 (0.5)	2.01 ± 2.16 1.5 (1.4)	0.001 [#]
Albumin (mg/dL)		3.96 ± 0.82 4.2 (0.8)	3.09 ± 0.81 3.1 (1.1)	0.001 [#]
AST (U/L)		55.43 ± 41.26 45 (34)	78.40 ± 115.99 59 (47)	0.001 [#]
ALT (U/L)		55.59 ± 48.14 45 (34)	57.41 ± 75.28 46 (39)	0.912 [#]
GGT (U/L)		64.47 87.14 32 (56.5)	63.70 ± 69.60 34 (52)	0.338 [#]
Hemoglobin (g/dL)		13.48 ± 1.51 13.5 (2.1)	12.25 ± 3.06 12 (2.8)	0.001 [#]
WBCs (/mm ³)		6.52 ± 7.16 5.9 (3)	4.60 ± 1.44 4.45 (2)	0.001 [#]
Platelets (10 ⁹ /L)		175.99 ± 66.72 175 (90)	92.42 ± 39.39 89 (54)	0.001
Platelets (/mm ³)	≥ 15010 ⁹ /L	308 (96%)	13 (4%)	0.001
	< 15010 ⁹ /L	150 (44.1%)	190 (55.9%)	
INR		1.17 ± 0.28 1.1 (0.2)	1.33 ± 0.28 1.3 (0.2)	0.001 [#]
Portal vein diameter (cm)		11.39 ± 1.53 11 (2)	13.17 ± 2.36 13 (2)	0.001 [#]
Splenic vein diameter (cm)		9.28 ± 1.09 9 (1)	9.60 ± 1.51 9 (1)	0.052 [#]
Transient elastography (kPa)		17.54 ± 6.46 16.8 (7.9)	31.92 ± 13.29 29.6 (16.7)	0.001 [#]
ALBI score		- 2.58 ± 0.84 - 2.84 (0.7)	- 1.71 ± 0.81 - 1.68 (1.16)	0.001 [#]
ALBI grade	1	310 (67.7%)	31 (15.3%)	0.001
	2	91 (19.9%)	106 (52.2%)	
	3	57 (12.4%)	66 (32.5%)	
ALBI-PLT score		2.83 ± 1.04 2 (2)	3.99 ± 0.88 4 (1)	0.001 [#]
ALBI-PLT grade	2	249 (54.4%)	17 (8.4%)	0.001
	3	85 (18.6%)	29 (14.3%)	
	4	78 (17%)	96 (47.3%)	
	5	46 (10%)	61 (30%)	
PALBI score		- 2.46 ± 0.51	- 2.09 ± 0.55	0.001
PALBI grade	1	252 (55%)	46 (22.7%)	0.001
	2	128 (27.9%)	55 (27.1%)	
	3	78 (17%)	102 (50.2%)	
GAR		1.82 ± 5.03 0.83 (1.28)	1.57 ± 1.61 0.99 (1.2)	0.197 [#]

EVs esophageal varices, IHA Sch indirect hemagglutination of schistosomiasis
[#]Mann-Whitney test. Data are represented as mean ± standard deviation, number (percentage) for nominal data and median (interquartile range) for data out of normal distribution

(ROC) curve analysis was used for detection of the cut-off value for the esophageal varices presence and for small versus large varices size discrimination. For each cutoff, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. The ROCs were compared using the DeLong tests to assess variable discrimination. Univariate and multivariate binary logistic regression were done for detecting the predictors of esophageal varices presence irrespective of the size.

Results

Table 1 demonstrates comparison between patients with and without esophageal varices. Patients with esophageal varices compared to those without varices, were older (51.16 ± 8.55 vs. 40.48 ± 11.38 years; p = 0.001) and positive for indirect hemagglutination of schistosomiasis (21.8% vs. 10.6%; p = 0.025).

