Preventive Medicine Reports 39 (2024) 102639

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Albumin-bilirubin score as a predictor of all-cause mortality in patients with hepatitis B virus infection: An analysis of National Health and Nutrition Examination Survey (NHANES) 1999–2018

Lixia Du [a,b,1], Hui Xu [b,1], Li Fang [b], Lijuan Qiao [b], Yu Xie [b], Chunli Yang [b], Linxiu Ji [b], Liqiong Zhao [b], Cong Wang [b], Weilan Zhang [b], Xue Feng [b], Ting Chen [b], Qin Yuan [a,*]

[a] Department of Infectious Diseases, The First People's Hospital of Shuangliu District, Chengdu 610020, PR China
[b] Department of Gastroenterology, Chengdu BOE Hospital, Chengdu 610219, PR China

ARTICLE INFO

Keywords:
Hepatitis B virus infection
Albumin-Bilirubin score
All-cause mortality
Prediction

ABSTRACT

Objectives: The Albumin-Bilirubin (ALBI) score has been widely used to assess the prognosis in patients with cirrhosis and hepatocellular carcinoma. This study aimed to analyze the relationship between ALBI score and all-cause mortality in patients with hepatitis B virus (HBV) infection in general.

Methods: Patients aged ≥ 18 years with previous or current HBV infection from the National Health and Nutrition Examination Survey (NHANES) in the United States between 1999 and 2018 were enrolled in this retrospective cohort study. Weight univariate and multivariate Cox regression models were used to assess the relationship between ALBI score and all-cause mortality. The area under the receiver operating characteristic curve (AUC) was utilized to assess the predictive effect of ALBI score for all-cause mortality.

Results: A total of 3,666 patients were included, of whom 925 (23.53 %) patients died. Compared with ALBI score ≤ -2.6, HBV-infected patients with ALBI score > -2.6 [hazard ratio (HR) = 1.75; 95 % confidence interval (CI): 1.43–2.14] were corrected with a higher all-cause mortality risk after adjusting for confounders. Stratified analyses showed that higher ALBI score was related to a higher risk of all-cause mortality in different patients with HBV infection (All $P < 0.05$). Furthermore, the ALBI score had good predictive ability for 1-year (AUC = 0.816, 95 %CI: 0.754–0.878), 3-year (AUC = 0.808, 95 %CI: 0.775–0.841), 5-year (AUC = 0.809, 95 %CI: 0.783–0.835), and 10-year (AUC = 0.806, 95 %CI: 0.784–0.827) all-cause mortality.

Conclusion: Higher ALBI score was related to a higher risk of all-cause mortality in patients with HBV infection, and the ALBI score showed a good predictive effect for short- and long-term all-cause mortality.

1. Introduction

Hepatitis B virus (HBV) is a hepatotropic virus that causes persistent infection in humans through immune anergy (Yuen et al., 2018). Chronic HBV infection is a major global healthcare problem, although infection rates have been greatly reduced since the introduction of the vaccine (Martinot-Peignoux et al., 2013). It was reported that chronic hepatitis B affects more than 250 million people worldwide and causes more than 880,000 deaths each year (Farias et al., 2016). Chronic hepatitis B may progress to cirrhosis, liver failure, and hepatocellular carcinoma in subsequent decades (Yuen et al., 2018). Monitoring liver function plays an important role in the assessment of the prognosis of patients with liver disease.

The Child-Pugh score is the most widely used tool for assessing liver function and has been used in the management of the patient with hepatocellular carcinoma (Bruix and Sherman, 2011; Hiraoka et al., 2019). However, some limitations of the Child-Pugh score were disclosed, such as the interaction between different variables and the subjective judgment of some variables (Durand and Valla, 2005, 2008). Recently, a new index to assess liver function, the Albumin-Bilirubin (ALBI) score, has been used. Serum albumin and total bilirubin levels are important indicators of liver function impairment (Hamoud et al., 2018; Oettl et al., 2013). ALBI score has been confirmed to be associated with the prognosis of patients with cirrhosis and hepatocellular carcinoma (Wang

* Corresponding author.
E-mail address: yuanqincd@outlook.com (Q. Yuan).
[1] Lixia Du and Hui Xu contributed equally to this work and co-first authors.

https://doi.org/10.1016/j.pmedr.2024.102639
Received 14 November 2023; Received in revised form 25 January 2024; Accepted 31 January 2024
Available online 3 February 2024

