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Original Article

Comparative Validity of the ALBI Grade and CTP Score in Predicting Overall Survival in Patients Receiving TACE Plus Sorafenib Therapy for Hepatocellular Carcinoma

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) significantly impacts global health, with liver function being a critical factor in patient prognosis. The ALBI grade and Child-Turcotte Pugh (CTP) score are both used to evaluate liver function in HCC patients, but their effectiveness in predicting survival outcomes varies.

Objective: This study aimed to evaluate and compare the effectiveness of the ALBI grade and CTP score in predicting overall survival (OS) in HCC patients undergoing combined therapy with sorafenib and transarterial chemoembolization (TACE).

Methods: Conducted at Jinnah Hospital Lahore and Hijaz Hospital between January 2019 and June 2023, this study included 103 HCC patients with CTP scores of 5 and 6. We analyzed the predictive values of the ALBI grade and CTP score for OS using multivariate analyses and time-dependent ROC curves.

Results: Multivariate analysis indicated significant differences in OS among patients categorized by both scoring systems, with hazard ratios of 2.16 (P<0.001) for the CTP score and 1.49 (P=0.035) for the ALBI grade. Time-dependent ROC analysis showed that the ALBI grade was more effective in discriminating long-term survival. It also remained a significant predictor of OS in a larger number of patient subgroups compared to the CTP score.

Conclusion: The ALBI grade demonstrates superior prognostic stratification compared to the CTP score in HCC patients treated with TACE and sorafenib who have stable liver function.

Keywords: ALBI; CTP score; Hepatocellular carcinoma (HCC); Overall survival; Sorafenib.

INTRODUCTION

Hepatocellular carcinoma (HCC) stands as a significant contributor to cancer-related mortality worldwide. The prognosis of HCC is influenced by several factors, including the extent of underlying liver disease, tumor burden, associated health complications, and the functional status of the patient (1, 2). Traditionally, the Child-Turcotte Pugh (CTP) score has been a staple in assessing liver function in patients with HCC and is widely incorporated into various staging systems (3). More recently, the Albumin-Bilirubin (ALBI) grade has emerged as a reliable alternative, focusing solely on albumin and bilirubin levels to evaluate liver function. This model has gained global recognition for its effectiveness in predicting survival outcomes in HCC, showcasing superior discriminatory capabilities (7, 8).

Transarterial chemoembolization (TACE) is endorsed by recent international guidelines as the standard treatment for intermediate-stage HCC. However, in more advanced stages, systemic therapies become pivotal. Sorafenib, as the first approved systemic treatment for inoperable HCC, is often used in combination with TACE. This combined approach has been substantiated by several prospective trials, affirming its efficacy and safety for advanced HCC cases (9, 10-14).

The primary objective of this study was to compare the predictive accuracy of the ALBI and CTP scores regarding overall survival in patients receiving TACE combined with sorafenib therapy. By analyzing outcomes in this specific patient group, the research aimed to clarify which scoring system provides a more accurate prognostic tool in the context of advanced liver cancer treatment.

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METHODS

This study enrolled 103 patients diagnosed with intermediate-stage hepatocellular carcinoma (HCC) at the Jinnah Hospital Hepatitis Clinic and Hijaz Hospital. All participants, classified as Child-Pugh A, were either receiving or scheduled to receive combination therapy of transarterial chemoembolization (TACE) and sorafenib between January 2019 and June 2023. The diagnosis of HCC conformed to the criteria set by the European Association for the Study of the Liver Disease (EASL) (9, 15). Exclusion criteria included patients with an Eastern Cooperative Oncology Group (ECOG) performance status greater than 1, as well as those exhibiting signs of decompensated cirrhosis such as jaundice, ascites, and encephalopathy. Informed consent was obtained from all individuals, adhering to the ethical guidelines of the Declaration of Helsinki, and the study received approval from the Institutional Review Board. Patients were referred to Sheikh Zaid Hospital, Lahore, and the Pakistan Kidney and Liver Institute (PKLI) for TACE therapy. Sorafenib was administered at a dose of 400 mg twice daily for thirty days before or after the initial TACE session. Routine follow-ups included laboratory evaluations every four to six weeks, and imaging studies, such as CT scans or MRIs, conducted six weeks post-therapy and subsequently every eight weeks. Additional TACE procedures were performed in cases of newly detected HCC lesions or remaining viable tumors, provided liver function remained within normal limits. Continuation of sorafenib was strongly recommended unless severe or life-threatening side effects occurred, with dosage adjustments made based on toxicity levels.

Statistical analysis involved calculating frequencies and percentages for qualitative data, while means and standard deviations described quantitative variables. Overall survival (OS) was defined as the time from the first TACE session to either the date of death or last follow-up. Survival rates were analyzed using the Kaplan-Meier method, log-rank tests, and Cox proportional hazards regression models. Three multivariate models were constructed in a stepwise manner to identify independent prognostic factors: the first included baseline characteristics, the second combined baseline characteristics with CTP scores excluding bilirubin and albumin, and the third incorporated the ALBI grade alongside baseline features, excluding albumin and bilirubin. The discriminatory power of the ALBI grade and CTP score for predicting OS was compared using time-dependent Receiver Operating Characteristic (ROC) curves. SPSS version 25.0 facilitated all statistical analyses, enabling further investigation into survival based on diverse baseline patient profiles.

RESULTS

In this study, the mean age of the 103 patients was 47.9 ± 10.7 years. The cohort predominantly consisted of males (87, 84.4%), with 44 (42.7%) patients suffering from HBV infection. Staging according to the BCLC system classified 9 (8.7%) patients in stage A, 42 (40.7%) in stage B, and 52 (50.4%) in stage C. A significant majority, 83 (80.58%), had not received any prior therapy for HCC, and most did not present with symptoms related to their tumors. The average tumor size was recorded at 6.6 ± 3.1 cm, and a unifocal presentation was observed in 62 (53.2%) patients. Notably, 69% of the patients exhibited no portal vein tumor thrombosis (PVTT).

