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Original Article

Assessment of Prognostic Accuracy of Albumin-Bilirubin and Platelet-Albumin-Bilirubin Grades in Hepatocellular Carcinoma Patients According to Different Treatment Modalities: A Prospective Study

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Abstract

Background: The prognosis of hepatocellular carcinoma (HCC) is complex and depends on multiple factors, including hepatic reserve function. The albumin-bilirubin (ALBI) and platelet-albumin-bilirubin (PALBI) grades were developed to objectively evaluate liver function. We aimed to explore the ability of ALBI and PALBI grades to predict overall survival (OS) in patients with HCC based on the treatment modality and to determine factors associated with mortality.

Methods: From January 2018 to December 2022, we prospectively enrolled 645 newly diagnosed HCC patients. Kaplan-Meier and Cox-regression analyses were used to assess OS. Receiver operating characteristics (ROC) curve analysis was used to analyze the efficacy of different grades in predicting mortality.

Results: The median OS was 12 months during the follow-up time (range 1-24 months), and 75.81% of the study cohort died. Except for patients who underwent surgical resection, the ALBI and PALBI grades were significantly associated with OS in HCC patients, in various stages of BCLC, and treatment modalities (P<0.0001). In predicting OS, the PALBI score outperformed the ALBI, CTP, and MELD scores (P<0.0001). Furthermore, the PALBI grade outperformed the ALBI grade in stratifying CTP classes into distinct survival groups. Multiple tumours >3, MELD grade 3, PALBI grade 3, BCLC stages B, C, and D, and patients receiving supportive treatment were independently associated with OS.

Conclusions: ALBI and PALBI grades are effective in the determination of OS among HCC patients in different clinical settings. The PALBI grade is an independent risk factor for mortality and is superior to the ALBI grade in predicting OS.

Keywords: Hepatocellular carcinoma; Albumin-bilirubin grade; Platelet-albumin-bilirubin grade; Prognosis; Overall survival
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Background

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths (8.3%) worldwide. [(1)] Since HCC occurs primarily in the presence of cirrhosis and even chronic liver disease, liver

impairment is relatively common at the time of diagnosis, which influences the prognosis of HCC. [2] In clinical settings, the Child-Turcotte-Pugh (CTP) class and the model for end-stage liver disease (MELD) score are frequently employed to evaluate hepatic function. [3, 4]

The CTP class which includes hepatic encephalopathy, ascites, prothrombin time/international normalized ratio (PT/INR), albumin, and bilirubin has several limitations including the equal weighting of the parameters, arbitrary cutoff values, subjective (encephalopathy and ascites) and interrelated (ascites and serum albumin) factors, in addition, encephalopathy and ascites can be altered by the treatment. Furthermore, it was developed for cirrhotic patients, and many HCC patients have chronic hepatitis with normal or slightly reduced hepatic functional reserve (CTP A patients) .[5] The MELD score, which is based on bilirubin, creatinine, and INR, is widely used to predict prognosis and timing for liver transplantation. However, the validity of the MELD score in patients with lesser degrees of liver impairment has been questioned .[6]

The albumin-bilirubin (ALBI) grade incorporating albumin and bilirubin only was developed to overcome the drawbacks of CTP classification, providing a more objective evaluation of liver function. [7] ALBI grade had proven more effective in predicting prognosis and overall survival (OS) than CTP class, especially in patients with good hepatic function. [8, 9] ALBI grade does not take into consideration the impact of portal hypertension which can leverage patients' outcomes. Accordingly, the platelet-ALBI (PALBI) grade was developed based on the ALBI grade, using platelet count as an indicator for portal hypertension severity. [10]

Egypt had a high HCC burden secondary to the high prevalence of hepatitis C virus (HCV) with a very poor prognosis being the most common cause of cancer-related mortality (29.8%) in 2020 [1, 11]. Even though direct-acting antivirals (DAAs) have dramatically altered the HCV landscape, the hazard of HCV-related HCC remains high, especially among patients with cirrhosis and severe liver fibrosis . [12] Although ALBI-based grades seem to be better than CTP and MELD scores in predicting survival among HCC patients. [8-10, 13], the CTP class is still widely used in Egyptian liver centers to evaluate liver function and to assign treatment accordingly. Therefore, this study aimed to investigate the ability of ALBI and PALBI grades to predict OS in Egyptian patients with HCC according to the treatment modality and to determine factors associated with mortality.

Patients and methods

PatientsFrom January 2018 to December 2022, we conducted a 60-month prospective study with a 24-month follow-up period at Sohag University Hospitals. A total of 683 cirrhotic patients with recently diagnosed HCC participated in the study. In all, 7 patients were excluded from the study due to the coexistence of other malignancies and 31 patients did not comply with the follow-up period. Finally, 645 patients were included in the study (Figure 1). The diagnosis of liver cirrhosis was based on clinical information, sonographic, and laboratory findings. The diagnosis of HCC was based on dynamic imaging studies (triphasic computed tomography (CT), and/or dynamic magnetic resonance imaging (MRI)) or histopathological examination. The presence of the typical imaging pattern of an arterial phase hyperenhancement followed by washout in the venous phase on a dynamic study or the characteristic pathological features establish the diagnosis of HCC.

The study protocol was revised and endorsed by the Ethics Committee of Sohag Faculty of Medicine, under (IRB number: Soh-Med-21-10-41) and ClinicalTrials.gov (ID: NCT05720195). Informed written consent was provided by all patients before enrolment. We excluded patients with proteinuria, pre-existing other malignancies, haematologic disorders, kidney, gall bladder, or biliary duct disease; and Missed follow-up.