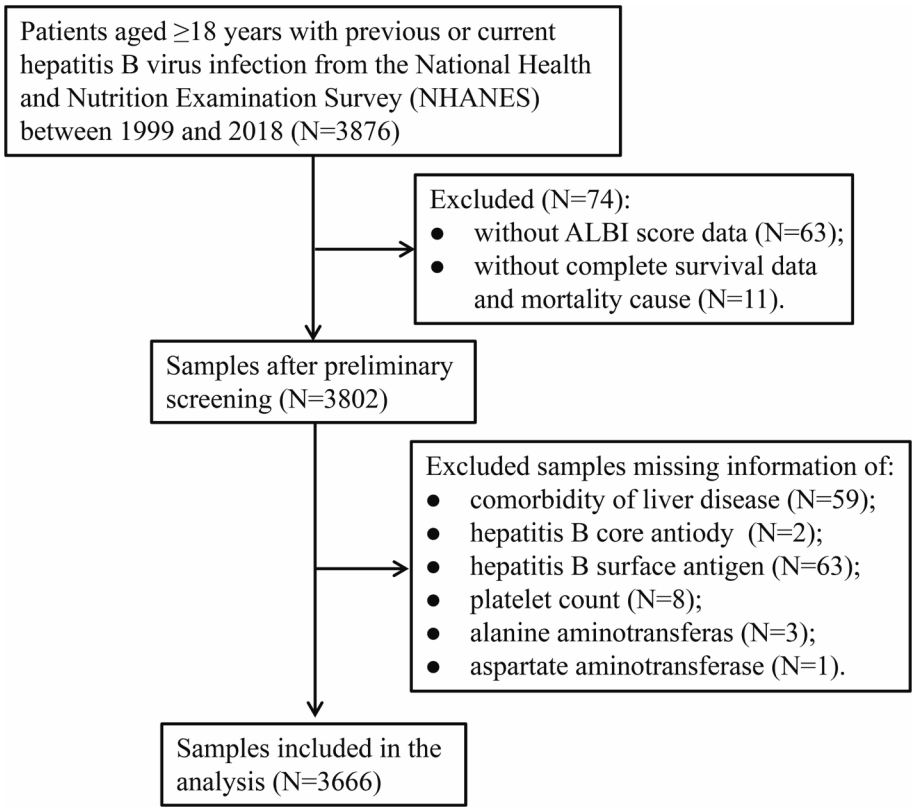

Fig. 1. Flow chart of screening of patients with hepatitis B virus infection in the National Health and Nutrition Examination Survey (NHANES), 1999–2018. ALBI, albumin-bilirubin score.

et al., 2019; Wang et al., 2016). Several studies reported that the ALBI score was correlated with liver fibrosis staging (Fujita et al., 2019) and cirrhosis severity in patients with HBV infection (Wang et al., 2019) and can be used to predict short- and long-term mortality risk in patients with cirrhosis (Chen et al., 2017; Wang et al., 2019). Similarly, the ALBI score can be used to assess the prognosis of patients with hepatocellular carcinoma (Fujita et al., 2019; Wang et al., 2016). However, the association between ALBI score and prognosis of HBV-infected patients in general remains unclear.

Whether the ALBI score could predict the prognosis of HBV-infected patients in general is not well established. This study aimed to explore the association between ALBI score and all-cause mortality in HBV-infected patients in general, and to analyze the predictive values of the ALBI score for short- and long-term mortality.

2. Methods

2.1. Data sources and study population

Data used in this retrospective cohort study were from the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2018. The NHANES sampling method uses a stratified, multistage, probability cluster design established by the National Center for Health Statistics for Disease Control and Prevention in the United States. The NHANES database is publicly available (https://www.cdc.gov/nchs/nhanes/index.htm) and contains information on the health, nutritional status, and health behaviors of the sample population. The inclusion criteria were that patients were ≥ 18 years of age, had previous or current HBV infection, and had complete laboratory test such as albumin and bilirubin levels. Patients with missing survival data and other important variables were excluded. Protocols of NHANES were approved by the National Center for Health Statistics Research Ethics Review Board. This study was exempted from ethical review by the Institutional Review Board of Chengdu BOE Hospital due to the retrospective design and de-identified data from the publicly database.

2.2. Study outcomes and definition

The outcome of this study was all-cause mortality, which was defined as all deaths that occurred during the study period. The follow-up period was until December 2019.

The ALBI score was calculated using the following formula: ALBI = (log10 bilirubin × 0.66) + (albumin × -0.085), where total bilirubin is measured in μmol/L and albumin in g/L. As reported previously (Johnson et al., 2015), the ALBI score was stratified into three grades: grade 1 (score ≤ -2.60), grade 2 (score > -2.60 and ≤ -1.39), and grade 3 (score > -1.39). Since there were only 5 patients in the grade 3 group, this study divided the ALBI score into two categories: ≤-2.60 and > -2.60.

The fibrosis-4 index (FIB-4) was used to assess the severity of fibrosis (Sterling et al., 2006). The FIB-4 was calculated using the formula: FIB-4 = aspartate aminotransferase (IU/L) × age (years) / [platelet count (10^9/L) × alanine aminotransferase (IU/L)$^{1/2}$]. The threshold of FIB-4 was determined according to Liu et al. (Liu et al., 2021), FIB-4 index ≤ 2.25 was considered non-fibrotic and the FIB-4 index > 2.25 (cirrhosis) was considered fibrotic.

2.3. Data collection

Patient demographic data, disease history, and laboratory test data were collected. Characteristics included in the analysis were recorded as follows: age, sex (male, female), race/ethnicity (Mexican American, non-Hispanic white, non-Hispanic black, other Hispanic, other race), educational level (less than 9th grade, 9-11th grade, high school graduate, college graduate or above), family income (<20,000 $, ≥20,000 $, unknown), smoke (never, smoking before but not present, current

Table 1
Characteristics of patients with hepatitis B virus infection in the National Health and Nutrition Examination Survey (NHANES), 1999–2018.

