Liver, Pancreas and Biliary Tract

Platelet-albumin-bilirubin grade: Risk stratification of liver failure, prognosis after resection for hepatocellular carcinoma

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ABSTRACT

Background and aims: The liver function reserve in Child-Pugh (C-P) grade A hepatocellular carcinoma (HCC) patients varies widely, and the value of platelet-albumin-bilirubin (PALBI) grade in predicting posthepatectomy liver failure (PHLF) grade B/C and overall survival (OS) remains unknown.
Methods: From Dec 2004 to Dec 2013, 2038 C-P grade A HCC patients after resection were enrolled. Univariate and multivariate analyses were performed to clarify the risk factors for PHLF grade B/C and OS.
Results: The PALBI grade had higher area under the curve values than albumin-bilirubin (ALBI) and C-P grade in predicting PHLF grade B/C (0.693, 0.683, 0.529 in the entire cohort; 0.677, 0.646, 0.516 in patients who underwent major resection). PALBI grade differentiated C-P grade A patients into three groups with distinct prognoses (P < 0.001), whereas ALBI grade differentiated C-P grade A patients into two groups (P < 0.001). Furthermore, PALBI grade identified three groups with clearly different prognoses in ALBI grade 1 patients (P = 0.032). Multivariate analyses showed that PALBI grade was one of the independent and significant prognostic factors of PHLF grade B/C and OS.
Conclusions: PALBI grade offers a simple, objective and discriminatory method for risk stratification of PHLF grade B/C and OS in C-P grade A HCC patients following resection.

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1. Introduction

Hepatocellular carcinoma (HCC) is the fifth most common solid tumor and the second leading cause of cancer-related death worldwide [1]. In contrast to other solid tumors, HCC patient prognosis is influenced not only by tumor burden but also by the degree of liver functional impairment [2,3]. Avoiding posthepatectomy liver failure (PHLF) grade B/C [4,5] and accurately evaluating long-term survival are two important goals in the management of HCC patients

following curative resection. However, studies that targeted these two outcomes were still lacking, and the Child-Pugh (C-P) grade, which has been widely used for the assessment of preoperative liver function in clinical practice [6–9], does not actually offer a wide range of discrimination among patients with HCC, as the majority of cases fall in grade A despite having radically unequal liver reserve. Thus, it is clinically valuable to develop a more objective and accurate method for better preoperative risk evaluation of PHLF grade B/C and long-term survival among C-P grade A HCC patients.

In 2015, the albumin-bilirubin (ALBI) grade [10], which is based solely on preoperative laboratory parameters, was introduced as an alternative measure of liver function, and an increasing number of external validations have tested the prognostic accuracy of this system [11–15]. Given that the ALBI grade does not incorporate any marker to indicate portal hypertension, the platelet-albumin-

bilirubin (PALBI) grade was proposed as a more objective measure of preoperative liver function reserve to adequately stratify patient survival [16,17]. However, the PALBI grade has been retrospectively generated and needs external validation in independent studies, and it remains controversial whether the capacity of the PALBI grade to predict prognosis is superior to that of the ALBI grade [12,16–19]. Moreover, no study has focused on the value of the PALBI grade in predicting PHLF grade B/C.

Thus, the purpose of this study was to assess the value of the PALBI grade in predicting PHLF grade B/C and long-term survival in a large cohort of C-P grade A HCC patients following curative resection.

2. Materials and methods

The study was conducted according to the ethical guidelines of the 1975 Declaration of Helsinki. The analysis of patient data was approved by the Institutional Review Board and Human Ethics Committee of Sun Yat-sen University Cancer Center. Informed consent was obtained from all patients included in this study.

2.1. Study population

From December 2004 to December 2013, a total of 2508 patients who underwent liver resection were prescreened for enrollment. Patients were enrolled according to the following criteria: (a) aged between 18 and 75 years; (b) patients with histological confirmation of HCC; (c) patients who were classified as C-P grade A preoperatively; (d) an Eastern Co-operative Group performance status of 0; and (e) resectable disease defined as the complete removal of all macroscopic tumor tissue and an expected remnant liver volume no less than $250 \, \text{ml/m}^2$. Exclusion criteria were as follows: (a) evidence of hepatic decompensation including ascites, esophageal or gastric variceal bleeding, or hepatic encephalopathy; (b) an American Society of Anesthesiologists (ASA) score of ≥ 3; and (c) patients with other malignant diseases or incomplete data.

Finally, 2038 patients ultimately fulfilled the inclusion criteria and were recruited for the study.