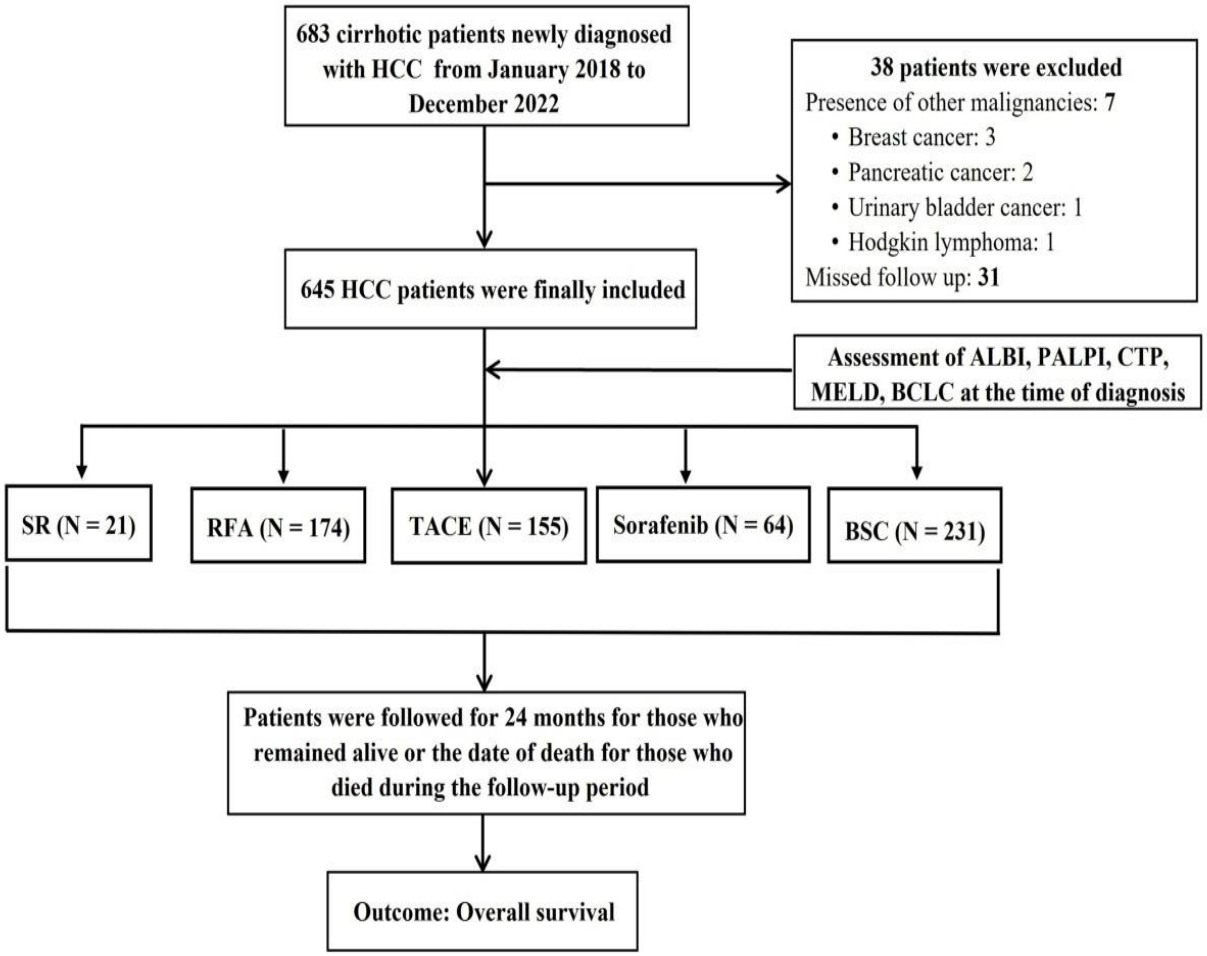


Figure 1: Flow chart of study patients

HCC: hepatocellular carcinoma; ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; CTP: Child-Turcotte-Pugh; MELD: Model for End-Stage Liver Disease; BCLC: Barcelona Clinic Liver Cancer; SR: surgical resection; RFA: radiofrequency ablation; TACE: transarterial chemoembolization; BSC: best supportive care.

Methods

All patients were subjected to a detailed medical history, thorough clinical examination, abdominal ultrasound, and laboratory investigations. Screening abdominal ultrasound was done on all cirrhotic patients before enrollment in the study and those with a hepatic focal lesion or heterogenous liver were subjected to a triphasic CT scan to establish HCC diagnosis. Dynamic MRI was done when triphasic CT results were inconclusive or combined with it for lesions < 2 cm. When radiography was unable to confirm the diagnosis, a biopsy with histopathological analysis was performed [14]. Diagnostic upper endoscopy was done on patients presenting with upper gastrointestinal bleeding (UGIB). Furthermore, screening upper endoscopy was performed on those who underwent surgical resection for their HCC; platelet count less than 100,000/µl; and/or splenomegaly.

Peripheral venous blood (12 ml) was collected from each patient at the time of initial diagnosis of HCC

by a clean venipuncture and the following investigations were done; 2 ml Ethylene Diamine Tetra acetic Acid (EDTA) blood for complete blood count (CBC), 4 ml heparinized and citrated plasma for liver function tests (albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and PT/INR), 2 ml heparinized plasma for serum creatinine, 2 ml serum for alpha-fetoprotein (AFP), and 2 ml serum for hepatitis B surface antigen and hepatitis C antibody. Random urine analysis was performed to exclude proteinuria.
We calculated the ALBI. [7] PALBI. [10] CTP. [3] and MELD.[4] scores and grades to evaluate the degree of hepatic dysfunction at the time of diagnosis. HCC was staged according to the Barcelona Clinic Liver Cancer (BCLC) staging system . [15] and the treatment was determined by the multidisciplinary hepatoma team based on the tumor stage following the BCLC guidelines whenever possible. We used the 2022-BCLC update in patients newly diagnosed after November 2021 .[6] Our patients received either curative (surgical resection (SR), radiofrequency ablation (RFA)), palliative (transarterial chemoembolization (TACE), sorafenib), or supportive (best supportive care (BSC)) treatment options. OS was measured from the time of HCC diagnosis until 24 months had passed for patients who survived or the date of death for those who died during the follow-up time.

Statistical analysis

Data were analyzed using STATA version 17.0 (Stata Statistical Software: Release 17.0 College Station, TX: Stata Corp LP.). The mean, standard deviation, median, range, and interquartile range (IQR) were used to depict quantitative data. Qualitative data were displayed as numbers and percentages. To determine the best cutoff point for liver function scores that predict mortality, receiver operating characteristic (ROC) curve analysis was employed. OS was evaluated using the Kaplan-Meier survival method and the log-rank test. Univariate and multivariate Cox regression analysis was employed to determine risk factors associated with OS. Graphs were created using an Excel or STATA program. The P-value was considered significant if it was < 0.05.