Variables	Total (n = 3,666)	ALBI ≤ -2.6 (n = 3,109)	ALBI > -2.6 (n = 557)	*P*
Age, years, Mean (S.E)	53.05 (0.36)	52.34 (0.38)	57.74 (0.89)	<0.001
Sex, n (%)				<0.001
Male	2,061 (56.04)	1,797 (57.65)	264 (45.25)	
Female	1,605 (43.96)	1,312 (42.35)	293 (54.75)	
Race/ethnicity, n (%)				<0.001
Mexican American	275 (3.63)	229 (3.55)	46 (4.22)	
Other Hispanic	339 (7.35)	295 (7.71)	44 (4.91)	
Non-Hispanic white	737 (39.45)	633 (39.87)	104 (36.59)	
Non-Hispanic black	1,350 (25.14)	1,076 (23.07)	274 (39.03)	
Other races	965 (24.42)	876 (25.80)	89 (15.24)	
Education level, n (%)				0.424
Less than 9th grade	638 (12.04)	533 (11.70)	105 (14.31)	
9-11th grade	657 (15.96)	540 (15.90)	117 (16.36)	
High school graduate	838 (23.81)	720 (23.68)	118 (24.68)	
College graduate or above	1,533 (48.20)	1,316 (48.73)	217 (44.65)	
Family income, n (%)				<0.001
< $20,000	1,236 (29.31)	1,009 (27.97)	227 (38.30)	
≥ $20,000	2,218 (65.82)	1,915 (66.95)	303 (58.24)	
Unknown	212 (4.87)	185 (5.08)	27 (3.46)	
Smoke, n (%)				0.618
Never	1,815 (47.51)	1,565 (47.92)	250 (44.79)	
Smoking before but not present	961 (24.67)	813 (24.46)	148 (26.12)	
Current smoking	890 (27.82)	731 (27.62)	159 (29.09)	
Drink, n (%)				0.398
No	1,065 (26.35)	911 (26.64)	154 (24.44)	
Yes	2,108 (60.67)	1,790 (60.69)	318 (60.50)	
Unknown	493 (12.98)	408 (12.67)	85 (15.06)	
Comorbidity of liver disease, n (%)				<0.001
No	3,257 (87.59)	2,803 (88.64)	454 (80.51)	
Yes	409 (12.41)	306 (11.36)	103 (19.49)	
Diabetes, n (%)				<0.001
No	2,392 (71.97)	2,074 (73.81)	318 (59.69)	
Yes	1,274 (28.03)	1,035 (26.19)	239 (40.31)	
Cardiovascular disease, n (%)				<0.001
No	1,199 (38.64)	1,053 (40.15)	146 (28.52)	
Yes	2,467 (61.36)	2,056 (59.85)	411 (71.48)	
BMI, kg/m^2, Mean (S.E)	27.60 (0.15)	27.20 (0.16)	30.32 (0.39)	<0.001
BMI groups, n (%)				<0.001
<18.5 kg/m^2	77 (2.26)	68 (2.43)	9 (1.18)	
18.5–25 kg/m^2	1219 (34.73)	1101 (37.11)	118 (18.77)	
25–28 kg/m^2	803 (20.92)	695 (21.05)	108 (20.04)	
≥28 kg/m^2	1,567 (42.09)	1,245 (39.41)	322 (60.01)	
Hepatitis B surface antigen, n (%)				0.166
Positive	248 (6.47)	205 (6.24)	43 (8.03)	
Negative	3,418 (93.53)	2,904 (93.76)	514 (91.97)	
Albumin, g/L, Mean (S.E)	42.29 (0.11)	43.18 (0.09)	36.34 (0.16)	<0.001
Bilirubin, μmol/L, Mean (S.E)	11.54 (0.14)	11.33 (0.14)	12.98 (0.43)	<0.001
Platelet, 1000/μL, Mean (S.E)	243.91 (1.70)	244.57 (1.70)	239.50 (5.45)	0.363
ALT, U/L, Mean (S.E)	28.42 (0.58)	27.55 (0.54)	34.25 (2.59)	0.012
AST, U/L, Mean (S.E)	28.55 (0.51)	27.05 (0.40)	38.64 (2.71)	<0.001
ALP, U/L, Mean (S.E)	71.98 (0.63)	70.19 (0.60)	83.98 (2.40)	<0.001
GGT, U/L, Mean (S.E)	36.64 (1.01)	33.35 (0.96)	58.66 (4.33)	<0.001
Sodium, mmol/L, Mean (S.E)	139.36 (0.08)	139.41 (0.08)	139.02 (0.18)	0.014
Creatinine, mg/dL, Mean (S.E)	0.90 (0.01)	0.89 (0.01)	1.02 (0.04)	0.001
Hemoglobin, g/dL, Mean (S.E)	14.19 (0.04)	14.30 (0.04)	13.43 (0.11)	<0.001
FIB-4, Mean (S.E)	1.35 (0.03)	1.24 (0.02)	2.04 (0.15)	<0.001
Hepatitis B treatment drugs, n (%)				0.497
No	3,617 (98.05)	3,068 (97.98)	549 (98.49)	
Yes	49 (1.95)	41 (2.02)	8 (1.51)	
All-cause mortality, n (%)				<0.001
Alive	2,741 (76.47)	2,421 (78.81)	320 (60.86)	
Dead	925 (23.53)	688 (21.19)	237 (39.14)	
Follow-time, months, Mean (S.E)	129.94 (2.97)	133.39 (3.21)	106.88 (4.84)	<0.001

Note: ALBI, Albumin-Bilirubin; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase; FIB-4, fibrosis-4 index.

smoking), drinking (no, yes, unknown), comorbidity of liver disease (no, yes), diabetes (no, yes), cardiovascular disease (no, yes), body mass index (BMI, <18.5 kg/m^2, 18.5–25 kg/m^2, 25–28 kg/m^2, ≥28 kg/m^2), hepatitis B surface antigen (positive, negative), albumin, total bilirubin, platelet, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), sodium, creatinine, hemoglobin, FIB-4, hepatitis B treatment drugs (no, yes), survival status (alive, dead), and follow-up time.

2.4. Statistical analysis

Continuous data were expressed as mean [standard error (SE)] or median with interquartile range [M (Q1, Q3)] and were compared using independent samples *t*-test or Mann-Whitney U rank-sum test. Categorical data were described as numbers and percentage [n (%)] and were analyzed by the chi-square test or rank-sum test.

Missing values of the variable education level, smoking, and BMI were imputed by the multiple imputations by chained equations for the random forest. Sensitivity analysis showed no statistically significant difference between before and after data interpolation. Descriptive statistics were performed based on patients with ALBI ≤ -2.60 and > -2.6. Weighted univariate Cox regression model was used to select factors that might be related to all-cause mortality. Weighted multivariate Cox regression model was applied to assess the association between ALBI and all-cause mortality. The association between ALBI and all-cause mortality was further stratified by age (<65 and ≥ 65 years)

Table 2
Univariate Cox regression analysis of the factors that may be associated with the risk of all-cause mortality in patients with hepatitis B virus infection.

