Original Article

Comparison of albumin-bilirubin grade versus Child-Pugh score in predicting the outcome of transarterial chemoembolization for hepatocellular carcinoma using time-dependent ROC

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Background: The Child-Pugh score has been used extensively to assess hepatic function and predict post-treatment outcomes in patients with hepatocellular carcinoma (HCC). Recently, the albumin-bilirubin (ALBI) grade has been put forward as an objective method of evaluating liver function and predicting overall survival (OS) in HCC patients. Transarterial chemoembolization (TACE) is considered to be effective in prolonging OS among intermediate-stage HCC patients. This study aimed to explore and compare the performance of ALBI grade and Child-Pugh score in predicting outcomes for HCC patients who underwent TACE.

Methods: There were a total of 221 consecutive HCC patients enrolled in this study, all of whom received TACE and were enrolled retrospectively. The Kaplan-Meier method and time-dependent receiver operating curves (ROC) were used to estimate the discriminatory ability and survival prediction accuracy of ALBI grade and Child-Pugh score in predicting postoperative OS. Univariate and multivariate Cox regression analyses were performed to evaluate the prognostic factors for OS.

Results: Of the patients enrolled in the study, 106 (48.0%) were ALBI grade 1 and 115 (52.0%) were ALBI grade 2. Overall survival differed significantly between patients with ALBI-1 and ALBI-2 [hazard ratio (HR), 3.032; 95% CI, 2.019–4.555, P<0.001]. With regard to Child-Pugh scores, 160 (72.4%) patients had a score of A5 and 61 (27.6%) had a score of A6. There was also a difference in overall survival between patients with Child-Pugh-A5 and Child-Pugh-A6 (HR, 1.548; 95% CI, 1.066–2.247, P=0.022). In multivariate analyses, both ALBI grade and Child-Pugh score could significantly stratify the patients with different OS (HR, 2.994 and 1.545, P<0.001 and P=0.026 for ALBI grade and Child-Pugh score, respectively). Furthermore, time-dependent ROC analysis and its subgroup analyses demonstrated that the ALBI grade had a better discriminatory ability than Child-Pugh score in predicting survival.

Conclusions: In stratifying prognosis for HCC patients who had received TACE therapy, the ALBI grade provided better prognostic performance and discrimination of liver function than Child-Pugh score. These results suggest that ALBI grade could provide an alternative liver function grading system for stratification of patients with HCC.

Keywords: Child-Pugh score; albumin-bilirubin grade (ALBI grade); hepatocellular carcinoma (HCC);

transarterial chemoembolization (TACE); time-dependent receiver operating characteristic curve

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Introduction

Liver cancer is one of the three leading causes of cancer-related deaths worldwide, and in terms of malignant tumors, it is the seventh most common type (1). Hepatocellular carcinoma (HCC) accounts for about 90% of liver cancer cases (2). The treatment options for HCC include liver transplantation, hepatectomy, local ablative therapy, transarterial chemoembolization (TACE), systemic therapies, and basic supportive care (3). However, on account of the highly aggressive and insidious nature of HCC, a large proportion of patients are classified as being at the intermediate to advanced stage by the time of diagnosis and, as such, beyond the indications for curative interventions such as liver transplantation, hepatectomy, and ablation therapy (4).

For patients with preserved liver function who are not eligible for curative treatments, TACE is the most commonly used nonsurgical treatment modality and, in several randomized controlled trials and meta-analyses, has been reported to prolong survival (5,6). Particularly for patients with intermediate-stage HCC according to Barcelona clinic liver cancer (BCLC) staging system, TACE is the standard treatment modality (7). A growing body of evidence supports the use of TACE for patients with early and advanced HCC (8-10).

Due to a combination of factors, the prognosis assessment of the HCC patients remains complicated and hepatic function, tumor characteristics and performance status must be taken into consideration (11,12). Among them, hepatic function is a vital determinant in the prognosis of HCC. Traditionally, the Child-Pugh score has been used extensively in liver function evaluation and even plays an important role in most of the prevalent HCC staging systems, which inform treatment decision making (13,14). However, the Child-Pugh scoring system has several limitations (15,16): the assessment of ascites and encephalopathy is subjective; all five parameters are given the same weight; moreover, ascites and albumin are interrelated.