2.2. Diagnosis and definitions

Diagnoses of HCC were based on histological evidence after operation. Clinically relevant portal hypertension was diagnosed as presence of esophageal varices and/or platelets <100 with splenomegaly. PHLF was defined as an increased international normalized ratio (INR) and concomitant hyperbilirubinemia on or after postoperative day 5 as defined by the International Study Group of Liver Surgery (ISGLS) [20,21]. PHLF grade A corresponded to a substantial regular postoperative course and required no specific treatment, whereas grade B led to a deviation from the regular clinical management but required non-invasive treatment, and grade C resulted in a deviation from the regular clinical management requiring invasive treatment. The ALBI and PALBI grades were retrospectively calculated from existing preoperative laboratory parameters [10,22]. The ALBI grade was calculated using the following equation: $0.66 \times \log_{10}$ bilirubin level $-0.085 \times$ albumin level. The ALBI grades were stratified into grade 1 (≤ -2.60), grade 2 (-2.59 to -1.39), and grade 3 (> -1.39). The PALBI grades were calculated using the following equation: $2.02 \times \log_{10}$ bilirubin level $-0.37 \times (\log_{10}$ bilirubin level$) [2] -0.04 \times$ albumin level $-3.48 \times \log_{10}$ platelet count (PLT) $+ 1.01 \times (\log_{10}$ PLT$) [2]$. The PALBI grade was categorized into grade 1 (≤ -2.53), grade 2 (-2.52 to -2.09), and grade 3 (> -2.09). Serum total bilirubin level was expressed in μmol/L; serum albumin level was expressed in g/L, and blood PLT was expressed in $1000/\mu$L.

2.3. Hepatic resection procedure

Hepatic resection was performed using the previously described technique [23,24]. Intraoperative ultrasound was routinely performed to evaluate the tumor burden, remnant liver, and possibility of a negative resection margin. Pringle's maneuver was routinely employed with a clamp/unclamp time of 10 min/5 min. Anatomic resection was our preferred surgical method for multiple nodules in one segment or neighboring segments as described by Couinaud [25]. For multiple bilobar nodules, the main tumor was usually removed using anatomic resection, whereas satellite nodules were resected using nonanatomic resection with a negative resection margin. If the volume of the remnant liver was inadequate, nonanatomic resection was performed with a negative resection margin. The major liver resection was defined as resection of three or more segments. A negative resection margin was defined as no residue under the microscope after resection at the margins nearest to the gross edge of the tumor.

2.4. Follow-up

Follow-up was performed until December 30, 2017. The first visit of most patients after hospital discharge occurred 4 weeks after surgery. Follow-up sessions of most patients were scheduled once every three months for the first two years and then at gradually increasing intervals. Laboratory tests (including liver function, serum alpha-fetoprotein, and blood parameter evaluation) and abdominal contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) were performed at every follow-up visit. All patients with HBV-related HCC who were prepared for resection for their HCC in our hospital were counselled by a hepatologist for antiviral therapy regardless of the serum HBV DNA result [26]. Recurrence after surgery was defined as the appearance of a new lesion with radiologic features typical of HCC, as confirmed by two or more imaging modalities. The choice of treatment for relapse was determined from the characteristics of the recurrent tumor, patient preference, and discussion among our multidisciplinary team [27].

2.5. Statistical analysis

Overall survival (OS) was defined as the interval between diagnosis and death or the end of the last follow-up period. The area under the receiver operating characteristic (ROC) curve (AUC) was calculated to measure the discriminatory power of the PALBI, ALBI and C-P grades in predicting PHLF grade B/C. To identify the independent predictors of PHLF grade B/C, factors with a probability threshold of less than 0.10 in univariate logistic regression analysis were entered into a multivariable logistic regression model. In terms of long-term survival, OS rates were estimated using the Kaplan–Meier method, and the log-rank test was used to compare the differences. Parameters with a P-value (log-rank) <0.10 in univariate analyses were subjected to multivariate analysis using Cox's proportional hazards models. A significant difference was considered at two-side $P < 0.05$. Data analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

3. Results

A total of 2038 patients were enrolled in this study. The demographic and clinical characteristics are summarized in Table 1. In total, 1907 (93.6%) patients were categorized into C-P grade A5, and 131 (6.4%) patients were C-P grade A6. According to the ALBI grade, 1570 (77.0%) patients were stratified as grade 1468 patients (23.0%) as grade 2, and no patients as grade 3. Based on the PALBI grade, 1223 (60.0%) patients were classified as grade 1730 (35.8%)

Table 1
Baseline characteristics of patients.

