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ALBI/ST ratio versus FIB-4 and APRI as a predictor of posthepatectomy liver failure in hepatocellular carcinoma patients

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Abstract

A precise and noninvasive method to predict posthepatectomy liver failure (PHLF) in clinical practice is still lacking. Liver fibrosis or cirrhosis accompanied with varying degrees of portal hypertension plays an important role in the occurrence of PHLF in hepatocellular carcinoma (HCC) patients. This study aims to compare the predictive ability of the albumin-bilirubin score to spleen thickness ratio (ALBI/ST) versus fibrosis-4 index (FIB-4) and aspartate aminotransferase to platelet count ratio index (ARPI) for the occurrence of PHLF. We retrospectively enrolled 932 patients who underwent liver resection for HCC between 2010 and 2017. The predictive accuracy of ALBI/ST ratio, FIB-4, and APRI for occurrence of PHLF was evaluated by receiver operating characteristic curve analysis. PHLF was diagnosed in 69 (7.4%) patients. The ALBI/ST ratio was found to be a significant predictor of PHLF. The AUC of ALBI/ST (AUC = 0.774; 95% CI, 0.731–0.817; P <.001) was larger than that of FIB-4 (AUC = 0.696; 95% CI, 0.634–0.759; P <.001) and APRI (AUC = 0.697; 95% CI, 0.629–0.764; P <.001). Multivariate analysis demonstrated that ALBI/ST ratio was a strong risk factor of PHLF in all hepatectomy subgroups. In conclusion, the ALBI/ST ratio has a superior predictive ability for PHLF compared with APRI and FIB-4.

Abbreviations: ALBI = albumin-bilirubin, ALBI/ST = albumin-bilirubin score to spleen thickness ration, ALT = alanine transaminase, APRI = aspartate aminotransferase to platelet count ratio index, AST = aspartate aminotransferase, AUC = area under receiver operating characteristic curve, CSPH = clinically significant portal pressure, CT = computed tomography, FIB-4 = fibrosis-4 index, HCC = hepatocellular carcinoma, ICG R15 = indocyanine green retention rate 15 min, MELD = model for end-stage liver diseases, MRI = magnetic resonance imaging, PHLF = posthepatectomy liver failure, PVP = portal vein pressure, RLV = remnant liver volume, ROC = receiver operating characteristic, ST = spleen thickness.

Keywords: albumin-bilirubin score to spleen thickness ratio, aspartate aminotransferase to platelet count ratio index, fibrosis-4 index, hepatocellular carcinoma, posthepatectomy liver failure

1. Introduction

Hepatocellular carcinoma (HCC) with varying degrees of cirrhosis is one of the most prevalent malignancies worldwide.[1,2] Partial liver resection is widely regarded as the first-line curative treatment modality for HCC patients.[3] Despite advancements in perioperative management, the invasiveness of surgical procedures in addition to coexisting chronic liver diseases still cause an incidence of posthepatectomy liver failure (PHLF). Due to lack of effective treatments, PHLF remains the main cause of postoperative mortality in HCC patients undergoing liver resection. Yet, the magnitude of PHLF events is still huge and there are still lacking accurate predictive markers. To our knowledge, accurate preoperative assessment of liver function and strict patient selection are the main strategies of preventing adverse postoperative outcomes.[4]

Hepatic fibrosis and cirrhosis, which are mostly associated with chronic viral hepatitis or steatosis, often accompany with impaired liver function. Recently, several noninvasive biomarkers of liver fibrosis based on laboratory parameters have been proposed. The fibrosis-4 index (FIB-4) [5] and aspartate aminotransferase (AST) to platelet count ratio index (ARPI) [6] are 2 alternative biomarkers which have been shown to be effective in assessing liver fibrosis and cirrhosis.[7–12] However, only a few studies investigated the accuracy of FIB-4 and ARPI indices in predicting short-term outcomes of liver resection in HCC patients.[13–16]

Liver function is a major determinant of postoperative outcomes. As a simple and objective assessment tool of liver function, the ALBI grading system has recently been proven to be a powerful predictor of short-term and long-term outcomes after liver resection.[17–25] However, the ALBI grading system is limited by its inability to account for portal vein pressure (PVP). As a key step in the pathophysiological mechanism of liver

cirrhosis, portal hypertension was reported to be correlated with adverse postoperative outcomes.[26–28] Being an indicator of severe portal hypertension, spleen thickness (ST) has been proven to be a reliable predictor of PHLF.[29] On this basis, we proposed an innovative biomarker, the ALBI score to spleen thickness ratio (ALBI/ST), to predict PHLF in HCC patients.