Variables	HR (95 %CI)	*P*
Age	1.05 (1.05–1.06)	<0.001
Sex		
Male	Ref	
Female	0.88 (0.75–1.02)	0.080
Race/Ethnicity		
Mexican American	Ref	
Other Hispanic	1.01 (0.58–1.74)	0.980
Non-Hispanic white	1.51 (1.13–2.01)	0.006
Non-Hispanic black	1.33 (1.01–1.76)	0.045
Other Races	0.83 (0.59–1.16)	0.268
ALBI score		
ALBI score ≤ -2.6	Ref	
ALBI score > -2.6	2.39 (1.91–2.98)	<0.001
Education level		
Less than 9th grade	Ref	
9-11th grade	0.86 (0.65–1.14)	0.292
High school graduate	0.67 (0.52–0.87)	0.003
College graduate or above	0.60 (0.46–0.78)	<0.001
Family income		
< $20,000	Ref	
≥$20,000	0.73 (0.59–0.90)	0.004
Unknown	0.71 (0.49–1.03)	0.069
Smoke		
Never	Ref	
Smoking before but not present	1.77 (1.45–2.18)	<0.001
Current smoking	1.35 (1.08–1.68)	0.008
Drink		
No	Ref	
Yes	1.15 (0.96–1.37)	0.130
Unknown	1.13 (0.82–1.56)	0.461
Comorbidity of liver disease		
No	Ref	
Yes	1.23(0.94–1.62)	0.133
Diabetes		
No	Ref	
Yes	2.12 (1.79–2.51)	<0.001
Cardiovascular disease		
No	Ref	
Yes	2.17 (1.75–2.68)	<0.001
BMI	1.00 (0.99–1.02)	0.613
BMI groups		
18.5–25 kg/m^2	Ref	
<18.5 kg/m^2	2.25 (1.21–4.19)	0.011
25–28 kg/m^2	1.04 (0.80–1.35)	0.752
≥28 kg/m^2	1.23 (0.98–1.55)	0.075
Albumin	0.91 (0.89–0.94)	<0.001
Bilirubin	0.99 (0.97–1.02)	0.586
Platelet	1.00 (1.00–1.00)	0.084
ALT	1.00 (1.00–1.00)	0.211
AST	1.00 (1.00–1.00)	1.000
ALP	1.01 (1.01–1.01)	<0.001
GGT	1.00 (1.00–1.00)	<0.001
Sodium	0.97 (0.94–1.01)	0.101
Creatinine	1.00 (0.72–1.39)	1.000
Hemoglobin	0.91 (0.85–0.97)	0.005
FIB-4	1.00 (0.93–1.08)	1.000
Hepatitis B treatment drugs		
No	Ref	
Yes	1.17 (0.47–2.95)	0.734

Note: HR, hazard ratio; 95 %CI, confidence interval; Ref, reference; ALBI, Albumin-Bilirubin; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase; FIB-4, fibrosis-4 index.

and hepatitis B surface antigen (positive and negative). Overall survival was determined using the Kaplan-Meier (K-M) method and the log-rank test was utilized to compare differences. Receiver operating characteristic (ROC) curves and area under the ROC curve (AUC) were utilized to assess the predictive accuracy of the ALBI score for all-cause mortality. Results were reported as hazard ratio (HR) and 95 % confidence interval (CI). Statistical analyses were completed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA), and R 4.0.3 software (Institute for Statistics and Mathematics, Vienna, Austria) for ROC curve plotting. Statistical significance was set at $P < 0.05$ (two-sided).

Table 3
Association between ALBI score and all-cause mortality in patients with hepatitis B virus infection.

Populations	Variable	Crude Model		Adjusted Model	
		HR (95 % CI)	*P*	HR (95 % CI)	*P*
Total	ALBI score > -2.6 (vs. ≤ -2.6)	2.39 (1.92–2.98)	<0.001	1.75 (1.43–2.14)	<0.001
Aged < 65 years	ALBI score > -2.6 (vs. ≤ -2.6)	2.11 (1.53–2.91)	<0.001	1.83 (1.32–2.54)	<0.001
Aged ≥ 65 years	ALBI score > -2.6 (vs. ≤ -2.6)	2.04 (1.56–2.67)	<0.001	1.73 (1.33–2.23)	<0.001
Positive hepatitis B surface antigen	ALBI score > -2.6 (vs. ≤ -2.6)	4.19 (1.99–8.80)	<0.001	2.20 (0.83–5.82)	0.111
Negative hepatitis B surface antigen	ALBI score > -2.6 (vs. ≤ -2.6)	2.32 (1.87–2.88)	<0.001	1.73 (1.41–2.13)	<0.001

Note: HR, hazard ratio; 95 %CI, confidence interval; ALBI, Albumin-Bilirubin score.
Adjusted model was a weighted multivariate Cox regression model adjusted for age, sex, race/ethnicity, education level, family income, smoking, diabetes, cardiovascular disease, BMI, ALP, GGT, and hemoglobin.

3. Results

3.1. Participant characteristics

A total of 3,876 patients aged ≥ 18 years with a history of HBV infection were extracted from the NHANES database from 1999 to 2018. After excluding 210 patients who did not meet the inclusion criteria, 3,666 patients were included in the analysis (Fig. 1). The characteristics of 3,666 patients were shown in Table 1. The mean age of all patients was 53.05 years, 2,061 (56.04 %) patients were male, and 1,350 (25.14 %) patients were non-Hispanic white. The mean BMI was 27.60 kg/m^2 and 1,567 (42.09 %) patients' BMI was ≥ 28 kg/m^2. There were 248 (6.47 %) patients with positive hepatitis B surface antigen and 49 (1.95 %) patients treated with hepatitis B drugs. The mean albumin level was 42.29 g/L and the mean bilirubin level was 11.54 μmol/L. There were 3,109 patients with ALBI score ≤ -2.6 and 557 patients with ALBI score > -2.6. At the end of the follow-up, 925 (23.53 %) patients died and the mean follow-up was 129.94 months.