Results

Baseline features of the studied population

The baseline features of study patients are highlighted in Table 1. The mean age of our patients was 61.53 ± 8.71 years, 75.66% were males, and HCV was the primary etiology of cirrhosis (92.56%) followed by hepatitis B virus (7.13%). Of all patients, 60.47% had a solitary nodule, and the right lobe was affected in 56.59%. The mean tumor size was 5.46 ± 3.23 cm (range 1-18 cm). Portal vein thrombosis (PVT) was present in 26.2% of patients, and extrahepatic spread in 4.96%. The median (IQR) of AFP was 258.22 (28-923) ng/ml. Curative, palliative, and supportive treatments were provided to 30.23%, 33.95%, and 35.81% of patients, respectively. The median follow-up time was 12 months (range, 1-24), and the median OS was 12 months (95% confidence interval (95% CI) 11.49-12.52). The overall mortality at the end of the follow-up was 75.81%.

Table 1: Baseline features of the studied population

Variable	All patients (N=645)
Age, mean±SD (years)	61.53±8.71
Gender, male/female, n (%)	488/157 (75.66/24.34)
Residence, urban/rural, n (%)	119/526 (18.45/81.55)
Smoking, n (%)	193 (29.92)
Hypertension, n (%)	170 (26.36)
Diabetes Mellitus, n (%)	177 (27.44)
Aetiology of cirrhosis, n (%)	
HCV/HBV/Negative/HBV and HCV coinfection	575/24/24/22 (89.15/3.72/3.72/3.41)
Jaundice, n (%)	198 (30.7)
Hepatic encephalopathy, n (%)	201 (31.16)
Varices, n (%)	203 (31.47)
Direct-acting antivirals (N=597), n (%)	424 (71.02)
Imaging data	
Splenomegaly, n (%)	401 (62.17)
Ascites, n (%)	
No	343 (53.18)
Mild	69 (10.7)
Moderate to marked	233 (36.12)
Site of HFL, n (%)	
Right	365 (56.59)
Left	121 (18.76)
Bilateral	159 (24.65)
Number of HFLs, n (%)	
Single	390 (60.47)
Two	80 (12.4)
Three	20 (3.1)
More than three	155 (24.03)
Size of HFL (cm)	
Mean±SD	5.46±3.23
Median (range)	4.5 (1:18)
Portal vein thrombosis, n (%)	169 (26.2)
Extrahepatic spread, n (%)	32 (4.96)
Laboratory parameters	
AFP (ng/ml), median (IQR)	258.22 (28:923)
ALT (U/l), median (IQR)	44 (25:75.5)
AST (U/l), median (IQR)	57 (34:90.5)
Total bilirubin (mg/dl), median (IQR)	1.6 (1:3.5)
Albumin (g/dl), mean±SD	2.97±0.8
INR, mean±SD	1.32±0.33
Creatinine (mg/dl), mean±SD	1.25±0.81
Platelets (10^3/µl), mean±SD	150.54±79.31
HCC treatment, n (%)	
SR	21 (3.26)
RFA	174 (26.98)
TACE	155 (24.03)
Sorafenib	64 (9.92)
BSC	231 (35.81)
Overall mortality, n (%)	489 (75.81)
Overall survival, months (95%CI)	12 (11.49:12.52)
Duration of follow-up (months)	
Mean±SD	12.45±8.45
Median (range)	12 (1:24)

HBV: hepatitis B virus; HCV: hepatitis C virus; HFL: hepatic focal lesion; AFP: alpha-fetoprotein; IQR: interquartile range; ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; HCC: hepatocellular carcinoma; SR: surgical resection; RFA: radiofrequency ablation; TACE: transarterial chemoembolization; BSC: best supportive care; CI: confidence interval.

Patient classification and OS according to liver function grading systems, BCLC stage, and treatment modality

We classified patients according to CTP, ALBI, PALBI, and BCLC staging systems. The most frequent CTP class was A (38.14%) followed by class C (32.87%), and the mean MELD score was 14.15 ± 6.86. The most frequent grade of ALBI was 2 (47.29%), followed by grade 3 (42.02%), and most patients were PALBI grade 3 (64.5%), followed by grade 2 (23.72%). BCLC stage D accounted for 32.87% of patients, followed by stage A (26.2%), and stage B (25.74%) (Table 2). The OS was associated with the liver function grading systems (ALBI, PALBI, CTP, and MELD grades, Figures 2A-D), BCLC staging system (Figure 2E), and the type of treatment offered to the patient, being better with curative treatments and worse with BSC (Figure 2F, all $P < 0.0001$).

Table 2 Distribution of patients with HCC according to the studied staging systems

Variable	All patients (N=645)
Child score, mean±SD	8.2±2.72
Child class, n (%)	
A	246 (38.14)
B	187 (28.99)
C	212 (32.87)
MELD score, mean±SD	14.15±6.86
MELD grade, n (%)	
Grade 1	184 (28.53)
Grade 2	224 (34.73)
Grade 3	237 (36.74)
ALBI score, mean ± SD	-1.53±0.85
ALBI grade, n (%)	
Grade 1	69 (10.7)
Grade 2	305 (47.29)
Grade 3	271 (42.02)
PALBI score, mean±SD	-1.83±0.57
PALBI grade, n (%)	
Grade 1	76 (11.78)
Grade 2	153 (23.72)
Grade 3	416 (64.5)
BCLC stage, n (%)	
0	6 (0.93)
A	169 (26.2)
B	166 (25.74)
C	92 (14.26)
D	212 (32.87)

MELD: Model for End-Stage Liver Disease; ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; BCLC: Barcelona Clinic Liver Cancer.