In the present study, we investigated and compared the accuracy of ALBI/ST ratio, FIB-4 index, and APRI in predicting PHLF among HCC patients who underwent liver resection.

2. Patients and methods

2.1. Patients

A total of 932 patients who were diagnosed with HCC and underwent hepatectomy at the Second Xiangya Hospital were retrospectively enrolled between 2010 and 2017. Eligibility criteria included: Child–Pugh grade A or B liver function, no therapy for neoplasm before hepatectomy, and no cardiopulmonary dysfunction, renal insufficiency or cerebropathy before surgery. Exclusion criteria included: coexisting malignancies, former splenectomy, splenomegaly caused by etiology beyond liver cirrhosis, and obstructive jaundice before surgery. This study complied with the principles of Helsinki Declaration and was approved by the Institutional Ethical Board of Central South University. Informed consent was waived for this retrospective research.

2.2. Diagnosis and definitions

Spleen thickness was routinely measured and reported by ultrasonography, and it was defined as the transversal distance between the splenic hilum and the point of tangency of the opposite convex surface. Operators were experienced in ultrasound and not aware of hemodynamic information of the patients. Classification of the Child–Pugh score was based on prepublished methodology.[30] Clinically significant portal pressure (CSPH) was confirmed as the development of esophageal/gastric varices or low platelet count ($< 100 \times 10^9$/L) with splenomegaly (major diameter > 12 cm).[31,32] The definition of PHLF was in accordance with the guidelines proposed by International Study Group of Liver Surgery, as a total serum bilirubin $> 50 \mu$mol/L and a prothrombin time index $< 50\%$ (which corresponds to international normalized ratio >1.7) on or after postoperative day 5.[33,34] Postoperative mortality was defined as death within 30 days of surgery or during the hospital stay if this was longer.

ALBI score, ALBI/ST, FIB-4 index, and APRI were calculated using the following formulas :[5,6,17]

ALBI score $= -0.085 \times$ (albumin [g/L]) $+ 0.66 \times \log_{10}$(bilirubin [μmol/L]);

FIB-4 $=$ age [years] $\times$ AST [U/L]/(platelet count [10^9/L] $\times$ ALT [U/L]$^{1/2}$);

APRI $=$ ([AST/upper limit of normal (ULN)]/platelet count [10^9/L]) $\times 100$;

ALBI/ST ratio $=$ ALBI score/spleen thickness (cm);

ALBI score was further stratified into 3 classifications: ALBI grade 1 (≤ -2.60), grade 2 (>-2.60 to ≤ -1.39) and grade 3 (> -1.39).

2.3. Surgical technique

The remnant liver volume (RLV) was assessed based on the imaging data, especially for patients who underwent major liver resection. An RLV of 30% was used as the lower limit for patients with normal liver function, whereas a minimum RLV of approximately 40% was used for patients with impaired hepatic function. Conventional open hepatectomy was performed in the majority of patients, with a small number undergoing laparoscopic surgery. Liver transection was conducted using an ultrasonic dissector or clamp crushing method under low central pressure based on the operator's preference. Intermittent Pringle maneuver was used if needed to control intraoperative hemorrhage. Hepatic resection was defined as major if a removal of 3 segments or more was performed and minor if fewer than 3 segments were resected.

2.4. Statistical analysis

Statistical analysis was conducted using SPSS version 17.0 (SPSS, Inc., Chicago, IL) and MedCalc version 15.2.2 (MedCalc Software bvba, Ostend, Belgium). Data were expressed as mean $\pm$ SD or absolute values and percentages. P values $< .05$ were considered significant. Student t-test, Chi-square test, and Fisher exact test were used for univariate analysis where appropriate. Univariate analysis and multivariate logistic regression analysis were applied to determine independent risk factors correlated with PHLF. The discriminative power of different noninvasive methods for the prediction of PHLF was evaluated using the receiver operating characteristic (ROC) curve analysis and expressed as area under the ROC curve (AUC). The cut-off points for the occurrence of PHLF were also determined by ROC curve analysis. Comparison between AUCs was made using Delong test.