Characteristic	No. of patients (n = 2038)
Age (y)	
≤50	1090 (53.5)
>50	948 (46.5)
Sex	
Male	1810 (88.8)
Female	228 (11.2)
Etiology	
HBV	1812 (88.9)
HCV	34 (1.7)
Others	217 (10.6)
Alpha-fetoprotein (ng/mL)	
≤200	1042 (51.1)
>200	996 (48.9)
Platelet count (×10⁹/L)	
≤100	219 (10.7)
>100	1819 (89.3)
Liver function	
Alanine aminotransferase (U/L)	
≤40	1122 (55.1)
>40	916 (44.9)
Prothrombin time (s)	
≤13.5	1726 (84.7)
>13.5	312 (15.3)
Serum albumin (g/L)	
≤35	62 (3.0)
>35	1976 (97.0)
Total bilirubin (μmol/L)	
≤17	1437 (70.5)
>17	601 (29.5)
Liver cirrhosis	
Absent	762 (37.4)
Present	1276 (62.6)
Portal hypertension	
Absent	1900 (93.2)
Present	138 (6.8)
Child-Pugh grade	
A5	1907 (93.6)
A6	131 (6.4)
ALBI grade	
1	1570 (77.0)
2	468 (23.0)
3	0 (0)
PALBI grade	
1	1223 (60.0)
2	730 (35.8)
3	85 (4.2)
Tumor burden	
Greatest tumor size (cm)	
≤5	923 (45.3)
>5	1115 (54.7)
Tumor number	
Single	1554 (76.3)
Multiple	484 (23.7)
Macroscopic vascular invasion	
Present	228 (11.2)
Absent	1810 (88.8)
Extent of liver resection[a]	
Major	537 (26.3)
Minor	1501 (73.7)
Surgical margin (cm)	
≤1	1283 (63.0)
>1	755 (37.0)
Time of Pringle's maneuver (min)	
≤20	1527 (74.9)
>20	511 (25.1)
Blood loss (ml)	
≤400	1441 (70.7)
>400	597 (29.3)
Short-term outcomes after surgery	
Transfusions	
Absent	2018 (99.0)
Present	20 (1.0)
PHLF	
A	1842 (90.4)
B&C	196 (9.6)

Table 1 (*Continued*)

Characteristic	No. of patients (n = 2038)
Hypoalbuminemia	
Absent	1865 (91.5)
Present	173 (8.5)
Bile leakage	
Absent	2033 (99.8)
Present	5 (0.2)
Ascites/pleural effusion	
Absent	1953 (95.8)
Present	85 (4.2)
Upper gastrointestinal/postoperative hemorrhage	
Absent	2018 (99.0)
Present	20 (1.0)

Variables are expressed as no. (%).
Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; ALBI, albumin-bilirubin; PALBI, platelet-albumin-bilirubin; PHLF, posthepatectomy liver failure.

[a] Major liver resection: resection of three or more segments; minor liver resection: resection fewer than three segments.

patients as grade 2, and 85 patients (4.2%) as grade 3. A total of 196 patients (9.6%) suffered PHLF grade B/C. At the time of censor, a total of 852 (41.8%) patients had died, including 30 (1.5%) patients who died within 3 months. The median follow-up time of patients was 56.0 ± 29.1 months (range, 0.67–157.8 months).