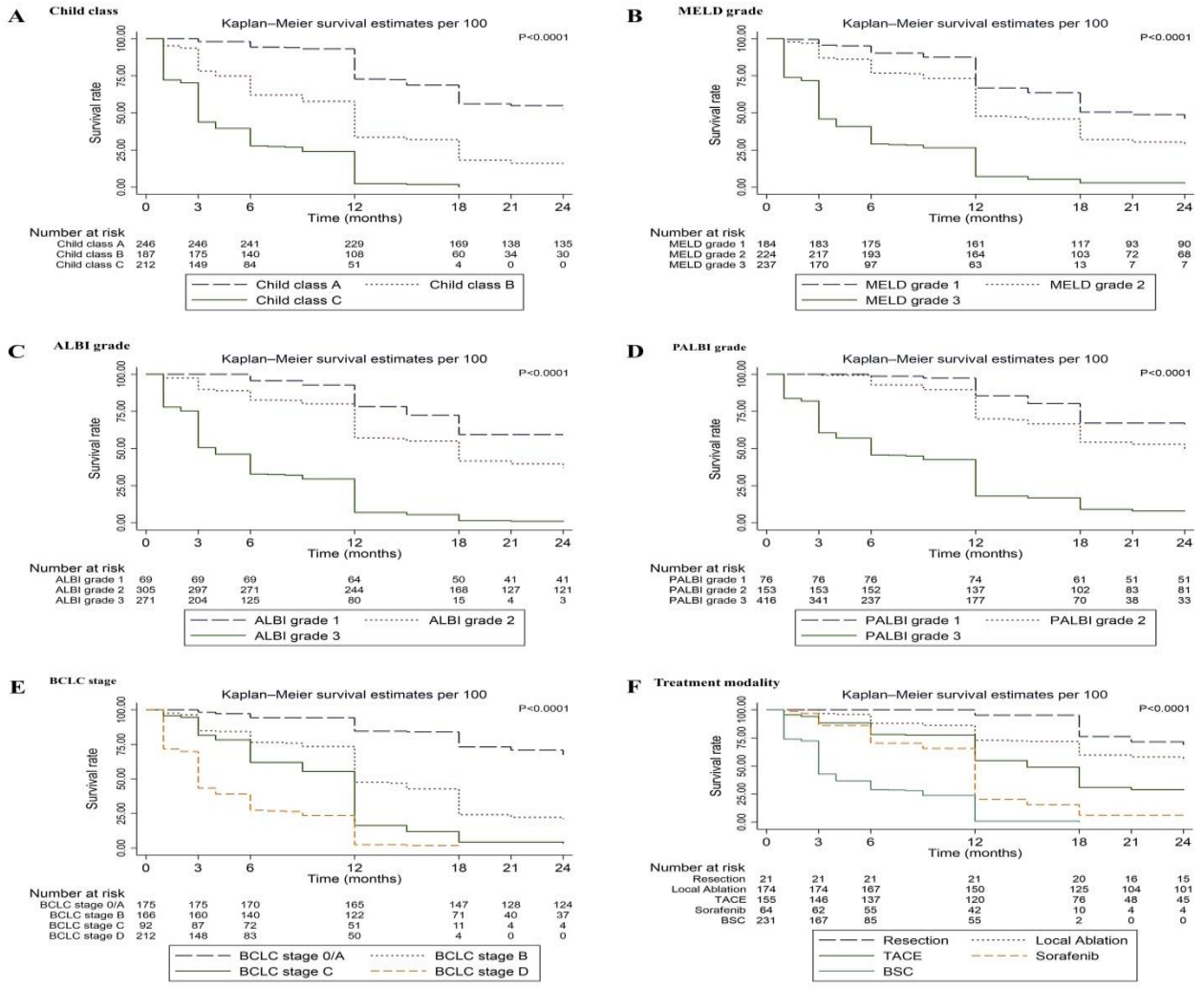
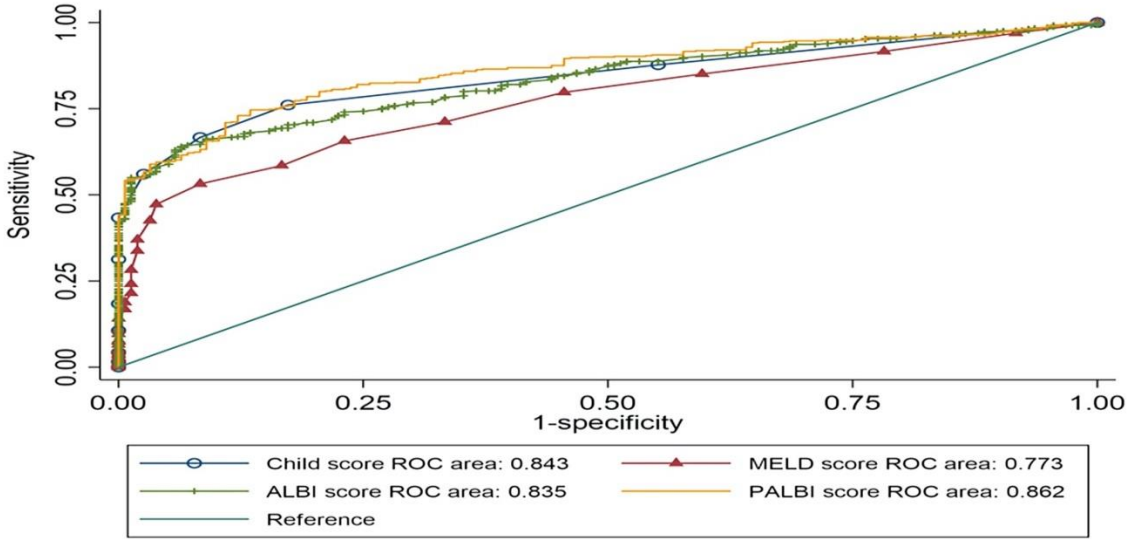


Figure 2 : Overall survival of study cohort stratified by (A) Child class, (B) MELD grade, (C) ALBI grade, (D) PALBI grade, (E) BCLC stage, and (F) treatment modality.
MELD: Model for End-Stage Liver Disease; ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; BCLC: Barcelona Clinic Liver Cancer; TACE: transarterial chemoembolization; BSC: best supportive care.

Efficacy of liver function scores to predict mortality

We conducted a ROC curve study, and the results revealed that the PALBI score had the highest area under the curve (AUC), followed by the CTP, ALBI, and MELD scores (AUC = 0.862, 0.843, 0.835, and 0.773, respectively). At a cutoff level > 6, the CTP score had 76.1% sensitivity and 82.7% specificity for predicting mortality among cirrhotic patients with HCC. MELD score at a cutoff level > 13 had a sensitivity of 53.2% and specificity of 91.7% for predicting mortality. The optimal cutoff level of the ALBI score for predicting mortality was > -1.6 with a sensitivity of 64% and specificity of 93.6%. Finally, the reported sensitivity and specificity of the PALBI score at a cutoff level > -1.99 were 74.6% and 86.5%, respectively (Figure 3).