Recently, a novel model based on serum albumin and bilirubin has been put forward to assist with liver function evaluation and has shown powerful discriminating ability over Child-Pugh classification in predicting overall survival for patients with HCC (17). However, until now, a consensus on whether the performance of albumin-bilirubin (ALBI) score can accurately reflect the liver function of HCC patients undergoing TACE therapy has not been reached. Besides, it is worth mentioning that the ALBI score appeared capable of classifying patients with Child-Pugh A who underwent liver resection, stereotactic body radiation and sorafenib treatment into two distinct prognostic cohorts (18-20).

This present study aimed to assess and compare the performance of ALBI grade and Child-Pugh score in predicting overall survival outcomes in HCC patients who underwent TACE.

Methods

Study population

In this retrospective study, a total of 221 consecutive HCC patients who underwent TACE therapy from January 2010 to December 2017 were enrolled at the Tangdu Hospital. Baseline parameters were retrieved from the hospital medical database. HCC was diagnosed based on the findings of abdominal ultrasonography. Dynamic computed tomography and magnetic resonance imaging, or a combination of both, were also used, in accordance with the guidelines of the American Association for the Study of the Liver Disease and the European Association for the Study of Liver disease (AASLD/EASL) (13,14).

The inclusion criteria were as follows: liver function of Child-Pugh-A; patients with only one malignant tumor; no HCC-specific-treatment before TACE therapy; and no insufficient heart, lung, kidney, or brain function before TACE therapy.

The exclusion criteria were as follows: curative treatments for HCC prior to TACE therapy; concurrent malignancies; and renal, cerebral or cardiopulmonary dysfunction. Written informed consent was obtained from all patients before the administration of TACE. This investigation was approved by the Clinical Research Ethics

Committee of the Tangdu Hospital.

Treatment and follow-up

Prior to TACE, abdominal ultrasound and contrast-enhanced CT or MRI were used to assess tumor status and resectability. The Seldinger technique was used and a 4.1-French RC1 catheter was introduced into the tumor feeding artery. Following this, the number, location, size and branches of the feeding vessels of the tumor were carefully identified. A mixture of 10–20 mL iodized oil, gelfoam particles with 30–50 mg doxorubicin and 50–100 mg cisplatinum was injected into the arterial branches. The number of TACE sessions ranged from 1 to 6, with the procedure scheduled at 1-month intervals and performed depending on the patients' physical condition.

All patients were followed up at 1 month after TACE therapy and then at 3-month intervals in the first year and every 3–6 months thereafter, as appropriate. Routine examinations were conducted at each follow-up. These included physical examinations, blood tests (serum AFP level, serum biochemistry, liver biochemistry) and imaging examinations (chest X-ray, abdominal ultrasonography, abdominal CT or MRI). The start of the follow-up was defined as the date when TACE therapy began. The end of follow-up was defined as the date of the final visit or death.

Child-Pugh score and ALBI score calculation

Child-Pugh score was calculated using total bilirubin, albumin, prothrombin time, and the clinical findings of encephalopathy and ascites. It was graded as: 5–6 points for Child-Pugh-A; 7–9 points for Child-Pugh-B; and 10–15 points for Child-Pugh-C (15). The ALBI score was calculated by $\log_{10}$Bilirubin (μmol/L) × 0.66 + albumin (g/L) × −0.085. ALBI score ≤−2.60 was defined as grade 1, >−2.60 but ≤−1.39 as grade 2, and >−1.39 as grade 3 (16). The parameters of the Child-Pugh and ALBI scores were obtained within the 1 week preceding TACE therapy to ensure that the patients did not receive albumin supplements, platelet infusion or other treatments beforehand.

Statistical analysis

Categorical variables are expressed as frequencies and percentages; continuous variables are expressed as means (interquartile range). Survival analyses were performed using the Kaplan-Meier method, and the log-rank test was used to examine the statistical differences between the ALBI grade and Child-Pugh score. The Cox proportional hazards model was used for univariate and multivariate analyses of prognostic factors of OS. Three multivariate models with stepwise methods were separately employed to select the independent prognostic factors: model 1 including the baseline characteristics; model 2 including the baseline characteristics and Child-Pugh score but excluding albumin and bilirubin; model 3 including the baseline characteristics and ALBI score but also excluding albumin and bilirubin. Model validation of different staging systems was compared using the C-index as a measure of discrimination. P values <0.05 for all analyses were identified at statistically significant. Statistical analyses were conducted using IBM SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA), and R software version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