3.2. Univariate analysis for all-cause mortality

Table 2 lists the univariate analysis of the factors that may be associated with the risk of all-cause mortality. Older age (HR = 1.05; 95 %CI: 1.05–1.06), non-Hispanic white (HR = 1.51; 95 %CI: 1.13–2.01), non-Hispanic black (HR = 1.33; 95 %CI: 1.01–1.76), higher ALBI score (HR = 2.39; 95 %CI: 1.91–2.98), smoking before but not present (HR = 1.77; 95 %CI: 1.45–2.18), current smoking (HR = 1.35; 95 %CI: 1.08–1.68), diabetes (HR = 2.12; 95 %CI: 1.79–2.51), cardiovascular disease (HR = 2.17; 95 %CI: 1.75–2.68), BMI < 18.5 kg/m^2 (HR = 2.25; 95 %CI: 1.21–4.19), higher ALP levels (HR = 1.01; 95 %CI: 1.01–1.01), might be correlated with a higher risk of all-cause mortality, whereas higher education levels [high school (HR = 0.67; 95 %CI: 0.52–0.87)

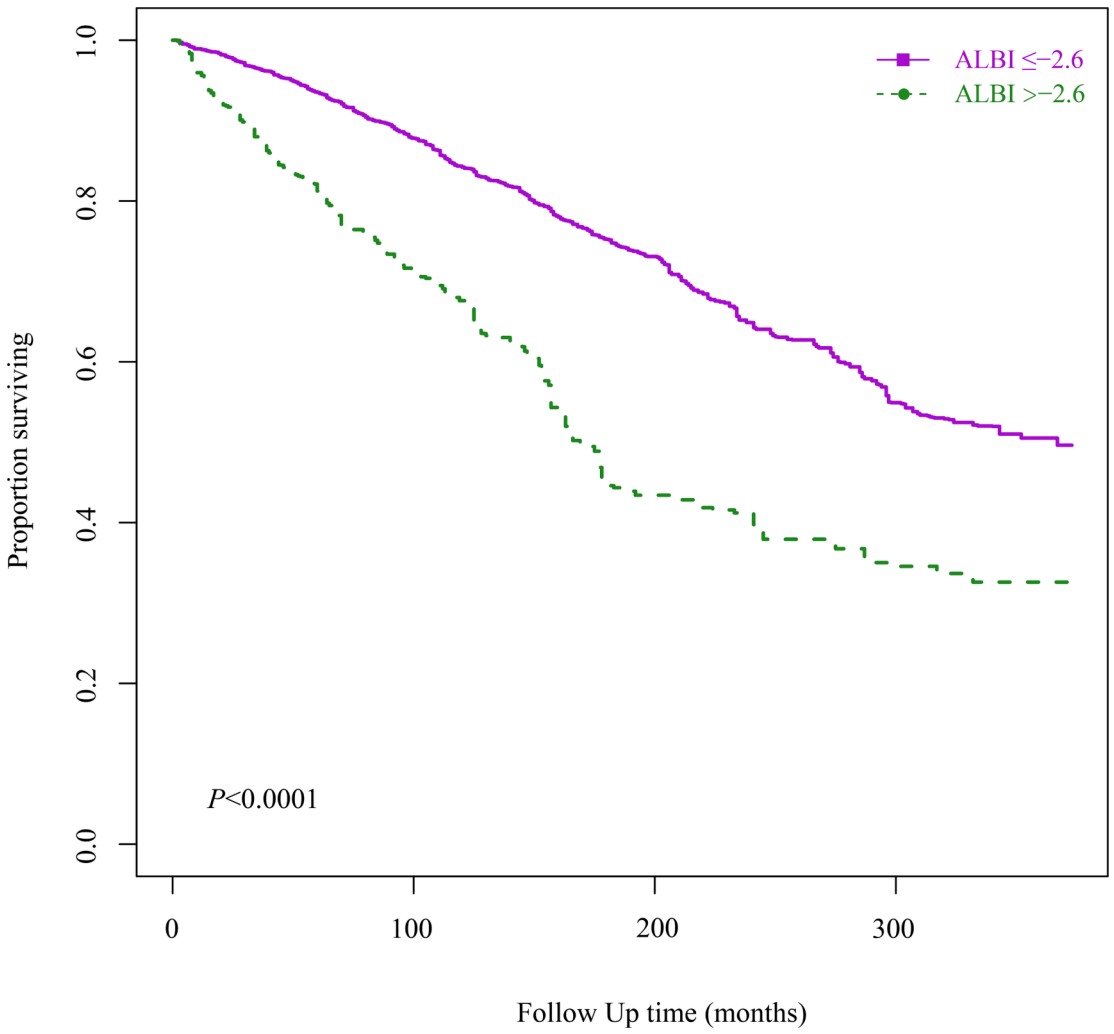

Fig. 2. Kaplan-Meier (K-M) survival curves of HBV-infected patients with albumin-bilirubin (ALBI) score ≤ -2.6 and > -2.6. HBV, hepatitis B virus.

and college or above (HR = 0.60; 95 %CI: 0.46–0.78)], higher family income (HR = 0.73; 95 %CI: 0.59–0.90), higher albumin levels (HR = 0.91; 95 %CI: 0.89–0.94), and higher hemoglobin levels (HR = 0.91; 95 %CI: 0.85–0.97) might be related to lower risk of all-cause mortality.

3.3. Relationship between ALBI and all-cause mortality in patients with HBV infection

Table 3 presents the association between ALBI score and all-cause mortality. Compared with ALBI score ≤ -2.6, HBV-infected patients with ALBI score > -2.6 (HR = 2.39; 95 %CI: 1.92–2.98) were related to higher all-cause mortality risk. After adjusting for age, sex, race/ethnicity, education level, family income, smoking, diabetes, cardiovascular disease, BMI, ALP, GGT, and hemoglobin, ALBI score > -2.6 (HR = 1.75; 95 %CI: 1.43–2.14) was associated with a higher risk of all-cause mortality. Stratified analyses found that patients with ALBI score > -2.6 were related to higher all-cause mortality in populations with age < 65 years (HR = 1.83; 95 %CI: 1.32–2.54), age ≥ 65 years (HR = 1.73; 95 %CI: 1.33–2.23), and negative hepatitis B surface antigen (HR = 1.73; 95 %CI: 1.41–2.13), while not in populations with positive hepatitis B surface antigen (HR = 2.20; 95 %CI: 0.83–5.82, $P = 0.111$). The K-M curves demonstrated that patients with ALBI score ≤ -2.6 had higher overall survival compared to patients with ALBI score > -2.6 ($P < 0.0001$; Fig. 2).