Patients with esophageal varices had statistically significant (p < 0.05) higher value [median (IQR)] of serum total bilirubin [1.5 (1.4) vs. 0.85 (0.5) mg/dL], serum AST [59 (47) vs. 45 (34) U/L], INR [1.3 (0.2) vs. 1.1 (0.2)], liver stiffness [29.6 (16.7) vs. 16.8 (7.9) kPa], portal vein diameter [13 (2) vs. 11 (2) cm], and splenic vein diameter.

Meanwhile, they had statistically significant (p < 0.05) lower value [median (IQR)] of serum albumin [3.1 (1.1) vs. 4.2 (0.8) mg/dL], hemoglobin [12 (2.8) vs. 13.5 (2.1) g/dL], WBCs [4.45 (2) vs. 5.9 (3) mm³] and platelets [89 (54) vs. 175 (90) 10⁹/L]. About 55.9% of the patients with EVs had platelets < 150,000 mm³.

Patients with esophageal varices compared to those without varices (Table 1 and Fig. 1) had statistically significant (p < 0.05) higher value [median (IQR)] of ALBI score [- 1.68(1.16) vs. - 2.84(0.7)], ALBI-PLT score [4(1) vs. 2(2)], and PALBI score (2.09 ± 0.55 vs. - 2.46 ± 0.51). Both groups were comparable as regards GAR (p = 0.197).

Table 2 shows discrimination of small and large varices. Large varices were statistically (p < 0.05) associated with higher [median (IQR)] liver stiffness [29.8 (14.7) vs. 29 (17.1) kPa], ALBI score [- 1.47 (0.7) vs. - 2.08 (1.1)], ALBI-PLT score [4 (1) vs. 4 (0.5)] and PALBI score [- 1.9 (0.5) vs. - 2.34 (0.7)]. Both small and large varices had comparable GAR (p = 0.535).

The ROC curve analysis was used to assess the usefulness of ALBI score, ALBI-PLT score, PALBI score, and GAR as non-invasive models for detection of esophageal varices and discrimination of its grade or size (Table 3).

For variceal detection whatever the size (Figs. 2 and 4); ALBI >- 2.43 had 81.28% sensitivity, 74.89% specificity, 58.9% PPV, and 90% NPV. The ALBI-PLT score > 3 had 77.34% sensitivity, 72.93% specificity, 55.86% PPV, and 87.90% NPV. The PALBI score >- 2.28 had 62.1% sensitivity, 76.4% specificity, 53.8% PPV, and 82% NPV. In

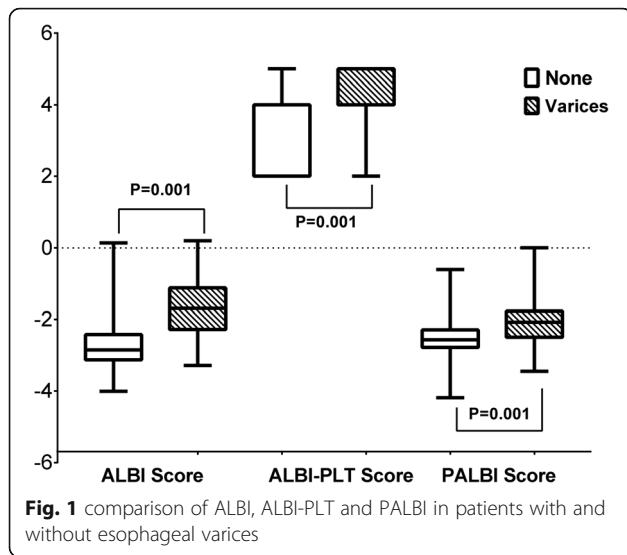


Fig. 1 comparison of ALBI, ALBI-PLT and PALBI in patients with and without esophageal varices

the current study, the cut-off of the liver stiffness adopted by the Baveno VI (> 20 kPa) had had 83.64% sensitivity, 91.62% specificity, 60.5% PPV, and 97.3% NPV.