According to the protocol, 221 patients were finally included, of whom 194 (87.8%) were male (with a mean age of 56.1 years) and 27 (22.2%) were female (with a mean age of 56.7 years). According to the ALBI grade, there were 106 (48.0%) and 115 (52.0%) patients belonging to the ALBI-1 group and ALBI-2 group, respectively. According to the Child-Pugh system for the evaluation of liver function, there were 160 (72.4%) patients of Child-Pugh-5, and 61 (27.6%) of Child-Pugh-6. In the ALBI-1 group, there were 105 patients of Child-Pugh-A5 and only 1 patient of Child-Pugh-A6. In the ALBI-2 group, there were 55 patients of Child-Pugh-A5 and 60 patients of Child-Pugh-A6. All patients enrolled in the study had unifocal tumors, with a mean tumor size (maximum diameter of the largest tumor) of 8.20 cm. Demographic and clinical features of the patients are summarized in *Table 1*. Correspondences between ALBI grades and Child-Pugh scores are listed in *Table 2*.

Survival analyses according to Child-Pugh score and ALBI grade

During a median follow-up time of 34.2 months, 121 patients had died and the median OS reached 25.8 months. Based on the Kaplan-Meier curves, both ALBI

Table 1 Baseline characteristics of patients

Characteristics	Outcome
No. of patients, n	221
Age (years), n (%)	
≥60	97 (43.9)
<60	124 (56.1)
Sex ratio (M:F)	194:27
Preoperative laboratory and clinical data	
Positive HBsAg, n (%)	197 (89.1)
Total bilirubin (μmol/L)	16.2 (11.97–22.80)
Albumin (g/L)	41.7 (36.8–45.0)
Platelet count ($\times10^9$/L)	164.0 (90.5–216.5)
ALT (units/L)	42.0 (27.0–66.5)
AST (units/L)	54.0 (36.0–77.0)
α-fetoprotein (ng/mL), n (%)	
>400	84 (38.0)
≤400	137 (62.0)
Child-Pugh score, n (%)	
Child-Pugh-5	160 (72.4)
Child-Pugh-6	61 (27.6)
Tumor size (cm)	8.20 (6.1–11.5)
ECOG, n (%)	
0	121 (54.8)
1	100 (45.2)
Blood urea nitrogen (μmol/L)	5.6 (4.4–6.7)
Creatinine (μmol/L)	69.0 (61.2–78.9)
ALBI grade, n (%)	
ALBI-1	106 (48.0)
ALBI-2	115 (52.0)

ALBI, albumin-bilirubin; ALT, alanine aminotransferase; ECOG, Eastern Cooperative Oncology Group; ALBI, albumin-bilirubin; AST, aspartate aminotransferase.

grade and Child-Pugh score were significantly associated with OS. In addition, patients with Child-Pugh-A5 showed better overall survival than those with Child-Pugh-A6 (OS at 1, 3 and 5 years was 81%, 37%, 13.3% *vs.* 63.4%, 19.9%, 7.4%, respectively; Log-rank P=0.020; *Figure 1A*). There was a significant difference in OS between patients with ALBI-1 and ALBI-2 grade. OS at 1,3 and 5 years was higher in patients with ALBI-1 (92.4%, 55.7%, and 27.5%, respectively) than those with ALBI-2 (63.3%, 17.3%, and 5.5%, respectively; Log-rank P<0.001; *Figure 1B*). Among patients with Child-Pugh-A5, the patients with ALBI-1 had a higher OS at 1,3 and 5 years than those with ALBI-2 (90.9%, 54.8%, 28.8% *vs.* 63.7%, 37.2%, 0%, respectively; Log-rank P<0.001; *Figure 1C*). Among patients with ALBI-2, there was no significant difference in OS at 1,3 and 5 years between the patients with Child-Pugh-A5 and Child-Pugh-A6 (63.7%, 34.9%, 0% *vs.* 62.7%, 18.1%, 12.0% months, respectively; Log-rank P=0.430; *Figure 1D*).

Table 2 Correspondences between ALBI grades and Child-Pugh scores

Variable	ALBI-1	ALBI-2
Child-Pugh-A5	105	55
Child-Pugh-A6	1	60

ALBI, albumin-bilirubin.