Variable	Cut-off	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	*P*-value
Child score	> 6	0.843 (0.813:0.87)	76.1%	82.7%	93.2%	52.4%	< **0.0001**
MELD score	> 13	0.773 (0.738:0.804)	53.2%	91.7%	95.2%	38.4%	< **0.0001**
ALBI score	> -1.6	0.835 (0.804:0.863)	64%	93.6%	96.9%	45.3%	< **0.0001**
PALBI score	> -1.99	0.862 (0.833:0.888)	74.6%	86.5%	94.5%	51.7%	< **0.0001**

Figure 3 ROC curve analysis for the ability of the liver function scores to predict mortality.
ROC: receiver operating characteristics; MELD: Model for End-Stage Liver Disease; ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; AUC: area under curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value.

CTP class redistribution by ALBI and PALBI grades

We stratified the CTP class based on the ALBI and PALBI grades (Figures 4A and B). Of 246 (38.14%) CTP class A patients, 67 (27.24%), and 179 (72.76%) were reclassified as ALBI grade 1, and 2, respectively; furthermore, 72 (29.27%), 119 (48.37%), and 55 (22.36%) were reclassified as PALBI grade 1, 2, and 3, respectively. Of 187 (28.99%) CTP class B patients, 2 (1.07%), 113 (60.43%), and 72 (38.5%) were reclassified as ALBI grade 1, 2, and 3, respectively; furthermore, 4 (2.14%), 32 (17.11%), and 151 (80.75%) were reclassified as PALBI grade 1, 2, and 3, respectively. Finally, of 212 (32.87%) CTP class C patients, 199 (93.87%) were reclassified as ALBI grade 3, and 210 (99.06%) as PALBI grade 3.

We noticed that the ALBI grade predicts survival in patients with CTP class B and C (P = 0.0007, 0.007, respectively), where ALBI grade 3 patients had poorer outcomes (Figures 4E and G). However, the ALBI grade was not predictive of OS for CTP class A patients (Figure 4C). Additionally, the PALBI grade predicts survival among all CTP classes (P = 0.0001, 0.0003, 0.08, for CTP class A, B, and C, respectively), where PALBI grade 3 patients had poorer outcomes (Figures 4D, F, and H).

Efficacy of ALBI and PALBI grades to identify survival among BCLC stages

We were able to categorize BCLC stages 0/A, B, and C into three different prognostic groups using the ALBI and PALBI grades. In the case of BCLC stages 0/A and B, both ALBI and PALBI grades substantially predict OS between all adjacent grades (Figures 5A-D). Except for grade 1 vs. 2 (P = 0.08 and 0.42, respectively), the ALBI and PALBI grades significantly predict OS in BCLC stage C

(Figures 5E and F). Finally, BCLC stage D can be divided into two prognostic groups (P = 0.03, 0.02, for ALBI and PALBI grades, respectively, Figures 5G and H).

Efficacy of ALBI and PALBI grades to identify survival among treatment modalities

We found that both ALBI and PALBI grades significantly predict OS among various treatment modalities offered to the study cohort except for patients undergoing SR (P = 0.19, and 0.39, for ALBI and PALBI grades, respectively, Figures 6A and B). In patients treated with RFA, the ALBI and PALBI grades substantially predict OS except for ALBI grade 1 vs. 2 (P = 0.06, Figures 6C and D). The ALBI and PALBI grades substantially predict OS in patients receiving TACE (P < 0.0001) and in all adjacent grades (Figures 6E and F). Except for PALBI grade 2 vs. 3 (P = 0.74), the ALBI and PALBI grades substantially predict OS in patients on sorafenib (Figures 6G and H). Finally, in patients on BSC, the ALBI and PALBI grades substantially predict OS except for PALBI grade 1 vs. 2 (P = 0.19, Figures 6I and J).