3. Results

3.1. Patient demographics

The clinical characteristics and laboratory data of the 932 patients are summarized in Table 1. This study included 827 males and 105 females, with a mean age of 51.3 years. The main etiology of liver diseases was hepatitis B, present in 799 (85.7%) patients. A total of 247 (26.5%) patients underwent major liver resection. Eighteen deaths occurred during 30 days of operation, with a mortality rate of 1.9%.

3.2. Univariate and multivariate analyses of risk factors for PHLF

PHLF occurred in 69 (7.4%) patients. In univariate analysis, factors associated with PHLF included age, ALT, tumor size, blood loss, major hepatectomy, FIB-4, APRI, ALBI score, ST, Child–Pugh score, and ALBI/ST (Table S1, http://Links.lww.com/MD/C915). Two multivariate analysis models were conducted to exclude collinearity (Table 2). In the APRI model, blood loss, major hepatectomy, APRI, and ALBI/ST were found to be significant predictors of PHLF. In the FIB-4 model, ALT, blood loss, major hepatectomy, FIB-4, and ALBI/ST were identified as independent predictors of PHLF. Interestingly, the ALBI/ST ratio exhibited a strong predictive accuracy of PHLF in both models.

3.3. Predictive power of the indices for PHLF

The ability of ALBI/ST, FIB-4, APRI, ALBI, and ST in predicting PHLF was evaluated by ROC analysis (Fig. 1). The AUC for ALBI/ST ratio (AUC = 0.774, P <.001) was larger than that of FIB-4 (AUC = 0.696, P <.001), APRI (AUC = 0.697, P <.001), ALBI (AUC = 0.701, P <.001), and ST (AUC = 0.710, P <.001).

Table 1

Baseline characteristics of 932 HCC patients.

Characteristics	Total cohort (n = 932)
Age, years*	51.3 ± 11.4
Male gender†	827 (88.7)
Etiology of liver diseases†	
HBV	799 (85.7)
HCV	15 (1.6)
Total bilirubin, μmol/L*	15.3 ± 7.6
Albumin, g/L*	38.3 ± 4.4
Creatinine, mg/L*	75.1 ± 19.9
ALT, U/L*	43.4 ± 29.3
AST, U/L*	49.6 ± 31.8
Prothrombin time, sec*	13.3 ± 1.4
INR*	1.07 ± 0.13
Platelet count, × 10^9/L*	161.7 ± 77.3
Maximum tumor size, cm*	7.0 ± 4.0
Blood loss, mL*	595.6 ± 868.9
Spleen thickness, cm*	3.7 ± 0.9
FIB-4 index*	3.28 ± 3.12
APRI*	1.15 ± 1.12
ALBI score*	−2.50 ± 0.39
ALBI/ST ratio*	−0.71 ± 0.21
Child–Pugh score*	5.5 ± 0.7
Extent of hepatectomy†	
Major	247 (26.5)
Minor	685 (73.5)
CSPH†	201 (21.6)
ALBI grade†	
1	384 (41.2)
2	541 (58.0)
3	7 (0.8)
Child–Pugh grade†	
A	854 (91.6)
B	78 (8.4)

ALBI = albumin-bilirubin, ALBI/ST = albumin-bilirubin score to spleen thickness ratio, ALT = alanine aminotransferase, APRI = aspartate aminotransferase to platelet count ratio index, AST = aspartate aminotransferase, HBV = hepatitis B virus, CSPH = clinically significant portal pressure, FIB-4 = fibrosis 4 index, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, INR = international normalized ratio, .

* Values are mean ± SD.

† Values are number (%).

The optimal cut-off values of ALBI/ST ratio, FIB-4, APRI, ALBI, and ST were −0.627, 2.58, 0.93, −2.496, and 3.8, respectively. The cut-off value of ALBI/ST showed a sensitivity of 67.3% and a specificity of 82.6%. We further compared the AUCs of ALBI/ST, FIB-4, and APRI using the Delong test. The difference between the AUCs of ALBI/ST and FIB-4 (P =.022), difference between ALBI/ST and APRI (P =.036) were both significant.