Univariate and multivariate analyses

According to the univariate analysis for OS, the ECOG performance status, tumor size, PLT, BUN, albumin and total bilirubin, as well as Child-Pugh score and ALBI grade were entered into multivariate analyses (*Table 3*). In multivariate model 1, BUN (HR 1.027, 95% CI: 1.012–1.042, P=0.020), PLT (HR 0.995, 95% CI: 0.993–0.997, P<0.001), total bilirubin (HR 1.029, 95% CI: 1.006–1.053, P=0.015), albumin (HR 0.944, 95% CI: 0.914–0.975, P<0.001) and tumor size (HR 1.144, 95% CI: 1.083–1.207, P<0.001) were identified as independent predictors of OS. According to multivariate model 2, the independent prognostic factors included tumor size (HR 1.121, 95% CI: 1.061–1.185, P<0.001), PLT (HR 0.995, 95% CI: 0.993–0.998, P<0.001), Child-Pugh score (HR 1.545, 95% CI: 1.053–2.267, P=0.026) and BUN (HR 1.028, 95% CI: 1.012–1.043, P<0.001). For multivariate model 3, the independent predictors of OS were tumor size (HR 1.148, 95% CI: 1.087–1.212, P<0.001), PLT (HR 0.996, 95% CI: 0.993–0.998, P<0.001), ALBI grade (HR 2.994, 95% CI: 1.968–4.556, P<0.001) and BUN (HR 1.030, 95% CI: 1.015–1.046, P<0.001) (*Table 4*). Therefore, according to the multivariate analyses, Child-Pugh score and the ALBI grade could independently predict OS in patients who underwent TACE therapy.