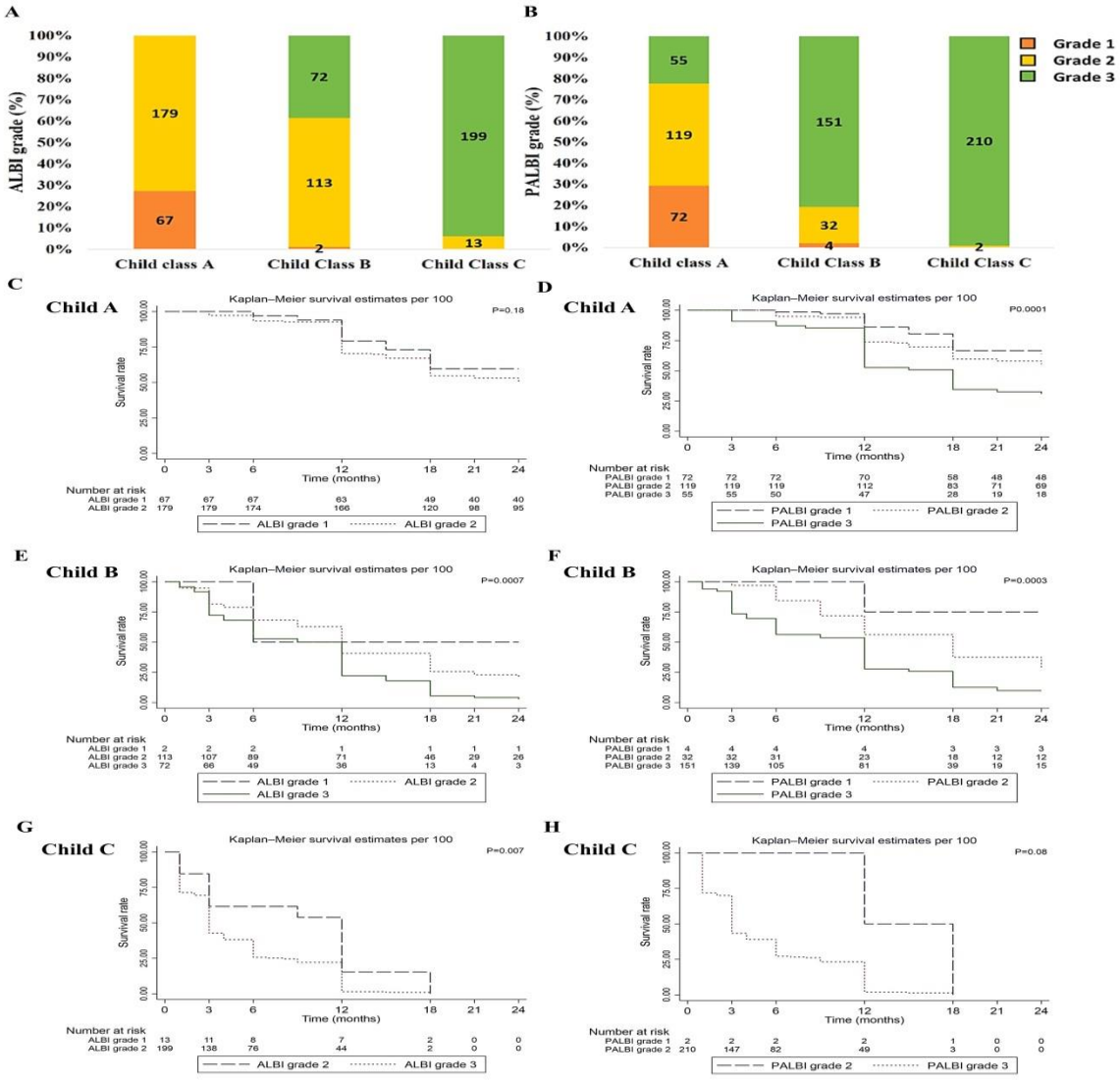


Figure 4: Stratification of Child classes by (A) ALBI and (B) PALBI grades, and the ability of ALBI (C, E, G) and PALBI (D, F, H) grades to differentiate survival among patients in different Child classes.

ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin.

Risk factors associated with OS among HCC patients

On univariate Cox regression analysis (Supplementary Table 1) increased tumor size, the presence of multiple tumors > 3, PVT/extrahepatic spread, CTP class, MELD, ALBI, and PALBI grades, BCLC stages B, C, and D, and patients receiving palliative and supportive treatment were substantially associated with OS. Multivariate Cox regression analysis (Table 3) confirmed that multiple tumors > 3 (HR (95% CI) = 1.263 (1.012-1.576), P = 0.039), MELD grade 3 (HR (95% CI) = 1.463 (1.052-2.034), P = 0.024), PALBI grade 3 (HR (95% CI) = 2.381 (1.345-4.216), P = 0.003), BCLC stage B (HR (95% CI) = 2.953 (1.982-4.399), P < 0.0001), BCLC stage C (HR (95% CI) = 3.831 (2.341-6.27), P < 0.0001), BCLC stage D (HR (95% CI) = 13.196 (1.557-111.827), P = 0.018) and patients received supportive treatment (HR (95% CI) = 2.043 (1.44:2-899), P < 0.0001), were independent predictors for OS in cirrhotic patients with HCC.

Table 3: Multivariate Cox regression analysis to identify risk factors associated with overall survival.

Variable	Hazard ratio (95% CI)	P-value
Smoking	0.971 (0.794:1.188)	0.777
HFL size (cm)	1.023 (0.994:1.054)	0.123
Number of HFL		
Single	Ref.	
Two	0.911 (0.675:1.23)	0.544
Three	0.96 (0.587:1.568)	0.87
More than three	1.263 (1.012:1.576)	**0.039**
PVT/Extrahepatic spread	1.168 (0.888:1.538)	0.267
Child class		
A	Ref.	
B	1.378 (0.99:1.917)	0.057
C	0.319 (0.038:2.718)	0.296
MELD grade		
Grade 1	Ref.	
Grade 2	0.959 (0.72:1.276)	0.772
Grade 3	1.463 (1.052:2.034)	**0.024**
ALBI grade		
Grade 1	Ref.	
Grade 2	1.158 (0.676:1.985)	0.592
Grade 3	1.65 (0.891:3.056)	0.111
PALBI grade		
Grade 1	Ref.	
Grade 2	1.676 (0.971:2.892)	0.064
Grade 3	2.381 (1.345:4.216)	**0.003**
BCLC stage		
0/ A	Ref.	
B	2.953 (1.982:4.399)	**<0.0001**
C	3.831 (2.341:6.27)	**<0.0001**
D	13.196 (1.557:111.827)	**0.018**
HCC treatment		
Curative *	Ref.	
Palliative †	1.137 (0.813:1.589)	0.454
BSC	2.043 (1.44:2.899)	**<0.0001**

* Resection or ablation, † TACE or sorafenib.

CI: confidence interval; HFL: hepatic focal lesion; PVT: portal vein thrombosis; MELD: Model for End-Stage Liver Disease; ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; BCLC: Barcelona Clinic Liver Cancer; HCC: hepatocellular carcinoma; BSC: best supportive care.