3.4. Predictive power of the indices for PHLF in the subgroups stratified by the extent of hepatectomy

To further investigate the predictive accuracy of the indices, we divided the entire cohort of patients into 2 subgroups according to the extent of liver resection. Multivariate analysis in minor hepatectomy subgroup revealed that age, Child–Pugh score and ALBI/ST were significant predictors of PHLF in the APRI model, while Child–Pugh score, FIB-4, and ALBI/ST were found to be significant risk factors of PHLF in the FIB-4 model (Table 3). In the major hepatectomy subgroup, multivariate analysis revealed that APRI and ALBI/ST were independent predictors of PHLF in the APRI model, while ALT and ALBI/ST were found to be independent risk factors of PHLF in the FIB-4 model (Table 4). The ROC analysis demonstrated that ALBI/ST has a superior or comparable predictive accuracy for PHLF compared with FIB-4, APRI, ALBI, and ST in both major and minor hepatectomy subgroups (Fig. 2, Table 5). The distribution of values of the indices are shown in Figure S1, http://Links.lww.com/MD/C915.

3.5. ALBI/ST and clinicopathological characteristics of patients

Table 6 displays the clinical and laboratory data based on the ALBI/ST values. Comparison between patients with an ABLI/ST ≤ −0.627 and patients with an ALBI/ST > −0.627 revealed statistical differences in etiology of liver diseases, total bilirubin, albumin, AST, prothrombin time, INR, platelet count, blood loss, ST, FIB-4, APRI, ALBI score, Child–Pugh score, CSPH, and PHLF (All P <.05, Table 6).

4. Discussion

A majority of HCC patients has a background of liver fibrosis or cirrhosis.[2] Liver fibrosis or cirrhosis accompanied with portal hypertension in HCC patients plays an important role in the occurrence of PHLF. Hence, accurate evaluation of liver fibrosis and cirrhosis before surgical operation is imperative. The APRI and FIB-4 indices have been proposed to be alternative

Table 2

Multivariate logistic regression analyses for posthepatectomy liver failure in the total cohort.

Variable	APRI model		FIB-4 model	
	OR (95% CI)	P	OR (95% CI)	P
Age, years	1.75 (0.99–3.10)	.054	1.54 (0.86-2.76)	.151
ALT, U/L	1.68 (0.95–2.97)	.074	2.11 (1.23-3.61)	.007
Tumor size, cm	1.39 (0.74–2.61)	.313	1.37 (0.73-2.58)	.322
Blood loss, mL	1.95 (1.06–3.56)	.031	1.98 (1.09-3.62)	.026
Major hepatectomy	2.02 (1.13–3.60)	.017	1.95 (1.10-3.48)	.023
Operation time, min	0.92 (0.53–1.63)	.783	0.96 (0.55-1.69)	.890
Prothrombin time, sec	0.65 (0.35–1.20)	.168	0.64 (0.35–1.19)	.159
Child–Pugh score	1.60 (0.78–3.27)	.202	1.59 (0.78–3.23)	.204
APRI	2.32 (1.23–4.40)	.010		
FIB-4			2.06 (1.11–3.83)	.022
ALBI/ST	6.87 (3.58–13.18)	<.001	7.05 (3.68–13.50)	<.001