3.1. Risk factors for posthepatectomy liver failure B/C

The discriminatory capabilities of the PALBI, ALBI, and C-P grades in predicting PHLF grade B/C in the entire cohort were tested by the AUC method (Fig. 1A) (AUC 0.693, 0.683, and 0.529, respectively). To avoid the confounding effect of the extent of liver resection, we also evaluated the AUC of each grade in patients who underwent the major resection (Fig. 1B) (AUC 0.677, 0.646, and 0.516, respectively). The incidence of PHLF grade B/C increase with increasing PALBI (grade 1: 4.4%, grade 2: 17.1%, grade 3: 20.0%), ALBI (grade 1: 7.1%, grade 2: 17.9%) and C-P grade (grade A5: 9.1%, grade A6: 17.6%). Among 1570 patients in ALBI grade 1, 1117 (71.1%) patients were stratified as PALBI grade 1, 436 (27.8%) patients as grade 2 and only 17 (1.1%) patients as grade 3. The incidences of PHLF grade B/C were 3.8% in PALBI grade 1 and 16.0% in PALBI grade 2. Factors associated with PHLF grade B/C in the univariable logistic analysis (P < 0.05) included age, PLT, alanine aminotransferase level, liver cirrhosis, portal hypertension, greatest tumor size, tumor number, macroscopic vascular invasion, major resection, surgical margin, blood loss, time of Pringle's maneuver, C-P grade, ALBI grade, and PALBI grade (Table 2). In the multivariable logistic analysis, the PALBI, ALBI, and C-P grades were incorporated into three different logistic regression models, respectively. To avoid collinearity, albumin and total bilirubin levels were not included in the C-P and ALBI models, while PLT, albumin and total bilirubin levels were not incorporated into the PALBI model. As a result, the PALBI grade (grade 3 vs. grade 1, odds ratio (OR): 5.136 (2.727–9.676), P < 0.001; grade 2 vs. grade 1, OR: 4.505 (3.164–6.413), P < 0.001) was selected an independent and significant predictor of PHLF grade B/C in the PALBI model, as was the ALBI grade (grade 2 vs. grade 1, OR: 2.125, 95% CI: 1.545–2.923, P < 0.001) in the ALBI model. As for the C-P model, the C-P grade was excluded in the multivariable analysis (Table 2). The c indexes of PALBI and ALBI in regard to PHLF were 0.782 (95% CI: 0.750–0.813), 0.739 (95% CI: 0.702–0.775). In the subgroup analysis among cirrhotic patients, the result of multivariable analysis showed that both PALBI grade (grade 3 vs. grade 1, OR: 3.525, 95% CI: 1.564–7.943, P = 0.002; grade 2 vs. grade 1, OR: 4.230, 95% CI: 2.848–6.283, P < 0.001) and ALBI grade (grade 2 vs. grade 1, OR: 1.853, 95% CI: 1.279–2.684, P = 0.001) were identified as inde-

Table 2

Univariate and multivariate logistic regression analyses of risk factors for posthepatectomy liver failure B/C.

Variables	Univariate		Multivariate					
			Child-Pugh model		ALBI model		PALBI model	
	OR	P	OR	P	OR	P	OR	P
Age (>60 years)	1.802 (1.335–2.432)	<0.001	1.537 (1.068–2.210)	0.021			1.547 (1.063–2.251)	0.023
Male sex	1.055 (0.656–1.697)	0.825						
Viral hepatitis	1.610 (0.917–2.827)	0.097						
PLT (>100 × 10^9/L)	0.436 (0.297–0.639)	<0.001	0.443 (0.292–0.672)	<0.001				
ALT (>40 U/L)	2.026 (1.499–2.738)	<0.001	1.714 (1.254–2.342)	0.001	1.647 (1.204–2.253)	0.002	1.675 (1.217–2.305)	0.002
AFP (>200 ng/mL)	1.075 (0.801–1.444)	0.629						
Liver cirrhosis	1.895 (1.353–2.653)	<0.001	1.904 (1.335–2.717)	<0.001	1.733 (1.210–2.482)	0.003	1.920 (1.337–2.756)	<0.001
Portal hypertension	2.491 (1.590–3.904)	<0.001			2.344 (1.448–3.795)	0.001	3.395 (2.050–5.622)	<0.001
Greatest tumor size (>5 cm)	1.998 (1.455–2.744)	<0.001	1.795 (1.257–2.564)	0.001	1.609 (1.129–2.293)	0.008		
Tumor number (>1)	1.685 (1.228k2.313)	0.001						
Macroscopic vascular invasion	1.783 (1.197–2.656)	0.004						
Major resection[a]	1.807 (1.329k2.457)	<0.001						
Blood loss (>400 ml)	3.093 (2.294–4.171)	<0.001	2.740 (1.991–3.772)	<0.001	2.579 (1.865–3.565)	<0.001	2.504 (1.810–3.466)	<0.001
Time of Pringle's maneuver (>20 min)	1.810 (1.327–2.468)	<0.001					1.526 (1.086–2.145)	0.015
Child-Pugh grade	2.135 (1.326–3.437)	0.002						
ALBI grade								
1								
2					2.125 (1.545–2.923)	<0.001		
PALBI grade								
1								
2							4.505 (3.164–6.413)	<0.001
3							5.136 (2.727–9.676)	<0.001

Values in the parentheses represent 95% confidence interval.

Abbreviations: OR, odds ratio; PLT, platelet; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; TBIL, total bilirubin; ALBI, albumin-bilirubin; PALBI, platelet-albumin-bilirubin.