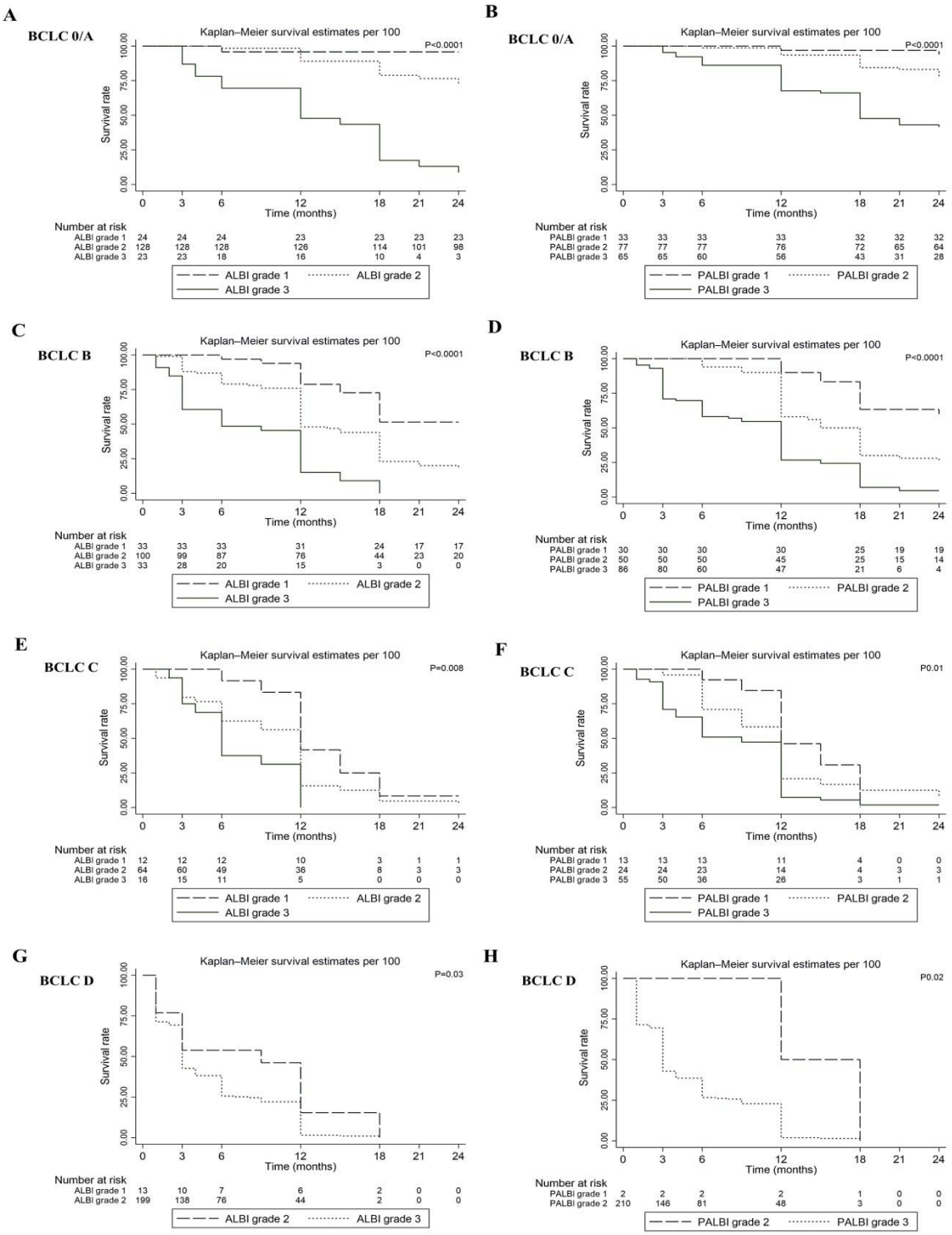


Figure 5: The ability of ALBI (A, C, E, G) and PALBI (B, D, F, H) grades to differentiate survival among patients in different BCLC stages.

ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; BCLC: Barcelona Clinic Liver Cancer

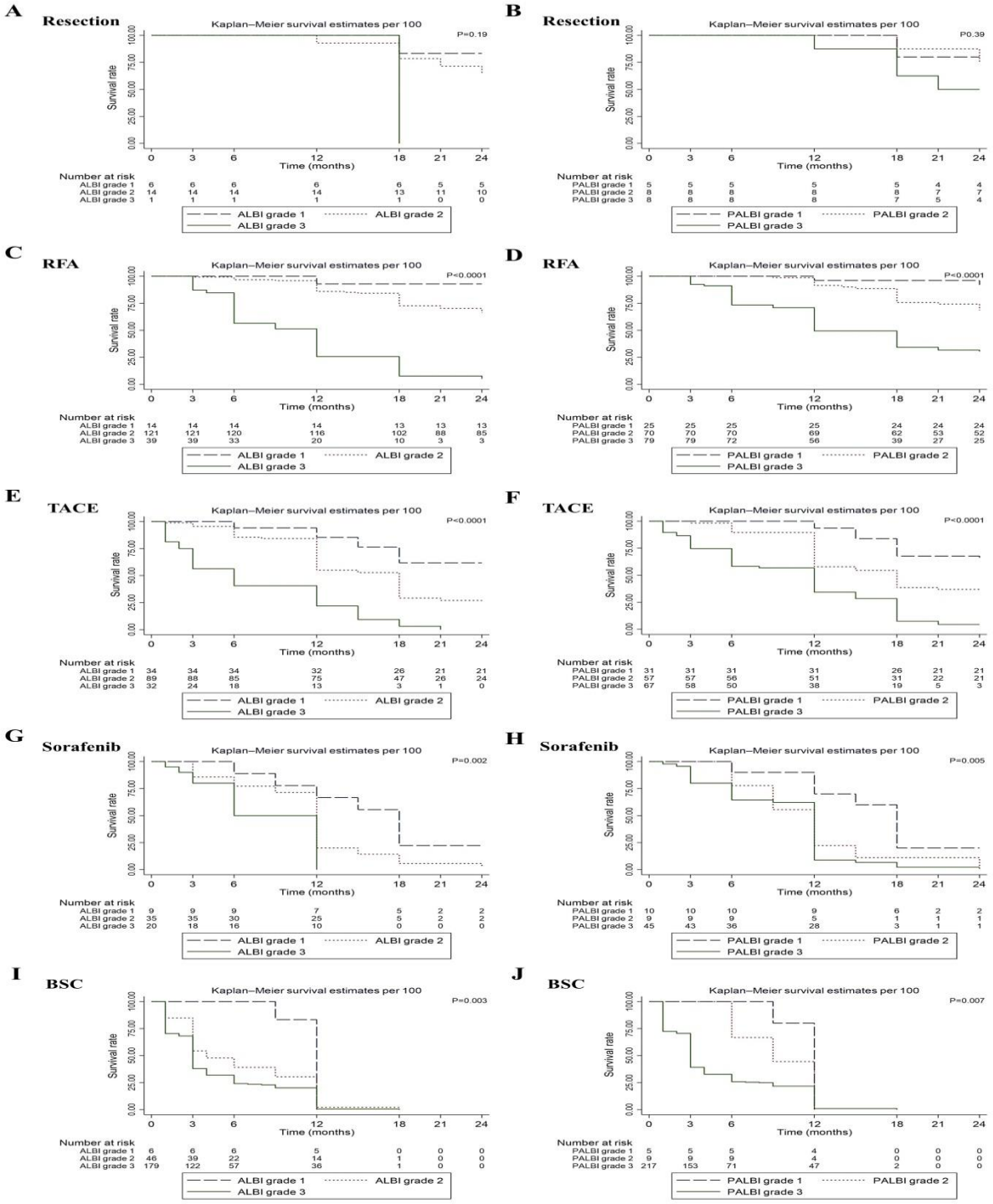


Figure 6: The ability of ALBI (A, C, E, G, I) and PALBI (B, D, F, H, J) grades to differentiate survival among patients according to different treatment modalities.