ALBI/ST = albumin-bilirubin score to spleen thickness ratio, ALT = alanine transaminase, APRI = aspartate aminotransferase to platelet count ratio index, CI = confidence interval, FIB-4 = fibrosis 4 index, OR = odds ratio.
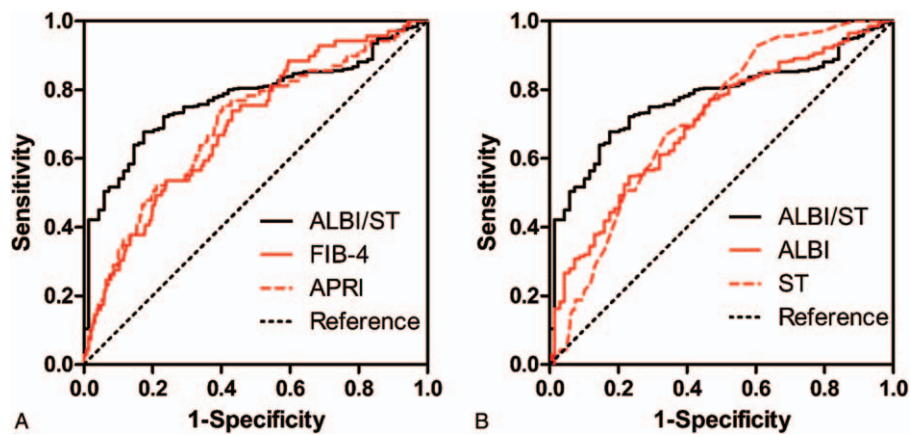
Figure 1. ROC curves for ALBI/ST, APRI, and FIB-4 in the total cohort (A) ROC curves for ALBI/ST, ALBI and ST in the total cohort (B). ALBI/ST, albumin-bilirubin score to spleen thickness ratio, ALBI = albumin-bilirubin score, APRI = aspartate aminotransferase to platelet count ratio index, FIB-4 = fibrosis 4 index, ROC = receiver operating characteristic, ST = spleen thickness.

Table 3

Multivariate logistic regression analyses for posthepatectomy liver failure in minor hepatectomy subgroup.

Variables	APRI model		FIB-4 model	
	OR (95%CI)	P	OR (95%CI)	P
Age, years	2.35 (1.13–4.87)	.022	1.90 (0.90–4.02)	.095
ALT, U/L	1.38 (0.65–2.92)	.396	1.64 (0.81–3.33)	.173
Tumor size, cm	1.53 (0.73–3.22)	.262	1.60 (0.76–3.38)	.218
Blood loss, mL	2.05 (0.96–4.36)	.064	2.00 (0.93–4.28)	.075
Operation time, min	0.77 (0.36–1.66)	.510	0.82 (0.38–1.77)	.614
Prothrombin time, sec	0.79 (0.36–1.72)	.551	0.77 (0.35–1.69)	.519
Child–Pugh score	2.71 (1.12–6.56)	.027	2.57 (1.05–6.30)	.039
APRI	2.00 (0.86–4.68)	.108		
FIB-4			3.20 (1.29–7.91)	.012
ALBI/ST	5.05 (2.11–12.13)	<.001	4.58 (1.92–10.96)	.001

ALBI/ST = albumin-bilirubin score to spleen thickness ratio, ALT = alanine transaminase, APRI = aspartate aminotransferase to platelet count ratio index, CI = confidence interval, FIB-4 = fibrosis 4 index, OR = odds ratio.

measurements of liver fibrosis to liver biopsy.[11,35,36] The 2 indices are widely used because they are noninvasive and possess high accuracy. The APRI formula consists of AST and PLT, while the FIB-4 formula includes age and ALT besides the 2 parameters above. FIB-4 and APRI are considered to be accurate measurements because they incorporate existing liver injury (as manifested by transaminases level) and sinusoidal injury (which influences platelet count).

To our knowledge, only a few studies have explored the predictive power of FIB-4 and APRI for PHLF.[14,16] Consistent

Table 4

Multivariate logistic regression analyses for posthepatectomy liver failure in major hepatectomy subgroup.

Variables	APRI model		FIB-4 model	
	OR (95%CI)	P	OR (95%CI)	P
Age, years	1.27 (0.48–3.37)	.638	1.26 (0.47–3.41)	.649
ALT, U/L	2.66 (1.03–6.87)	.054	3.66 (1.48–9.06)	.005
Tumor size, cm	1.30 (0.35–4.92)	.696	1.21 (0.34–4.39)	.767
Blood loss, mL	1.38 (0.48–3.97)	.552	1.61 (0.57–4.50)	.369
Operation time, min	1.19 (0.47–2.97)	.715	1.19 (0.49–2.92)	.702
Prothrombin time, sec	0.52 (0.18–1.45)	.208	0.54 (0.19–1.51)	.236
Child–Pugh score	0.70 (0.19–2.60)	.593	0.67 (0.18–2.46)	.543
APRI	2.84 (1.04–7.77)	.042		
FIB-4			1.13 (0.44–2.90)	.798
ALBI/ST	10.89 (3.95–29.99)	<.001	12.19 (4.39–33.84)	<.001