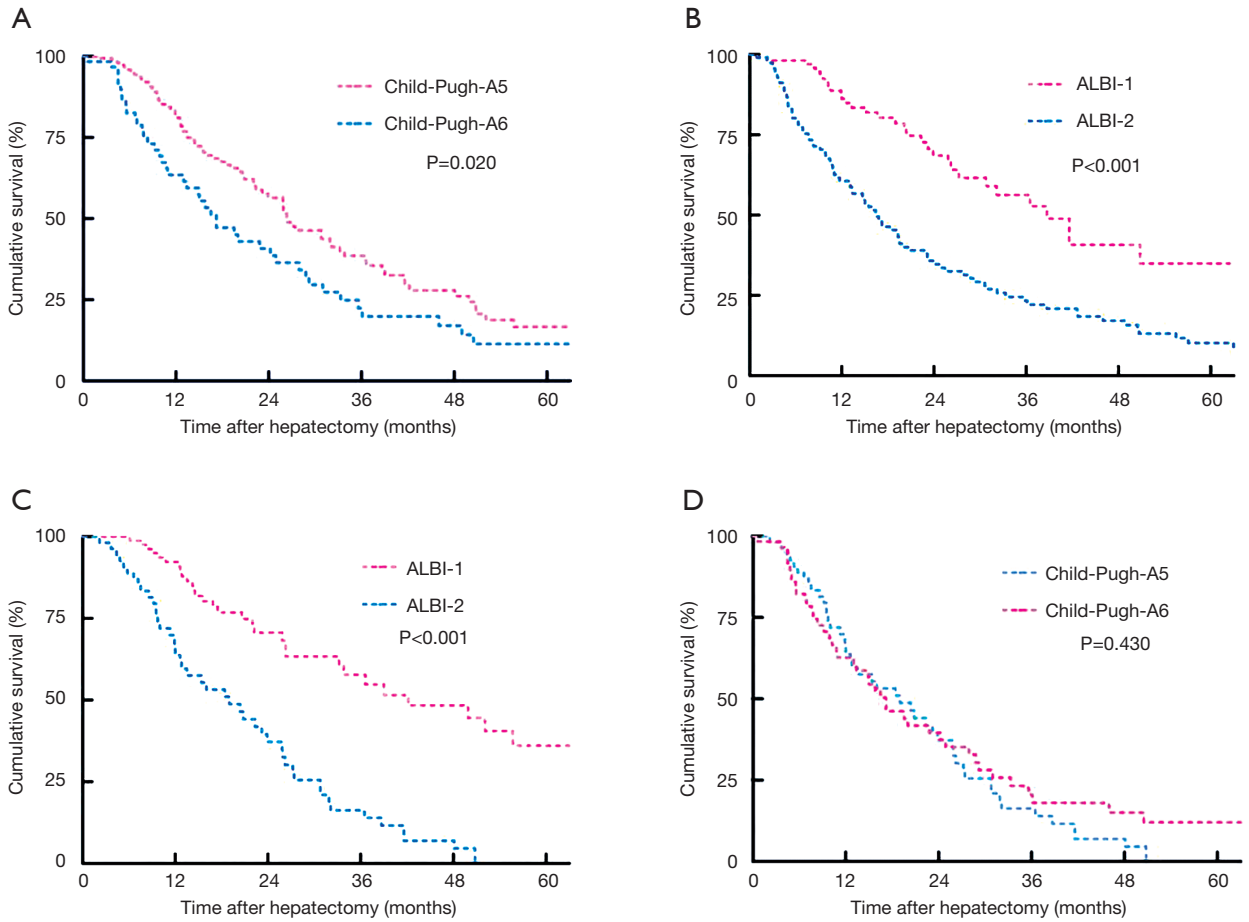

Figure 1 Kaplan-Meier curves for overall survival (OS). (A) Comparison of survival between patients with Child-Pugh score of 5 and 6; (B) comparison of survival between patients with ALBI grade 1 and 2; (C) comparison of survival between patients with Child-Pugh-A5 disease; (D) comparison of survival between patients with ALBI grade 2 disease.

Comparison of the discriminatory abilities for Child-Pugh score and ALBI grade in predicting survival

Figure 2 shows AUCs for Child-Pugh score and ALBI grade and overall survival from 6 to 36 months after the start of follow-up using time-dependent receiver operating curve (ROC) analysis. The ALBI grade had higher predictive power than Child-Pugh score for overall survival based on time-dependent AUCs (*Table 4*). In addition, their predictive abilities for subsets of patients with different baseline characteristics were investigated. ALBI grade showed better prognostic performance than Child-Pugh score in the all of the subsets apart from the female subgroup (*Table 5*).

Discussion

In the present study on HCC patients with Child-Pugh A who received TACE therapy, we demonstrated that ALBI grade had greater discriminatory power than Child-Pugh score in predicting OS. Importantly, the ALBI grade could classify the patients into two distinct prognostic cohorts.

In predicting the outcomes of HCC patients, assessing liver function reserve in order to select appropriate candidates for various kinds of treatments is the key issue. For many years, the traditional Child-Pugh rating system has been the most widely used method for assessing liver function and predicting therapeutic efficacy. Recently,

however, due to its limitations, the accuracy of Child-Pugh score has been questioned. Previous studies tried to assess the ALBI grade for patients treated with TACE, but lacked patients with ALBI-2 grade as well as results for long-term outcomes (21).

Table 3 Univariable analyses to identify predictors of postoperative survival in patients with hepatocellular carcinoma

Factors	Univariable Cox regression	
	Hazard rate (95% CI)	P value
Age (≥60 years)	1.041 (0.727–1.491)	0.824
Male sex	1.312 (0.751–2.292)	0.340
Positive HBsAg	0.991 (0.546–1.801)	0.977
Total bilirubin (μmol/L)	1.030 (1.007–1.054)	0.011
Albumin (g/L)	0.939 (0.909–0.971)	<0.001
Platelet count ($\times10^9$/L)	0.995 (0.993–0.997)	<0.001
ALT (units/L)	1.001 (0.997–1.005)	0.595
AST (units/L)	1.001 (0.999–1.004)	0.353
α-fetoprotein (>400 ng/mL)	1.308 (0.906–1.889)	0.151
Child-Pugh score	1.548 (1.066–2.247)	0.020
Tumor size (cm)	1.132 (1.074–1.192)	<0.001
ECOG	1.527 (1.069–2.182)	0.020
Blood urea nitrogen (μmol/L)	1.041 (1.006–1.078)	0.022
Creatinine (μmol/L)	0.994 (0.983–1.006)	0.320
ALBI grade	3.032 (2.019–4.555)	<0.001

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ECOG, Eastern Cooperative Oncology Group; ALBI, albumin-bilirubin.

In this study, we demonstrated that ALBI grade and Child-Pugh score could separately predict the overall survival of HCC patients with Child-Pugh A who underwent TACE therapy. Almost all of the patients included in our research who had a Child-Pugh score of 5 were graded as ALBI-1. However, patients with ALBI-2 had a different Child-Pugh score. In the entire cohort, there was a significant difference in OS between ALBI-1 grade and ALBI-2 grade. Moreover, in patients with Child-Pugh A, the patients with Child-Pugh-6 had a worse prognosis than patients with Child-Pugh-5. It was noteworthy that even in the cohort of patients with Child-Pugh-5—which indicated the best level of liver function—the prognosis could be further divided into two groups by the ALBI grade according to the log-rank test, which illustrated that patients in the same stratum identified by Child-Pugh scoring system had different liver function reserve. Thus, ALBI grade might be a more reasonable and accurate evaluation tool of liver function.