[a] Major liver resection: resection of three or more segments; minor liver resection: resection fewer than three segments.
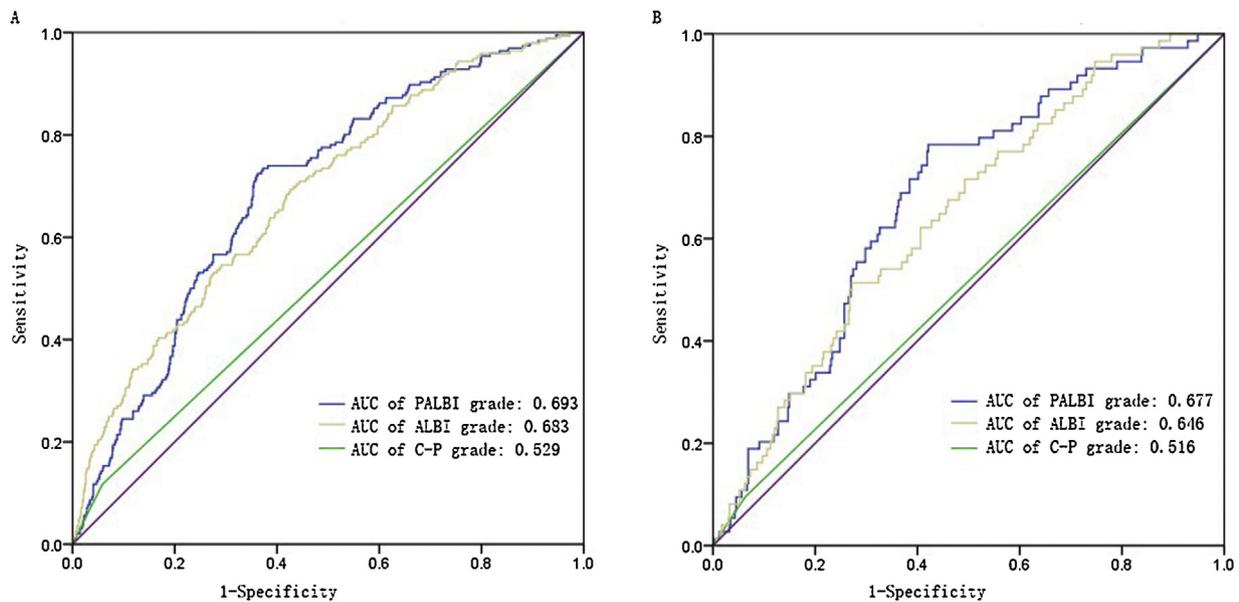
Fig. 1. ROC curves for PALBI, ALBI, and C-P grades in predicting PHLF grade B/C; (A) the entire cohort; (B) patients who underwent major resection.

pendent and significant predictors of PHLF grade B/C, respectively (Table 4).

3.2. Discriminatory power of the PALBI, ALBI and grades for long-term survival

Of the 2038 patients enrolled in this study, the 1-, 3- and 5-year OS rates were 82.7%, 62.7%, 48.2%, respectively. For the C-P grade A5 and A6 patients, the 1-, 3-, and 5-year OS rates were 82.8%, 64.2%, 47.2%, and 75.6%, 49.6%, 32.1% (P < 0.001) (Fig. 2A), respectively. Regarding the ALBI grades, the 1-, 3- and 5-year OS rates were higher in patients with ALBI grade 1 disease (83.8%, 64.2%, and 49.8%, respectively) than in patients with ALBI grade 2 (76.9%, 58.1%, and 38.2%, respectively) (P < 0.001) (Fig. 2B). Regarding the PALBI grades, the 1-, 3-, 5-year OS rates were 85.7%, 66.8%, and 51.1% for PALBI grade 1, 78.8%, 55.6%, and 42.2% for PALBI grade 2, and 62.3%, 44.7%, and 30.6% for PALBI grade 3 (P < 0.001), respectively (Fig. 2C). Moreover, the PALBI grade could further divide patients in ALBI grade 1 into three groups with different prognoses (P = 0.032) (Fig. 2D). In the multivariate analysis of OS in the PALBI model, the PALBI grade (grade 3 vs. grade 1, OR: 1.393; 95% CI: 1.023-1.897;1.023–1.897; P = 0.009; grade 2 vs. grade 1, OR: 1.187; 95% CI: 0.943–1.254; P = 0.024) was selected as an independent and significant predictor of OS, as was ALBI grade (grade 2 vs. grade 1, OR: 1.351; 95% CI: 1.130–1.531; P < 0.001) in the ALBI model and grade (OR: 1.440; 95% CI: 1.137–1.825; P = 0.003) in the C-P model (Table 3). The c indexes of PALBI, ALBI and C-P grade in regard to overall survival were 0.720 (95% CI: 0.650−0.771), 0.710 (95% CI: 0.649−0.772), and 0.707 (95% CI: 0.646−0.769), respectively. In the subgroup analysis among cirrhotic patients, the result of multivariable analysis showed that both PALBI grade (grade 3 vs. grade 1, OR: 1.291, 95% CI: 0.834–1.846, P = 0.007; grade 2 vs. grade 1, OR: 1.197, 95% CI: 0.920–1.308, P = 0.031) and ALBI grade (grade 2 vs. grade 1, OR: 1.237, 95% CI: 1.085–1.550, P = 0.004) were identified as independent and significant predictors of OS.