Pairwise comparison of ROC curves for esophageal varices detection whatever the size revealed TE was better than ALBI ($p < 0.05$), ALBI-PLT, ($p < 0.05$), and PALBI ($p < 0.05$). ALBI was better than ALBI-PLT ($p < 0.05$) and PALBI ($p < 0.05$). Both ALBI-PLT and PALBI are comparable ($p > 0.05$).

For large varices discrimination (Figs. 3 and 4); ALBI > 1.88 had 92.96% sensitivity, 60.61% specificity, 55.9% PPV, and 94.1% NPV. The ALBI-PLT score > 4 had 39.44% sensitivity, 75% specificity, 45.9% PPV, and 69.7% NPV. The PALBI score > 2.12 had 87.32% sensitivity, 64.39% specificity, 56.9% PPV, and 90.4% NPV.

Table 2 Comparison of TE, ALBI, ALBI-PLT, and PALBI in patients with small and large esophageal varices

	Esophageal varices		<i>p</i>
	Small <i>N</i> = 132	Large <i>N</i> = 71	
Transient elastography (kPa)	30.84 ± 12.68 29(17.1)	33.33 ± 14.18 29.8 (14.7)	0.44 [#]
ALBI score	- 1.92 ± 0.83 - 2.08(1.1)	- 1.29 ± 0.57 - 1.47(0.7)	0.001 [#]
ALBI-PLT score	3.89 ± 0.92 4(0.5)	4.18 ± 0.78 4(1)	0.039 [#]
PALBI score	- 2.24 ± 0.55 - 2.34 (0.7)	- 1.80 ± 0.43 - 1.9 (0.5)	0.001 [#]
GAR	1.63 ± 1.64 1.08(1.37)	1.54 ± 1.61 0.86(1.02)	0.535 [#]

[#]Mann-Whitney test. Data are represented as mean ± standard deviation and median (interquartile range) for data out of normal distribution

Table 3 Receiver operating characteristic (ROC) curve analysis of TE, ALBI, ALBI-PLT, and PALBI in patients with and without esophageal varices and small versus large varices

Varices detection					
	ALBI	ALBI-PLT	PALBI	TE	GAR
AUC	0.794	0.784	0.708	0.956	0.562
SE	0.0184	0.0178	0.0225	0.0106	
P	0.001	0.001	0.001	0.001	0.197
95% CI	0.758– 0.831	0.748– 0.821	0.664– 0.752	0.931– 0.973	0.469– 0.654
Cut-off	> - 2.43	> 3	> - 2.28	> 20	
Sensitivity	81.28	77.34	62.1	83.64	
Specificity	74.89	72.93	76.4	91.62	
PPV	58.9	55.86	53.8	60.5	
NPV	90	87.90	82	97.3	
Large varices detection					
	ALBI	ALBI-PLT	PALBI	TE	GAR
AUC	0.744	0.582	0.754	0.561	0.545
P	0.001	0.036	0.001	0.441	0.5431
95% CI	0.678– 0.803	0.511– 0.651	0.688– 0.811	0.421– 0.695	0.422– 0.663
Cut-off	> - 1.88	> 4	> - 2.12		
Sensitivity	92.96	39.44	87.32		
Specificity	60.61	75	64.39		
PPV	55.9	45.9	56.9		
NPV	94.1	69.7	90.4		

TE transient elastography, PPV positive predictive value, NPV negative predictive value