Univariable and multivariable analyses were conducted to identify contributing factors to OS. For multivariable analysis, the albumin and total bilirubin, the Child-Pugh score and the ALBI grade were entered into three different Cox proportional hazards regression models in order to avoid collinearity. Poorer prognosis for patients corresponded with higher Child-Pugh score and ALBI grade. Other than Child-Pugh score and ALBI grade, tumor size, BUN and PLT were also independent predictors of overall survival. Nevertheless, the ECOG score and prothrombin time were not regarded as being statistically significant, although this is a finding to which the small

Table 4 Multivariate analyses to identify predictors of postoperative survival in patients with hepatocellular carcinoma

Factors	Multivariate model 1		Multivariate model 2		Multivariate model 3	
	Hazard rate (95% CI)	P value	Hazard rate (95% CI)	P value	Hazard rate (95% CI)	P value
Tumor size (cm)	1.144 (1.083–1.207)	<0.001	1.121 (1.061–1.185)	<0.001	1.148 (1.087–1.212)	<0.001
Albumin (g/L)	0.944 (0.914–0.975)	<0.001	–	–	–	–
Total bilirubin (μmol/L)	1.029 (1.006–1.053)	0.015	–	–	–	–
Platelet count ($\times10^9$/L)	0.995 (0.993–0.997)	<0.001	0.995 (0.993–0.998)	<0.001	0.996 (0.993–0.998)	<0.001
Child-Pugh score	–	–	1.545 (1.053–2.267)	0.026	–	–
ALBI grade	–	–	–	–	2.994 (1.968–4.556)	<0.001
Blood urea nitrogen (μmol/L)	1.027 (1.012–1.042)	0.020	1.028 (1.012–1.043)	<0.001	1.030 (1.015–1.046)	<0.001
Creatinine (μmol/L)	1.184 (0.814–1.723)	0.377	1.204 (0.830–1.747)	0.327	0.974 (0.668–1.420)	0.889

ALBI, albumin-bilirubin.

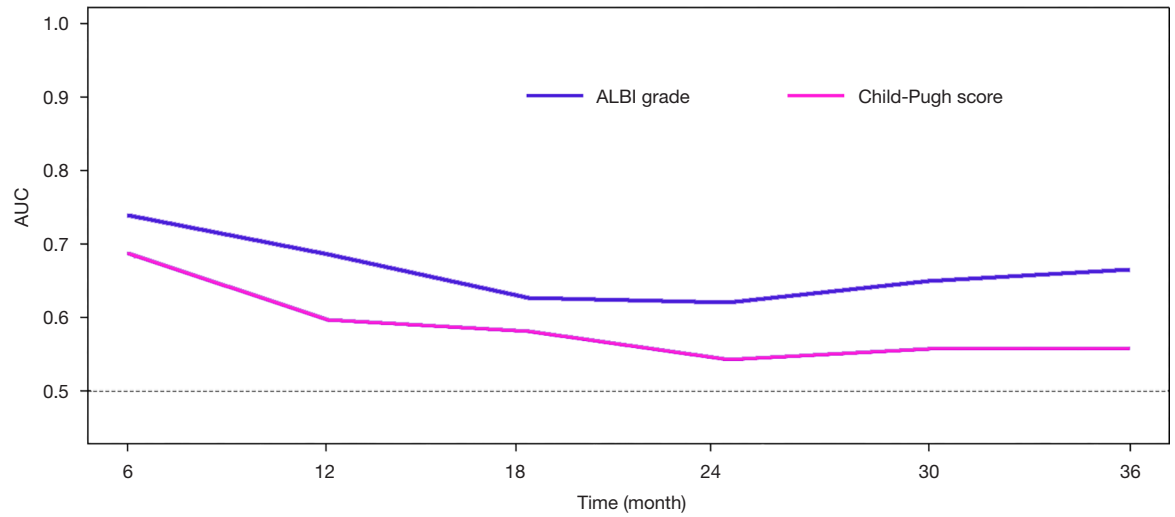

Figure 2 Time-dependent receiver operating curves (ROC) for ALBI grade and Child-Pugh score for predicting overall survival (OS). ALBI, albumin-bilirubin.