4. Discussion

A more objective and accurate method for predicting PHLF grade B/C and long-term survival is key for the management of C-P grade A HCC patients following resection. Our study revealed the potential role of the PALBI grade in estimating PHLF grade B/C and OS among the C-P grade A HCC patients.

To overcome the deficiency of C-P grade, the ALBI and PALBI grades were recently proposed. However, their discrimination capacity for the long-term survival of HCC patients remained controversial, Ho et al. showed that the ALBI and PALBI grade were both robust for discriminating survival, but the ALBI grade had the highest homogeneity for survival prediction [19]; Liu et al. proposed that the PALBI grade was consistently better for all HCC patients [17]. This finding was most likely due to differences in the selection of patients and their small sample sizes. Moreover, few studies to date have specifically focused on the value of the PALBI grade in predicting PHLF grade B/C among C-P grade A HCC patients whose liver function reserve varies widely. Thus, by using a large patient cohort (2038 patients), our study is the first to evaluate the value of the PALBI grade in predicting PHLF grade B/C and validate its discriminative power for the long-term survival of C-P grade A HCC patients following resection.

As PHLF is presumably caused by an insufficient quantity and function of the remnant liver [5,28], we investigated the predictive power of the PALBI grade in the entire cohort as well as in the subgroup of patients who underwent major resection to eliminate the impact of small remnant liver volume on PHLF. Except for PLT, major resection, and time of Pringle's maneuver, the other effective variables used in the multivariate logistic analysis of the PALBI and ALBI models were almost identical. As a result, it was more appropriate to incorporate PLT into the prognostic system, such as the PALBI grade, which is consistent with previous reports [29,30]. In terms of long-term survival, both ALBI and C-P grades sorted the C-P grade A HCC patients into two groups. However, the PALBI grade was capable of stratifying the C-P grade A patients into three groups with distinct prognoses and three survival groups in the ALBI grade 1 patients, which demonstrated a more adequate and clinical meaningful stratifying potential than that of the ALBI grade and C-P grade. Based on routine blood tests without subjective observation, the PALBI grade is objectively evaluated, easily available, and non-invasive and can be rapidly computed in clinical practice without the need for other special analysis. As the detection of PHLF often occurs too late and treatment pertains mainly to symptomatic management [5], the availability of a more accurate pretreatment prognostic predictor of PHLF may permit timely med-

Table 3
Univariate and multivariate analyses of risk factors for overall survival.

| Variables | Univariate | | Multivariate | | | | | |
| | | | Child-Pugh model | | ALBI model | | PALBI model | |
	OR	P	OR	P	OR	P	OR	P
Age (>60 years)	1.059 (0.896–1.152)	0.504						
Male sex	1.046 (0.845–1.295)	0.676						
Viral hepatitis	1.355 (1.068–1.720)	0.012	1.337 (1.050–1.702)	0.019	1.319 (1.035–1.680)	0.25	1.389 (1.093–1.765)	0.007
PLT (>100 × 10^9/L)	0.894 (0.727–1.098)	0.286						
ALT (>40 U/L)	1.273 (1.113–1.456)	<0.001						
AFP (>200 ng/mL)	1.818 (1.587–2.083)	<0.001	1.500 (1.306–1.722)	<0.001	1.514 (1.318–1.738)	<0.001	1.497 (1.304–1.720)	<0.001
Portal hypertension	1.197 (0.934–1.534)	0.155						
Greatest tumor size (>5 cm)	2.336 (2.024–2.696)	<0.001	1.906 (1.637–2.218)	<0.001	1.876 (1.610–2.184)	<0.001	1.805 (1.550–2.101)	<0.001
Tumor number (>1)	2.531 (2.200–2.913)	<0.001	1.994 (1.727–2.303)	<0.001	1.971 (1.706–2.277)	<0.001	2.029 (1.758–2.341)	<0.001
Macroscopic vascular invasion	4.067 (3.417–4.841)	<0.001	2.692 (2.246–3.227)	<0.001	2.722 (2.271–3.263)	<0.001	2.780 (2.321–3.329)	<0.001
Surgical margin (>1 cm)[a]	0.806 (0.700–0.929)	0.003						
Child-Pugh grade	1.669 (1.318–2.113)	<0.001	1.440 (1.137–1.825)	0.003				
ALBI grade								
1								
2					1.351 (1.130–1.531)	<0.001		
PALBI grade								
1								
2	1.337 (1.162–1.538)	<0.001					1.187 (0.943–1.254)	0.024
3	1.842 (1.357–2.502)	<0.001					1.393 (1.023–1.897)	0.009