ALBI/ST = albumin-bilirubin score to spleen thickness ratio, ALT: alanine transaminase, APRI = aspartate aminotransferase to platelet count ratio index, FIB-4 = fibrosis 4 index, OR = odds ratio, CI = confidence interval.
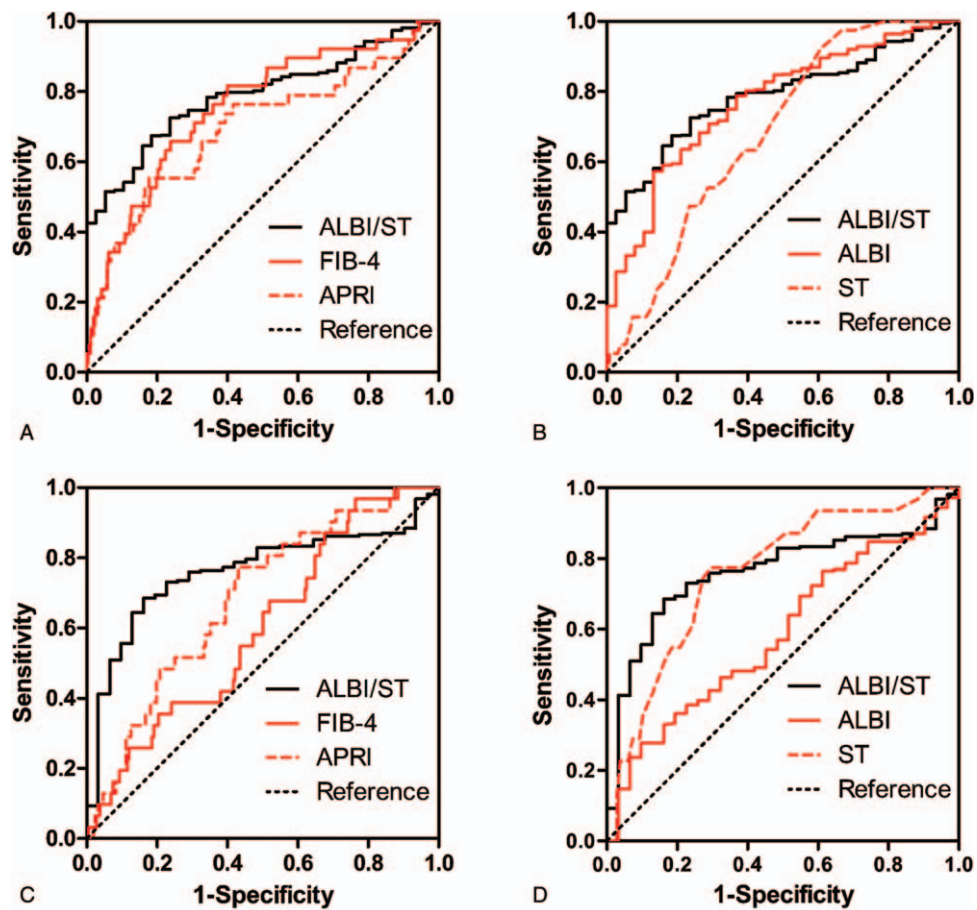
Figure 2. ROC curves for ALBI/ST, APRI, and FIB-4 in the minor hepatectomy subgroup (A) and major hepatectomy (C) ROC curves for ALBI/ST, ALBI, and ST in the minor hepatectomy subgroup (B), and major hepatectomy subgroup (D). ALBI/ST = albumin-bilirubin score to spleen thickness ratio, APRI = aspartate aminotransferase to platelet count ratio index, FIB-4 = fibrosis 4 index, ALBI = albumin-bilirubin score, ROC = receiver operating characteristic, ST = spleen thickness.

with these studies, our study found that FIB-4 and APRI were significant predictors of PHLF. Multivariate analysis revealed that FIB-4 and APRI were both significant risk factors. The ROC analysis revealed that the AUCs of FIB-4 and APRI for predicting PHLF were 0.696 (P <.001) and 0.697 (P <.001), respectively. These results showed that the 2 indices have a high discriminative power for PHLF.