Table 5 Subgroup analyses for ALBI grade and Child-Pugh score to predict overall survival (OS)

Factors	ALBI grade		Child-Pugh score	
	C-index (SE)	$Exp^{(coef)}$ (95% CI)	C-index (SE)	$Exp^{(coef)}$ (95% CI)
Gender				
Male	0.643 (0.024)	3.246 (2.066–5.101)	0.558 (0.027)	1.393 (0.939–2.067)
Female	0.609 (0.076)	2.118 (0.737–6.089)	0.670 (0.066)	5.502 (1.430–21.170)
Age (years)				
≥60	0.661 (0.032)	3.608 (1.927–6.756)	0.589 (0.037)	1.767 (1.033–3.024)
<60	0.631 (0.031)	2.663 (1.553–4.569)	0.559 (0.035)	1.368 (0.806–2.322)
HBsAg				
Positive	0.640 (0.023)	2.853 (1.860–4.375)	0.565 (0.027)	1.419 (0.956–2.106)
Negative	0.660 (0.076)	4.452 (1.175–16.870)	0.610 (0.076)	2.510 (0.757–8.321)
ECOG				
ECOG-0	0.664 (0.032)	3.253 (1.882–5.623)	0.583 (0.036)	1.670 (0.990–2.816)
ECOG-1	0.609 (0.031)	0.941 (1.374–4.773)	0.566 (0.037)	1.503 (0.876–2.578)
AFP (ng/mL)				
>400	0.678 (0.033)	3.765 (1.903–7.450)	0.606 (0.042)	1.831 (1.008–3.325)
≤400	0.622 (0.030)	2.773 (1.654–4.650)	0.553 (0.032)	1.419 (0.875–2.301)

ALBI, albumin-bilirubin; ECOG, Eastern Cooperative Oncology Group.

sample size may have contributed.

Time-dependent ROC curves have been introduced to assess the predictive power of diagnostic markers for time-dependent disease outcomes (22). Although both Child-Pugh score and ALBI grade have been confirmed as independent factors associated with OS by means of

multivariate analysis, in this study, time-dependent ROC analysis showed that the discriminatory ability of ALBI grade was superior to that of Child-Pugh score for OS of more than 3 years, especially with regard to long-term outcomes. Additionally, subgroup analysis revealed that both ALBI grade and Child-Pugh score were significant predictors of OS in the entire subsets. However, ALBI grade showed better prognostic performance than Child-Pugh score in all subsets apart from the female subgroup.

Although, unlike the Child-Pugh score system, the ALBI grade system excludes subjective factors, its limitations should also be acknowledged. In this system, only two factors (albumin and bilirubin) reflecting liver function are included and considered. However, several factors like positive HBsAg, AST and ALT are excluded. The serum albumin level has a relatively short half-life period and its level is affected by clinical treatment (albumin supplements), as a result, patients with ALBI-1 do not necessarily have good liver function. Furthermore, patients with poor albumin and bilirubin caused by other relevant reasons do not necessarily have severely impaired liver function. As for these above, more accurate models to evaluate liver function are still needed and joint assessment which combines multiple approaches is advisable.

However, this study has several limitations. Firstly, although quality control was ensured because all procedures and administrations were conducted by the same experienced team, the single-centered and retrospective nature of this study may have instilled some bias. Secondly, this study included a relatively small sample size, in which patients with Child-Pugh B and C and ALBI-3 grade were excluded. Whether the results of our study could be applied to the patients with a poorer liver function requires further studies with a larger sample size and effective controls. Finally, most of the study population in our study were Chinese patients with hepatitis B viral infection as the etiology of HCC. This is in contrast to patients in most Western countries, where the etiologies of HCC are mainly hepatitis C virus infection and alcoholic liver disease. Thus, the generalization of our findings should be cautious and future prospective studies are needed.

In summary, for HCC patients with preserved liver function (Child-Pugh A) who are treated with TACE therapy, our study demonstrates that ALBI grade could be used as an alternative assessment of liver function and might be superior to Child-Pugh score in terms of stratifying prognosis. These observations may have major implications for future study design insofar that it is vital to apply this high-quality and evidence-based ALBI grade model to the present HCC staging system to enhance its discriminatory ability.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.02.124). SZ serves as the unpaid editorial board member of *Annals of Translational Medicine* from Apr 2020 to Mar 2022. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This investigation was approved by the Clinical Research Ethics Committee of the Tangdu Hospital.

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