Values in parentheses represent 95% confidence intervals.
Abbreviations: OR, odds ratio; PLT, platelet; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; PALBI, platelet-albumin-bilirubin.

[a] Surgical margin: the shortest measured distance from the edge of the tumor to the plane of liver transection.

Table 4
Multivariate analyses of risk factors for posthepatectomy liver failure B/C and overall survival in cirrhotic patients.

| Variables | PHLF | | | | | | OS | | | | | |
| | Child-Pugh model | | ALBI model | | PALBI model | | Child-Pugh model | | ALBI model | | PALBI model | |
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
Age (>60 years)	1.651 (1.151–2.369)	0.006	1.529 (1.062–2.202)	0.022	1.563 (1.082–2.258)	0.017						
Viral hepatitis							1.651 (1.121–2.433)	0.011	1.624 (1.102–2.394)	0.014	1.653 (1.121–2.435)	0.011
PLT (>100 × 10^9/L)												
ALT (>40 U/L)	1.771 (1.227–2.558)	0.002	1.695 (1.173–2.448)	0.005	1.716 (1.180–2.496)	0.005						
AFP (>200 ng/mL)							1.532 (1.292–1.816)	<0.001	1.536 (1.296–1.821)	<0.001	1.530 (1.291–1.814)	<0.001
Portal hypertension	1.937 (1.036–3.624)	0.038	2.389 (1.461–3.904)	0.001	3.403 (2.035–5.690)	<0.001						
Greatest tumor size (>5 cm)	2.032 (1.383–2.985)	<0.001	2.036 (1.400-2.961)	<0.001	1.777 (1.207–2.617)	0.004	1.912 (1.600-2.286)	<0.001	1.882 (1.573–2.252)	<0.001	1.884 (1.291–1.814)	<0.001
Tumor number (>1)	1.467 (1.002–2.146)	0.049					1.715 (1.439–2.044)	<0.001	1.689 (1.417–2.014)	<0.001	1.708 (1.433–2.037)	<0.001
Macroscopic vascular invasion							2.556 (2.059–3.172)	<0.001	2.614 (2.106–3.243)	<0.001	2.597 (2.093–3.223)	<0.001
Surgical margin (>1 cm)	0.644 (0.430-0.964)	0.032	0.649 (0.434-0.970)	0.035	0.615 (0.407-0.929)	0.021						
Child-Pugh grade							1.514 (1.511–1.990)	0.003				
ALBI grade												
1												
2			1.853 (1.279–2.684)	0.001					1.237 (1.085–1.550)	0.004		
PALBI grade												
1												
2					4.230 (2.848–6.283)	<0.001					1.197 (0.920–1.308)	0.031
3					3.525 (1.564–7.943)	0.002					1.291 (0.834–1.846)	0.007