It was previously reported that the severity of portal hypertension could predict the occurrence of PHLF.[27,28] This is because PVP may increase after surgery due to a smaller liver size hence increased portal flow per tissue unit mass. The resultant acute portal hypertension may cause endothelial

damage and suppress liver regeneration, all of which play key roles in the mechanism of PHLF.[28] As a parameter that can be easily measured, spleen thickness (ST) has been confirmed to be an indicator of portal hypertension which associates with PHLF.[11,29,37,38] The newly proposed ALBI score was found to have a higher prognostic value compared with conventional methods such as Child–Pugh score, ICG R15 and MELD score.[21,23,25] Given that, we put forward the ALBI/ST ratio and explored its capability in predicting PHLF.

The results confirmed our hypothesis that ALBI/ST ratio was a significant predictor of PHLF as revealed by multivariate analysis. ROC curves further showed that the AUC value of ALBI

Table 5

AUCs of several biomarkers for predicting PHLF.

Biomarkers	Total cohort			Minor hepatectomy subgroup			Major hepatectomy subgroup		
	AUC	95%CI	P	AUC	95%CI	P	AUC	95%CI	P
ALBI/ST	0.774	0.73−0.82	<.001	0.789	0.74−0.84	<.001	0.761	0.69−0.84	<.001
FIB-4	0.696	0.63−0.76	<.001	0.752	0.67−0.84	<.001	0.598	0.50−0.70	.077
APRI	0.697	0.63−0.76	<.001	0.694	0.59−0.79	<.001	0.683	0.59−0.78	<.001
ALBI	0.701	0.64−0.76	<.001	0.770	0.70−0.84	<.001	0.586	0.49−0.69	.123
ST	0.710	0.66−0.76	<.001	0.682	0.61−0.75	<.001	0.761	0.67−0.85	<.001

ALBI = albumin-bilirubin score, ALBI/ST = albumin-bilirubin score to spleen thickness ratio, APRI = aspartate aminotransferase to platelet count ratio index, AUC = area under the receiver operating characteristic curve, FIB-4 = fibrosis 4 index, PHLF = posthepatectomy liver failure, ST = spleen thickness.

Table 6

Comparison between patients with ALBI/ST ≤ −0.627 and ALBI/ST > −0.627.

Characteristic	ABLI/ST ≤ −0.627 n = 598	ABLI/ST > −0.627 n = 334	P
Age, years*	50.9 ± 11.7	52.1 ± 10.7	.137
Gender (male/female)	74/524	31/303	.152
Etiology of liver diseases†			<.001
HBV	501 (83.8)	298 (89.2)	
HCV	7 (1.2)	8 (2.4)	
Total bilirubin, μmol/L*	13.6 ± 5.8	18.3 ± 9.4	<.001
Albumin, g/L*	39.7 ± 3.9	35.6 ± 4.0	<.001
Creatinine, mg/L*	75.2 ± 18.7	74.7 ± 21.8	.725
ALT, U/L*	42.4 ± 28.9	45.3 ± 29.9	.147
AST, U/L*	47.6 ± 30.9	53.3 ± 33.2	.009
Prothrombin time, sec*	13.0 ± 1.2	13.8 ± 1.6	<.001
INR*	1.05 ± 0.12	1.11 ± 0.14	<.001
Platelet count, × 10⁹/L*	176.9 ± 70.7	134.5 ± 81.1	<.001
Maximum tumor size, cm*	7.0 ± 4.0	7.2 ± 4.3	.453
Blood loss, mL*	540.9 ± 773.9	693.4 ± 1011.1	.010
Spleen thickness, cm*	3.2 ± 0.5	4.6 ± 0.9	<.001
FIB-4 index*	2.58 ± 2.14	4.52 ± 4.07	<.001
APRI*	0.92 ± 0.86	1.56 ± 1.38	<.001
ALBI score*	−2.65 ± 0.32	−2.23 ± 0.35	<.001
ALBI/ST*	−0.83 ± 0.15	−0.49 ± 0.09	<.001
Child–Pugh score*	5.2 ± 0.5	5.9 ± 0.9	<.001
Extent of hepatectomy†			.204
Major	154 (25.8)	93 (27.8)	
Minor	444 (74.2)	241 (72.2)	
CSPH†	60 (10.0)	141 (42.2)	<.001
Postoperative liver failure†	14 (2.3)	55 (16.5)	<.001