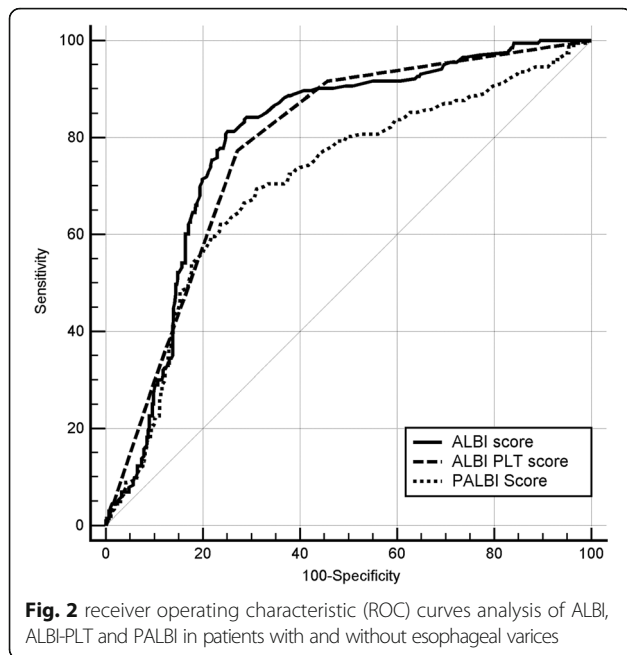
Pairwise comparison of ROC curves for discrimination of large varices revealed both the ALBI score and PALBI score were comparable ($p = 0.526$). Both ALBI score and PALBI score were better than ALBI-PLT score; ($p = 0.001$) and ($p = 0.001$), respectively.

By univariate logistic regression, the following variables were statistically independent predictors for esophageal varices presence (Table 4); positive indirect hemagglutination of schistosomiasis (odd = 2.35, 95% CI = 1.14–4.84), portal vein diameter (odd = 1.71, 95% CI = 1.52–1.92), splenic vein diameter (odd = 1.24, 95% CI = 1.05–1.45), TE (odds = 1.25, 95% CI = 1.19–1.32), ALBI score (odd = 2.94, 95% CI = 2.40–3.62), ALBI-PLT score (odd = 2.78, 95% CI = 2.32–3.34), and PALBI score (odd = 3.45, 95% CI = 2.50–4.76).

On multivariate analysis, portal vein diameter, TE, and ALBI score were statistically independent predictors for esophageal varices presence.

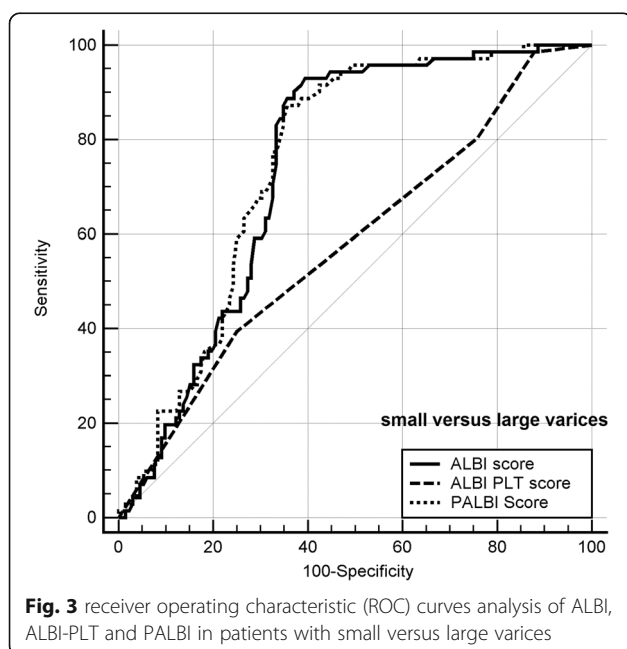
Discussion

PHTN and subsequently EVs varices are the main complications of liver cirrhosis. Once the EVs bleed, the hepatic reserve begins to decrease with each attack since the



liver is dependent in such condition on the hepatic artery. Screening for EVs is needed to detect and eradicate them and so prevent variceal bleeding. Endoscopy is the gold standard for the diagnosis but it is invasive maneuver that a lot of patients are afraid to undergo it.

According to the Baveno VI consensus [6], patients with the following criteria can avoid screening endoscopy, namely, TE < 20 kPa and platelets > 150,000/mm³. These criteria though easily to be applied, depended mainly on the presence of FibroScan that is not available



in all hospitals and primary care units. Another point that the FibroScan is costly regarding the machine price and the maintenance costs. As a result, we still need scores or models that depend on routine laboratory investigations.