Values in the parentheses represent 95% confidence interval.
Abbreviations: OR, odds ratio; PLT, platelet; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; PALBI, platelet-albumin-bilirubin.
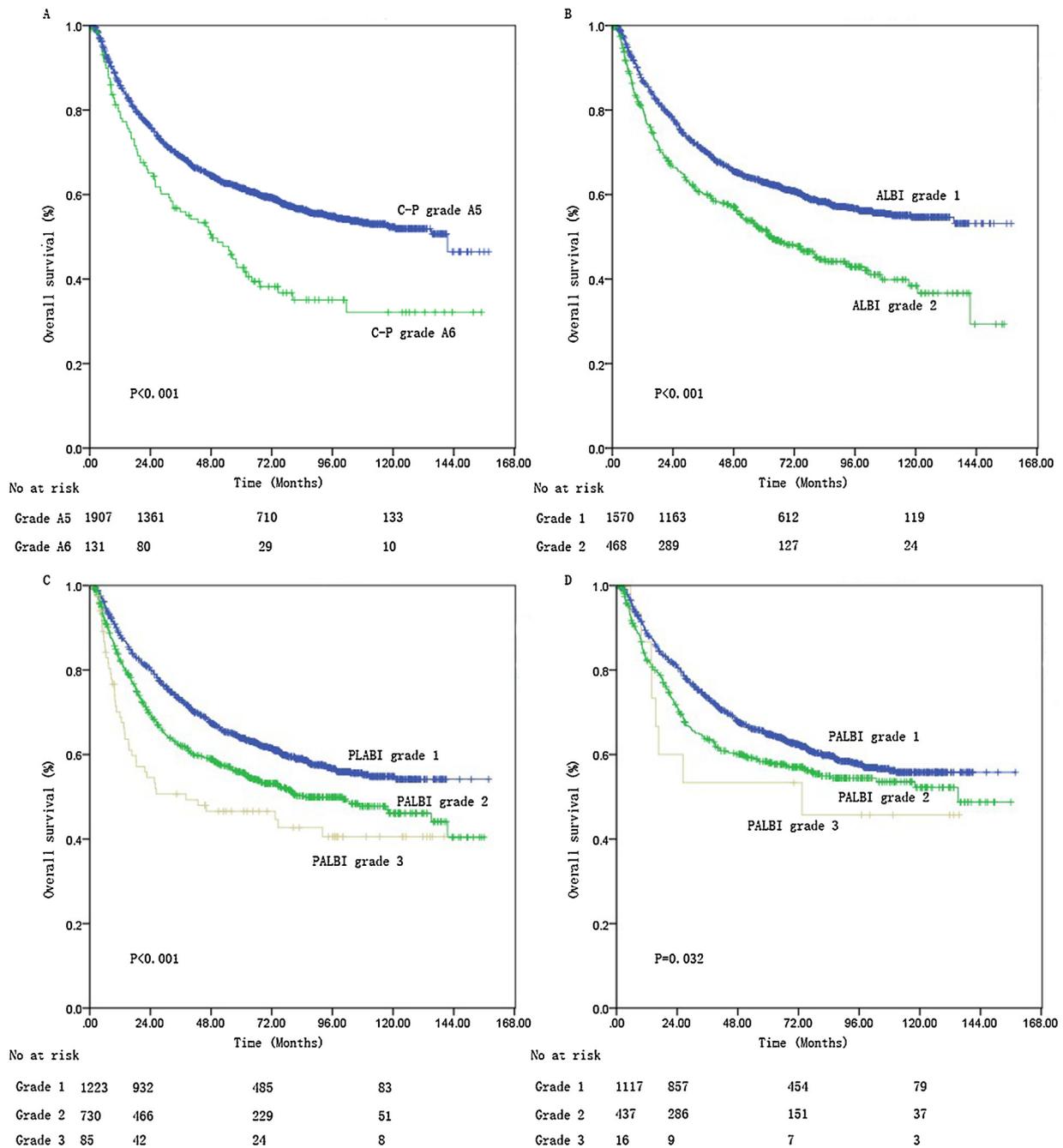
Fig. 2. Kaplan–Meier estimates of overall survival by C-P, ALBI, and PALBI grades. (A) C-P grade in the entire cohort; (B) ALBI grade in the entire cohort; (C) PALBI grade in the entire cohort; (D) PALBI grade among ALBI grade 1 patient.

ical treatments to prevent PHLF. Thus, the findings of our study can be extended to develop a more clinically relevant tool for modeling risk among HCC patients undergoing hepatic resection.

There are some limitations of this study. Due to the retrospective nature of our study, deviation from this clinical design was unavoidable. To address this limitation, we enrolled a large cohort consisting of 2038 patients. Second, as all patients enrolled in this study were C-P grade A HCC patients, further study was needed for C-P grade B patients, as a portion of them could be evaluated as candidates for hepatic resection. As all patients enrolled in this study underwent open hepatectomy, further exploration of those treated by means of laparoscopic approach is of importance. Finally, the AUC values in this study, while meaningful, were still relatively low, which needs further study.

Thus, the current study confirmed that PALBI grade can be employed as a promising prognostic predictor of PHLF grade B/C and long-term survival in C-P grade A HCC patients following curative resection. Consideration should be given to the prospective validation of the scoring system in future clinical studies to facilitate its use in routine clinical practice.

Conflict of interest

None declared.

Acknowledgments

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