3.4. Predictive effect of ALBI score for all-cause mortality

Fig. 3 shows the predictive ability of ALBI score for 1-year, 3-year, 5-year, and 10-year all-cause mortality in patients with HBV infection. The AUC of the model was 0.816 (95 %CI: 0.754–0.878) for 1-year all-cause mortality, 0.808 (95 %CI: 0.775–0.841) for 3-year all-cause mortality, 0.809 (95 %CI: 0.783–0.835) for 5-year all-cause mortality, and 0.806 (95 %CI: 0.784–0.827) for 10-year all-cause mortality.

4. Discussion

The current study investigated the relationship between ALBI score and all-cause mortality in HBV-infected patients in general. High ALBI score was found to be associated with a higher risk of all-cause mortality in HBV-infected patients. Furthermore, the ALBI score had good predictive ability for 1-year, 3-year, 5-year, and 10-year all-cause mortality, with AUC values above 0.80.

Liver function is an important indicator to evaluate the prognosis of patients with liver disease, especially cirrhosis and hepatocellular carcinoma (Fagenson et al., 2020; Oikonomou et al., 2019; Zhang et al., 2019). Poor liver function can cause high postoperative morbidity and worse long-term survival in patients with liver disease (Zou et al., 2018). The Child-Pugh score is the most widely used tool for assessing liver function and consists of serum albumin, serum bilirubin, coagulation profile, ascites, and hepatic encephalopathy. However, the use of the Child-Pugh score is limited by the fact that ascites and albumin are

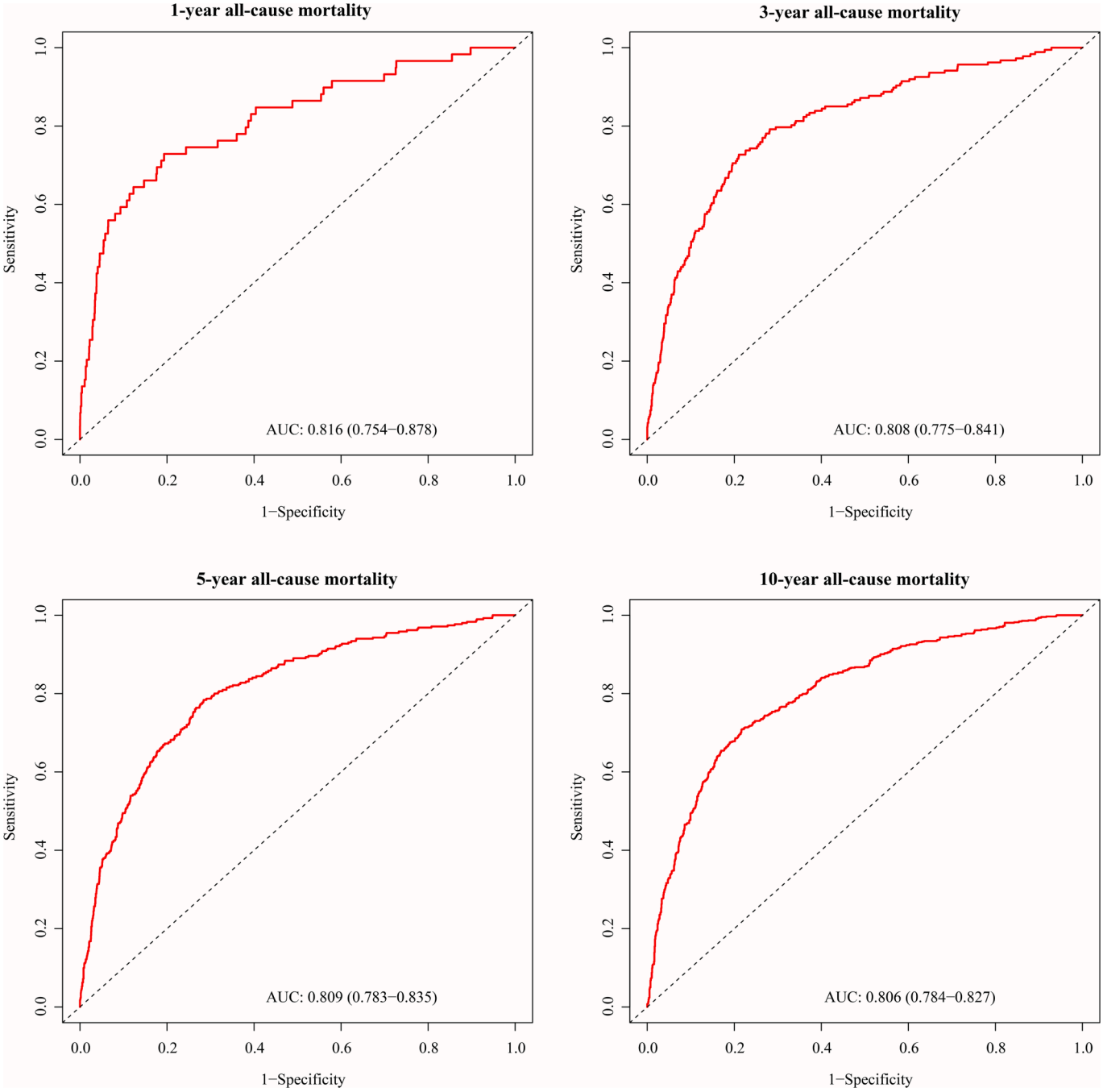

Fig. 3. Receiver operating characteristic (ROC) curves of albumin-bilirubin (ALBI) score for predicting 1-year, 3-year, 5-year, and 10-year all-cause mortality in HBV-infected patients. AUC, area under the ROC curve; HBV, hepatitis B virus.