Johnson et al. [11] in a large number international study assessed the liver function among patients with hepatocellular carcinoma and correlation with the survival after treatment. They developed the ALBI score that correlated with the liver dysfunction. In comparison with Child Pugh score (CTP), it is simple, non-objective, using two routine labs and being discriminatory for the liver dysfunction. It also correlated with survival. Various publications studied ALBI score in all the aspects of hepatocellular carcinoma from the diagnosis to treatment [16–18].

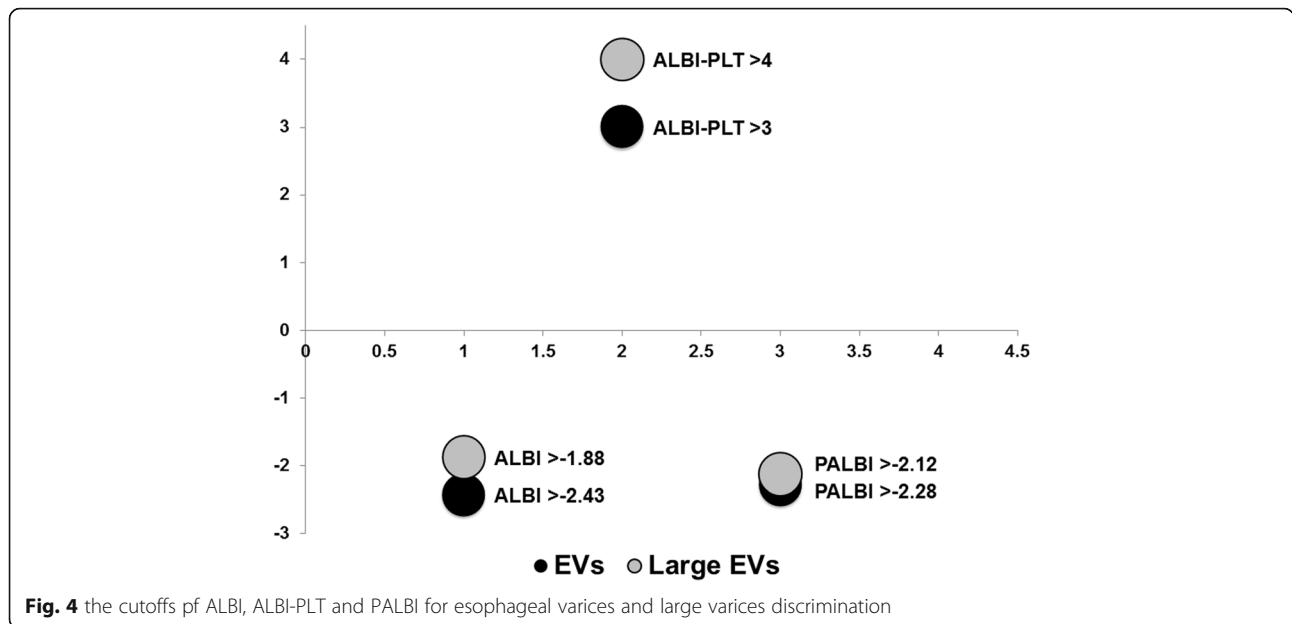
Roayaie et al. [12, 19] incorporated the platelet count into the ALBI score and called the new model PALBI score. They incorporated the liver function status and the PHTN indirectly. PALBI was divided it into 3 grades (PALBI 1 ≤ - 2.53, PALBI 2 - 2.53 to - 2.09, PALBI 3 > - 2.09). PALBI score was developed to stratify HCC patient and assessing the survival post-treatment. Liu et al. [20] reinforced the beneficial role of PALBI score.

ALBI and PALBI scores were initiated mainly for hepatocellular carcinoma patients but its success have encouraged researches to assess them in other liver diseases.