ALBI = albumin-bilirubin; ALBI/ST = albumin-bilirubin score to spleen thickness ratio, ALT = alanine aminotransferase, APRI = aspartate aminotransferase to platelet count ratio index, AST = aspartate aminotransferase, CSPH = clinically significant portal pressure, FIB-4 = fibrosis 4 index, HBV = hepatitis B virus, HCV = hepatitis C virus, INR = international normalized ratio.

* Values are mean ± SD.

† Values are number (%).

in predicting PHLF was 0.701, which is closer to 0.723 reported by Wang et al.[9] In addition, the AUC value for ST in predicting PHLF was 0.710, which is smaller than 0.754 reported by Chen et al.[29] This discrepancy may be due to the composition of patients enrolled; in the study by Chen et al, only HBV-related HCC patients were enrolled while a small number of non-HBV HCC patients were recruited in our study. By combining the ALBI and ST indices, we obtained a larger AUC value of ALBI/ST than ALBI or ST alone, which were confirmed to be good predictors of PHLF in previous studies.[21–23,29] In addition, we compared the predictive ability of ALBI/ST with FIB-4 and APRI, and found that ALBI/ST had a higher diagnostic accuracy for PHLF than FIB-4 and APRI.

In general, the relatively small liver after a major liver resection often increases the risk of developing PHLF. As expected, major hepatectomy was identified as an independent risk factor of PHLF in this study. To rule out the effects caused by the reduction of liver volume, we further conducted a stratification analysis based on the extent of hepatectomy. We observed that ALBI/ST ratio was a significant risk factor of PHLF in all hepatectomy subgroups as revealed by the multivariate analysis, while FIB-4 was only an independent predictor of PHLF in minor hepatectomy subgroup, and APRI only showed significance in major hepatectomy subgroup. Moreover, ROC curve analysis showed that the AUC value of ALBI/ST ratio was higher than that of FIB-4 and APRI, both in the minor and major hepatectomy

subgroups, which suggested that ALBI/ST had a higher diagnostic accuracy for PHLF compared with APRI and FIB-4. Being a combination of ALBI and ST, the ALBI/ST ratio not only considers the liver function, but also takes into account portal hypertension indicating that it has higher predictive power for PHLF which can be applied in clinical practice.

The cut-off value of ALBI/ST as determined by ROC analysis was −0.627. Statistical differences were found in the majority of clinical characteristics between patients with ALBI/ST ≤ −0.627 and those with ALBI/ST > −0.627. Interestingly, patients with ALBI/ST > −0.627 had a higher risk of blood loss and occurrence of PHLF, implying that HCC patients with an ALBI/ST > −0.627 should be given more attention during perioperative care.

The current study suffered several limitations. Firstly, majority of patients had a history of HBV infection. Therefore, to improve the findings of this study, the predictive power of the indices for PHLF should be investigated in HCC patients with different etiologies. Secondly, parameters related to splenomegaly such as spleen width, spleen length, or spleen volume were not measured by computed tomography or magnetic resonance imaging in the present research. Lastly, though previous studies reported that ALBI, FIB-4 and APRI had an influence on prognosis of HCC after surgery,[12,39] we did not compare their ability in predicting postoperative long-term outcomes, which remained to be investigated in our future studies.

In conclusion, this study found that a combination of ALBI score with spleen thickness (ALBI/ST ratio) was a significant predictor of PHLF. We also found that APRI and FIB-4 indices, the commonly used noninvasive measurements of liver cirrhosis, had high discriminative power for PHLF. More importantly, the diagnostic accuracy of ALBI/ST ratio for PHLF was superior to that of APRI and FIB-4. Hence, we recommend the clinical application of ALBI/ST as supplement of liver functional reserve assessment before surgery to achieve better postoperative results for HCC patients.

Author contributions

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Investigation: Bo Yang.
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