interrelated and that ascites and encephalopathy may be affected by inter-observer differences (Durand and Valla, 2008). Previous studies have confirmed that the ALBI score was a superior liver function assessment tool to the Child-Pugh score (Li et al., 2017; Na et al., 2018). The ALBI score includes only two objective serum indicators, albumin and bilirubin, to evaluate the patient's liver function and prognosis. Several studies have reported the use of the ALBI score to assess the prognosis of patients with cirrhosis (Oikonomou et al., 2019), post-hepatectomy (Fagenson et al., 2020), and hepatocellular carcinoma (Hiraoka et al., 2019). However, the association between ALBI score and prognosis of HBV-infected patients in general remains unclear. The current study investigated the relationship between ALBI score and all-cause mortality in HBV-infected patients in general. The results found that high ALBI score (score $>$ -2.6) was correlated with a higher risk of all-cause mortality. Similar results were observed in patients aged $<$ 65 years, aged $\geq$ 65 years, and those with negative hepatitis B surface antigen. Among patients with positive hepatitis B surface antigen, no statistical significance was found between ALBI score and all-cause mortality, and the associated causes need to be further investigated.

This study further analyzed the predictive ability of the ALBI score for short- and long-term all-cause mortality in HBV-infected patients. The ALBI score had good predictive ability for 1-year, 3-year, 5-year and 10-year all-cause mortality, and the AUC for these models exceeded 0.80. Fagenson et al. showed that the AUC of the ALBI score was 0.70 in predicting 30-day mortality after hepatectomy in patients with hepatocellular carcinoma, which was higher than that of the Model for End-

Stage Liver Disease (AUC 0.58) (Fagenson et al., 2020). Taylor et al. reported that the ALBI score had good a performance in predicting post-hepatectomy 30-day mortality with a model AUC of 0.80 (Taylor et al., 2021). Liu et al. used several tools to predict mortality in patients with hepatocellular carcinoma, with an AUC of 0.704 for the ALBI score to predict patient 3-year mortality (Liu et al., 2017). Furthermore, the use of the ALBI score in combination with other indicators for predicting the prognosis of patients with hepatocellular carcinoma was reported, such as the combined ALBI score-FIB-4 indicator (Zhang et al., 2019) and the combined ALBI score-aspartate aminotransferase-to-platelet count ratio index (APRI) (Luo et al., 2019). The ALBI score was used to assess liver function, and both the FIB-4 index and the APRI indicator were used to assess the severity of liver fibrosis. The combination of the ALBI score and the other indicators had better prognostic predictive ability than a single index. Future studies may need to explore more combined indicators of ALBI score for the prediction of prognosis in patients with liver disease.

Since the ALBI score was first described in 2015, it has been used to assess the prognosis of patients with different liver diseases. This study examined the relationship between ALBI score and all-cause mortality in HBV-infected patients in general. Furthermore, we assessed the predictive ability of the ALBI score for short- and long-term all-cause mortality. However, there were some limitations in this study. First, this study classified ALBI scores into two categories: $\leq$-2.6 and $>$ -2.6 due to only five individuals were included in ALBI grade 3 (score $>$ -1.39). This may affect the accuracy of the results in the populations with ALBI scores $>$ -2.6. Second, the ALBI score in combination with other indicators may be better predictors than a single ALBI score. Further studies may need to evaluate the predictive effect of combined indicators.

5. Conclusions

This study analyzed the relationship between ALBI score and all-cause mortality in HBV-infected patients in general. High ALBI score was related to a higher risk of all-cause mortality and the ALBI score showed a good predictive effect for short- and long-term all-cause mortality. The ALBI score may provide a biomarker for prognostic monitoring in a wide range of patients with HBV infection. Future studies may need to explore the predictive effect of the combination of the ALBI score with other indicators in the prognosis of patients with liver disease.

Funding

This study was funded by the Chengdu Municipal Health Commission (grant number: 20220818).

CRediT authorship contribution statement

Lixia Du: Writing – original draft, Conceptualization. **Hui Xu:** Methodology, Formal analysis, Conceptualization. **Li Fang:** Methodology, Investigation, Data curation. **Lijuan Qiao:** Visualization, Software, Data curation. **Yu Xie:** Methodology, Investigation. **Chunli Yang:** Methodology, Investigation, Data curation. **Linxiu Ji:** Methodology, Formal analysis, Data curation. **Liqiong Zhao:** Investigation, Data curation. **Cong Wang:** Visualization, Software, Data curation. **Weilan Zhang:** Methodology, Investigation, Data curation. **Xue Feng:** Software, Investigation, Data curation. **Ting Chen:** Investigation, Data curation. **Qin Yuan:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgment

None.

This study was funded by the Chengdu Municipal Health Commission (grant number: 20220818).

References

Bruix, J., Sherman, M., 2011. Management of hepatocellular carcinoma: an update. Hepatology (Baltimore, MD) 53, 1020–1022.

Chen, R.C., Cai, Y.J., Wu, J.M., Wang, X.D., Song, M., Wang, Y.Q., Zheng, M.H., Chen, Y. P., Lin, Z., et al., 2017. Usefulness of albumin-bilirubin grade for evaluation of long-term prognosis for hepatitis B-related cirrhosis. J. Viral Hepat. 24, 238–245.

Durand, F., Valla, D., 2005. Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD. J. Hepatol. 42 (Suppl), S100–S107.

Durand, F., Valla, D., 2008. Assessment of prognosis of cirrhosis. Semin. Liver Dis. 28, 110–122.

Fagenson, A.M., Gleeson, E.M., Pitt, H.A., Lau, K.N., 2020. Albumin-Bilirubin Score vs Model for End-Stage Liver Disease in Predicting Post-Hepatectomy Outcomes. J. Am. Coll. Surg. 230, 637–645.

Farias, D.R., Franco-Sena, A.B., Vilela, A., Lepsch, J., Mendes, R.H., Kac, G., 2016. Lipid changes throughout pregnancy according to pre-pregnancy BMI: results from a prospective cohort. BJOG 123, 570–578.