Chen et al. [21] found that ALBI score was superior to MELD and CTP score for predicting 1-, 2-, 3-year mortality in HBV-related cirrhosis patients. The lower the ALBI score the more the survival. Shao et al. [22] found that generally ALBI, CTP, and MELD score were comparable for assessing the in-hospital mortality in patients with cirrhosis. In subgroup analysis, CTP score and ALBI score were the best for HBV patients, meanwhile CTP score and MELD were the best for alcoholic hepatitis patients.

Chen and Lin [23] found that high admission ALBI score was a predictor of 3-month mortality in patients with HBV-related acute-on-chronic liver failure. Hou et al. [24] found that patients with hepatic encephalopathy had higher ammonia and ALBI grade, and their combination was useful for predicting advent of encephalopathy. ALBI score was prognostic in patients with primary biliary cholangitis [25]. Both MELD and ALBI predicted the post transjugular intrahepatic portosystemic shunt (TIPS) creation mortality but the performance of MELD score was superior than ALBI score [26].

Xavier et al. [27] conducted a study on 111 patients with acute upper gastrointestinal hemorrhage. Compared to CTP score and MELD score, only ALBI could predict in hospital stay and 30 days mortality. All the



three score were the same statistically for the 1 year mortality.

Zou et al. [28] found that ALBI score >-1.492 had 100% sensitivity, 69.62% specificity, 7.4% PPV, and 100% NPV for predicting acute upper gastrointestinal hemorrhage-related in-hospital mortality of in liver cirrhosis. The etiology of cirrhosis was, HBV, HCV, alcohol, or mixed. Unfortunately, the AUC of ALBI score was statistically comparable to the CTP and MELD score, so it did not add benefit [28].

Recently, Chen et al. [14] developed new score (ALBI-PLT) to screen for high-risk esophageal varices (HRVs) in patients with HCC. He combined the ALBI grade (I–III) to platelets grade (I–II) so the sum ranged from 2 to 5. HRVs were common with ALBI grade II $>$ I. ALBI-PLT score $>$ 2 had 90% sensitivity, 27% specificity, 21%

PPV, and 97% NPV for detecting HRVs. It is very simple score that also incorporated the dysfunction grade and PHTN indirectly. ABLI-PLT could discriminate patients with HRVs so it is a simple non-invasive screening tool and obviated unnecessary endoscopy.

In the current study, patients with EVs had more incidence of Schistosomiasis 21.8% against 10.6%. Schistosomiasis per se is a major cause of presinusoidal PHTN but it may augment the effect of HCV on the liver subsequently PHTN [29, 30]. The increased serum bilirubin, portal vein diameter and the decreased level of serum albumin, hemoglobin, WBCs and platelets reflect liver dysfunction, PHTN, and splenic sequestration or hypersplenism in patients with EVs.

In fact ALBI, PALBI, and ALBI-PT scores could reflect the degree of liver dysfunction and PHTN since higher

Table 4 Univariate and multivariate analysis of predictors of esophageal varices presence

	Univariate			Multivariate		
	Odds	95% CI	<i>p</i>	Odds	95% CI	<i>p</i>
Positive IHA Sch.	2.35	1.14–4.84	0.021	0.41	0.08–1.98	0.264
Portal vein diameter	1.71	1.52–1.92	0.001	1.76	1.13–2.74	0.012
Splenic vein diameter	1.24	1.05–1.45	0.010	0.73	0.42–1.27	0.263
Transient elastography	1.25	1.19–1.32	0.001	1.21	1.14–1.30	0.001
ALBI score	2.94	2.40–3.62	0.001	30.19	2.37–383.82	0.009
ALBI-PLT score	2.78	2.32–3.34	0.001	0.71	0.31–1.61	0.407
PALBI score	3.45	2.50–4.76	0.001	0.31	0.02–5.96	0.438
GAR	0.98	0.90–1.08	0.698			

IHA Sch indirect hemagglutination of schistosomiasis

values were seen in patients with EVs. Furthermore, they were of higher values in patients with large varices compared to small varices.