ALBI: albumin-bilirubin; PALBI: platelet-albumin-bilirubin; RFA: radiofrequency ablation; TACE: transarterial chemoembolization; BSC: best supportive care

Discussion

The prognosis of HCC is complex and depends on multiple factors, including tumor burden, patient performance status, and hepatic reserve function.

For many decades the CTP classification system was used as a general tool to evaluate hepatic reserve function and prognosis in cirrhotic patients since its introduction by Child and Turcotte in 1964, and its refinement by Pugh et al. in 1973 .[3] The CTP class is incorporated into the BCLC staging system to assess hepatic reserve function and to guide treatment selection. However, as previously mentioned, the CTP classification system has several limitations. Therefore, ALBI-based grades were developed to offer a simple, objective tool to assess hepatic reserve function .[5] In this prospective study, we demonstrated that, except for patients who underwent SR, the ALBI and PALBI grades were significantly associated with OS in HCC patients, throughout various BCLC stages and treatment modalities. Furthermore, in cirrhotic patients with HCC, the PALBI grade is an independent risk factor for mortality and is superior to the ALBI grade in predicting OS.

In the current study, we evaluated the performance of different liver function scoring systems in predicting OS among HCC patients. The PALBI score outperformed the ALBI and CTP scores (AUC 0.862 vs. 0.835 and 0.843, respectively) in predicting OS. Our results are consistent with previous reports .[10, 13] which demonstrated the superiority of PALBI grade which incorporates platelets as an indicator of portal hypertension, and this highlights the importance of portal hypertension in the prognosis of HCC .[16] The MELD score, which is used mainly to prioritize patients on the liver transplant waiting list, yields the least prognostic performance (AUC 0.773), which agrees with previous studies. [10, 13]

One of the main disadvantages of CTP class is reduced sensitivity in patients with mild hepatic impairment (CTP A patients). There is strong evidence that the number of HCC patients with CTP A class has substantially increased in the last years, and this could be a consequence of efficient antiviral treatments, lifestyle improvements (controlling alcohol and obesity), and possibly better HCC outcomes. [5, 17] HCC CTP class A patients have different clinical settings, including an absence of chronic liver disease, chronic hepatitis (both account for 10%-20% of cases), and well-compensated cirrhosis. [5, 13] This diverse presentation of CTP A patients is reflected on the prognosis; therefore, we stratified the CTP class based on the ALBI and PALBI grades. In agreement with previous reports. [7, 10, 13, 18] the ALBI and PALBI grades enabled the categorization of CTP class into 2 and 3 distinct prognostic groups, respectively. However, ALBI grade failed to predict OS in CTP A patients, and this could be explained by the fact that contrary to previous studies which included both cirrhotic and non-cirrhotic CTP A patients, we included only patients with cirrhosis.

We offered treatment to our patients following BCLC recommendations whenever possible, so we assessed the efficacy of ALBI and PALBI grades to predict OS based on BCLC stage and treatment modality. Both grades accurately predict OS across various BCLC stages except for BCLC stage C patients where ALBI and PALBI grades 1 and 2 overlapped. Several studies agree with our results and demonstrate the prognostic power of the ALBI and PALBI grades. [10, 13, 19, 20] in each of the BCLC stages. Furthermore, we evaluated the prognostic performance of both grades according to the curative (SR and RFA), palliative (TACE and sorafenib), and BSC treatment modalities. Consistent with previous studies, we found that both ALBI and PALBI grades were predictive of OS among patients who underwent RFA, TACE, those on Sorafenib, and BSC. [10, 13, 20-24] Contrary to previous reports. [10, 13, 19] the ALBI and PALBI grades failed to predict OS among patients undergoing SR, this could be attributed to the small number of these patients in the current study (n = 21).

Several studies investigated risk factors linked to mortality in HCC patients with variable observations. Generally, mortality was associated with hepatic functional reserve and tumor burden. In the current study, multivariate Cox regression

revealed that grade 3 MELD and PALBI were associated with a 1.463- and 2.381-fold increased hazard ratio (HR) of HCC mortality, respectively. Previous investigations had shown that PALBI. [13, 18, 25, 26] and MELD. [25, 27, 28] grades may accurately predict OS among HCC patients in different clinical settings and treatment modalities. Furthermore, in accordance with previous studies . [7, 18, 19, 25, 26, 28-30], we demonstrated that the existence of multiple tumors> 3, and the tumor stage defined by the BCLC staging system were independent predictors of mortality in cirrhotic patients with HCC. Finally, patients who received supportive treatment had a higher HR of mortality, which is reasonable given that they did not receive HCC-targeted therapy and had an advanced BCLC stage . [29, 30]

The association of PALBI, not ALBI, with the mortality risk in HCC patients highlights the significance of platelets in the prognosis of HCC. Multiple mechanisms might explain the ability of platelets to anticipate mortality risk in HCC patients. First, platelets are known to promote angiogenesis, HCC growth, vascular invasion, and metastasis through the production of several stimulants, including platelet-derived growth factor, serotonin, and vascular endothelial growth factor. [31] Second, mortality may be affected by the presence of portal hypertension for which platelet count serves as a marker of severity. [26]

There were a few limitations in the current study. First, it was a single-center study, conducted on a relatively small number of patients over a short follow-up period. Second, all patients were cirrhotic and most of them had chronic HCV infection, so future prospective studies conducted on large numbers of non-cirrhotic patients with various etiologies of liver disease are required to generalize our results. Third, the small number of patients treated by SR limited the efficacy of the ALBI and PALBI grades to evaluate this group of patients. Fourth, some patients did not receive treatment precisely according to BCLC recommendations . [10, 13], and treatment is offered according to the decision made by the multidisciplinary hepatoma team, which considers a variety of factors besides the stage of the tumour, such as the availability of the treatment modality as well as the financial aspects

Conclusions

In conclusion, except for patients who underwent SR, the ALBI and PALBI grades were significantly associated with OS in HCC patients, throughout various BCLC stages and treatment modalities. Furthermore, in cirrhotic individuals with HCC, the PALBI grade is an independent risk factor for mortality and a stronger predictor of OS than the ALBI grade.

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