Fujita, K., Nomura, T., Morishita, A., Oura, K., Yoneyama, H., Kobara, H., Tsutsui, K., Himoto, T., Masaki, T., 2019. Albumin-Bilirubin Score Differentiates Liver Fibrosis Stage and Hepatocellular Carcinoma Incidence in Chronic Hepatitis B Virus Infection: A Retrospective Cohort Study. Am. J. Trop. Med. Hyg. 101, 220–225.

Hamoud, A.R., Weaver, L., Stec, D.E., Hinds Jr., T.D., 2018. Bilirubin in the Liver-Gut Signaling Axis. Trends Endocrinol. Metab. 29, 140–150.

Hiraoka, A., Kumada, T., Michitaka, K., Kudo, M., 2019. Newly Proposed ALBI Grade and ALBI-T Score as Tools for Assessment of Hepatic Function and Prognosis in Hepatocellular Carcinoma Patients. Liver Cancer 8, 312–325.

Johnson, P.J., Berhane, S., Kagebayashi, C., Satomura, S., Teng, M., Reeves, H.L., O'Beirne, J., Fox, R., Skowronska, A., et al., 2015. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J. Clin. Oncol. 33, 550–558.

Li, M.X., Zhao, H., Bi, X.Y., Li, Z.Y., Huang, Z., Han, Y., Zhou, J.G., Zhao, J.J., Zhang, Y. F., et al., 2017. Prognostic value of the albumin-bilirubin grade in patients with hepatocellular carcinoma: Validation in a Chinese cohort. Hepatol. Res. 47, 731–741.

Liu, P.H., Hsu, C.Y., Hsia, C.Y., Lee, Y.H., Chiou, Y.Y., Huang, Y.H., Lee, F.Y., Lin, H.C., Hou, M.C., et al., 2017. ALBI and PALBI grade predict survival for HCC across treatment modalities and BCLC stages in the MELD Era. J. Gastroenterol. Hepatol. 32, 879–886.

Liu, K., Qin, M., Tao, K., Liang, Z., Cai, F., Zhao, L., Peng, P., Liu, S., Zou, J., et al., 2021. Identification and external validation of the optimal FIB-4 and APRI thresholds for ruling in chronic hepatitis B related liver fibrosis in tertiary care settings. J. Clin. Lab. Anal. 35, e23640.

Luo, H., Li, C., Chen, L., 2019. Preoperative albumin-bilirubin grade combined with aspartate aminotransferase-to-platelet count ratio index predict outcomes of patients with hepatocellular carcinoma within Milan criteria after liver resection. Biosci. Trends 13, 176–181.

Martinot-Peignoux, M., Carvalho-Filho, R., Lapalus, M., Netto-Cardoso, A.C., Lada, O., Batrla, R., Krause, F., Asselah, T., Marcellin, P., 2013. Hepatitis B surface antigen serum level is associated with fibrosis severity in treatment-naïve, e antigen-positive patients. J. Hepatol. 58, 1089–1095.

Na, S.K., Yim, S.Y., Suh, S.J., Jung, Y.K., 2018. ALBI versus Child-Pugh grading systems for liver function in patients with hepatocellular carcinoma. 117:912-21.

Oettl, K., Birner-Gruenberger, R., Spindelboeck, W., Stueger, H.P., Dorn, L., Stadlbauer, V., Putz-Bankuti, C., Krisper, P., Graziadei, I., et al., 2013. Oxidative albumin damage in chronic liver failure: relation to albumin binding capacity, liver dysfunction and survival. J. Hepatol. 59, 978–983.

Oikonomou, T., Goulis, L., Doumtsis, P., Tzoumari, T., Akriviadis, E., Cholongitas, E., 2019. ALBI and PALBI Grades Are Associated with the Outcome of Patients with Stable Decompensated Cirrhosis. Ann. Hepatol. 18, 126–136.

Sterling, R.K., Lissen, E., Clumeck, N., Sola, R., Correa, M.C., Montaner, J.M.S.S., Torriani, F.J., Dieterich, D.T., et al., 2006. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology (Baltimore, MD) 43, 1317–1325.

Taylor, G.A., Fagenson, A.M., Kuo, L.E., Pitt, H.A., Lau, K.N., 2021. Predicting Operative Outcomes in Patients with Liver Disease: Albumin-Bilirubin Score vs Model for End-Stage Liver Disease-Sodium Score. J. Am. Coll. Surge. 232:470-80.e2.

Wang, J., Zhang, Z., Yan, X., Li, M., Xia, J., Liu, Y., Chen, Y., Jia, B., Zhu, L., et al., 2019. Albumin-Bilirubin (ALBI) as an accurate and simple prognostic score for chronic hepatitis B-related liver cirrhosis. Digest. Liver Dis.: Off. J. Italian Soc. Gastroenterol. Italian Associat. Study Liver 51, 1172–2118.

Wang, Y.Y., Zhong, J.H., Su, Z.Y., Huang, J.F., Lu, S.D., Xiang, B.D., Ma, L., Qi, L.N., Ou, B.N., et al., 2016. Albumin-bilirubin versus Child-Pugh score as a predictor of

outcome after liver resection for hepatocellular carcinoma. Br. J. Surg. 103, 725–734.
Yuen, M.F., Chen, D.S., Dusheiko, G.M., Janssen, H.L.A., Lau, D.T.Y., Locarnini, S.A., Peters, M.G., Lai, C.L., 2018. Hepatitis B virus infection. Nature reviews. Disease Primers 4, 18035.
Zhang, J., Luo, Y., Li, C., Liu, J., Xiang, H., Wen, T., 2019. The combination of the preoperative albumin-bilirubin grade and the fibrosis-4 index predicts the prognosis of patients with hepatocellular carcinoma after liver resection. Biosci. Trends 13, 351–1337.
Zou, H., Wen, Y., Yuan, K., Miao, X.Y., Xiong, L., Liu, K.J., 2018. Combining albumin-bilirubin score with future liver remnant predicts post-hepatectomy liver failure in HBV-associated HCC patients. Liver Int. Off. J. Int. Associat. Study Liver 38, 494–502.