Despite the promising studies of GAR value in patients with HBV-related fibrosis [15, 20, 31], some studies did not find this advantage compared to other score in patients with HBV fibrosis [32, 33]. Shimakawa et al. [34] conducted the first study of GAR in patients with HCV fibrosis. GAR was comparable to APRI and Fib-4 score. In our study, it was useless for the diagnosis and discrimination of EVs though the number of patient with data was relatively low.

For EVs prediction, ALBI >− 2.43 had 81.28% sensitivity and 74.89% specificity. The ALBI-PLT score > 3 had 77.34% sensitivity and 72.93% specificity. The PALBI score >− 2.28 had 62.1% sensitivity and 76.4% specificity.

ALBI >− 1.88 (92.96% sensitivity, 60.61% specificity), ALBI-PLT score > 4 (39.44% sensitivity, 75% specificity), and PALBI score >− 2.12 (87.32% sensitivity, 64.39% specificity) could discriminate large from small varices. Again which one is the best? The ALBI-PLT score was less effective than ALBI and PALBI for EVs size discrimination.

The ROC analysis of the TE cutoff (> 20kPa) adopted by the Baveno VI consensus [6] in our study showed 83.64% sensitivity and 91.62% specificity. Thrombocytopenia < 150,000/mm³ was statistically associated with EVs but the percentage is not too high (55.9%).

On comparison of the different ROCs liver stiffness measured by FibroScan was better than all other scores, namely, ALBI, ALBI-PLT, and PALBI. In fact, ALBI was better than ALBI-PLT and PALBI. Both ALBI-PLT and PALBI were comparable.

Regarding the size of the varix, TE did not add benefit unlike the other scores where the ALBI and PALBI were the best for variceal size discrimination.

Positive indirect hemagglutination of schistosomiasis, portal vein diameter, splenic vein diameter, liver stiffness, ALBI score, ALBI-PLT score, and PALBI score were independent predictors of EVs existence. On multivariate analysis, portal vein diameter, TE, and ALBI score were statistically independent predictors for esophageal varices presence.

As aforementioned, three studies were conducted on relationship of ALBI and ALBI-PLT and portal hypertension reflected by variceal bleeding [27, 28] or the presence of HRVs [14]. None of them assessed the PALBI score. We are the first study to assess PALBI score and the role of the three scores in screening for EVs in cirrhosis patients without hepatocellular carcinoma.

The cutoff of ALBI-PLT was lower than our study (2 vs. 4–5) [14]. The possible explanations that the authors compared to us chose a cutoff value with high sensitivity

(90% vs. 77.34%) and very low specificity (27% vs. 72.93%).

The limitations of the study are that it is single-center experience, did not assess the longitudinal follow-up mortality, and did not assess them in non-HCV liver diseases or patients with ascites nor HCC. Large number multi-centric studies are needed.

Conclusion

The ALBI, ALBI-PLT, and PALBI are useful predictors of EVs presence and the need of diagnostic endoscopy especially in centers that lack FibroScan.

Abbreviations

PHTN: Portal hypertension; HVPG: Hepatic venous pressure gradient; EVs: Esophageal varices; ALBI: Albumin-bilirubin; PALBI: Platelets-albumin-bilirubin; ALBI-PLT: Albumin-bilirubin-platelets; GAR: γ -Glutamyl transferase-platelets; IHA Sch: Indirect hemagglutination; AUC: Area under the curve; CTP: Child-Pugh; HRVs: High risk esophageal varices; PPV: Positive predictive value; NPV: Negative predictive value; CI: Confidence interval; TE: Transient elastography

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Authors' contributions

Data collection: AA, HMA, MAE. Study design: AA, HMA, MAE. Manuscript writing and final revision: AA. All authors have read and approved the manuscript

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

It is approved by National Liver Institute IRB 0085/2014. Informed written consent was signed by all patients.

Consent for publication

Not applicable

Competing interests

None

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