The cohort was followed for a median duration of 48 months, during which the median overall survival (OS) was determined to be 16.4 months, with a 95% confidence interval ranging from 12.0 to 17.9 months. Among these patients, 73 (70.8%) had a CTP score of 5, and 30 (29.1%) had a CTP score of 6. Survival analysis indicated that patients with a CTP score of 5 experienced a longer OS compared to those with a score of 6 (17.6 vs. 11.5 months). Similarly, ALBI grading divided the patients into two groups: 51 (49.5%) at grade 1 and 52 (50.5%) at grade 2. Patients with an ALBI grade of 1 exhibited a significantly higher median OS of 22.0 months compared to 13.6 months for those classified under grade 2.

Univariate analysis identified several significant prognostic factors for OS, including ALBI grade, CTP score, tumor size, PVTT presence, AST levels, AFP levels, bilirubin, albumin, and ECOG score ($P<0.05$). Multivariate analysis further delineated independent predictors of OS. Category 1 analysis highlighted ECOG status, tumor size, PVTT presence, albumin, and bilirubin as significant factors. Category 2 analysis confirmed ECOG status, tumor size, PVTT presence, and CTP score as independent predictors. For Category 3, significant predictors included tumor size, PVTT presence, ALBI grade, and ECOG status.

ROC analysis underscored that the ALBI grade, particularly over extended periods, was a more robust discriminator of survival outcomes compared to the CTP score. Subgroup analyses based on different baseline characteristics revealed that the predictive capacity of the ALBI grade remained significant in most groups. However, its predictive utility was diminished among female patients, those without HBV, or those presenting with PVTT, where it failed to achieve statistical significance ($P>0.05$).

Table 1: Demographic details and clinical features of the patients (N=103)

Characteristics	Number (%) or Mean ± SD
Age (in years)	47.9±10.7
Gender (Female/Male)	16/87(15.6 /84.4)
Etiology (HBV/non-HBV)	44/59 (42.7/57.3)
Barcelona Classification of Liver Cancer stage (A/B/C)	9/42/52((8.7/40.8/50.5)
ECOG score (0/1)	58 /45 (56.4/43.6)
Prior treatments (yes/no)	20/83(19.42/80.58)
Tumor numbers (unifocal/multifocal)	62 /41 (53.2/46.8)
Portal vein tumor Thrombosis (PVTT) (absent/present)	72/31 (69.9/30.1)
Tumor size (cm)	6.6±3.1

Characteristics	Number (%) or Mean ± SD
Serum AFP level (≤400/>400 ng/mL)	53/50 (51.4/48.5)
Platelets (×109/L)	126.5±87.2
AST (U/L)	55.9±40.3
ALT (U/L)	45.6±37.6
Bilirubin (mg/L)	1.1±0.82
INR	1.13±0.12
Albumin (mg/dl)	3.92±0.54
Urea nitrogen (mmol/L)	4.8±1.4
Creatinine (mg/dl)	0.87±0.55
CTP score (5/6)	73 /30 (70.8/29.2)
ALBI grade (1/2)	51/52 (49.5/50.5)

Table 2 Baseline features for overall survival by Univariate analysis

Variable	HR (95% CI)	P value
Age, increase per year	0.99 (0.97–1.01)	0.29
Gender male ECOG score 0/1 Earlier treatments	0.91 (0.59–1.47) 2.64(1.87-3.71) 0.99 (0.55–1.76)	0.73 <0.001 0.99
Etiology	0.82 (0.51–1.25)	0.34
Size of Tumor , per 1 cm increase	1.08 (1.05–1.17)	<0.001
Multifocal tumors	1.23 (0.91–1.73)	0.20
Portal Vein Tumor Thrombosis AFP (Ref: ≤400 ng/mL)	3.25 (2.23–4.77) 1.85 (1.32–2.54)	<0.001 <0.001
INR, per 1% increase	0.98 (0.97–1.02)	0.98
ALT, per 1 U/L increase	0.99 (0.98–1.02)	0.96
AST, per 1 U/L increase Bilirubin, per 1 µmol/L increase	(1.01–1.11) 1.08(1.02-1.06)	<0.001 <0.001
Albumin, per 1 g/L increase	0.96(0.91–0.98)	<0.001
CTP score 6	1.72 (1.28–2.45)	0.003
ALBI grade 2	2.42 (1.60–3.64)	<0.001

Table 3: Adjustment of the predictive value of CTP score and ALBI grade by using Multivariate analysis

Variable	Category 1		Category 2		Category 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Size of Tumour,(per 1 cm increase)	1.09 (1.04–1.14)	0.006	1.06 (1.01–1.12)	0.005	1.06 (1.01–1.13)	0.004
ECOG ≥1	1.66 (1.13–2.42)	0.008	1.91 (1.33–2.75)	0.002	1.89 (1.31–2.70)	0.002
PVT	2.01 (1.41–3.11)	<0.001	2.22 (1.49–3.28)	<0.002	2.05 (1.39–3.04)	<0.002
Albumin, per 1 g/L increase	0.96 (0.91–0.98)	0.006	-	-		
T Bilirubin, per 1µmol/L increase	1.06 (1.01–1.08)	<0.002	_	_	_	
CTP score 6	–	–	1.49 (1.02–2.16)	0.03	–	–

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Variable	Category 1		Category 2		Category 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
ALBI grade 2	–	–	–	–	2.14 (1.40-3.28)	<0.002

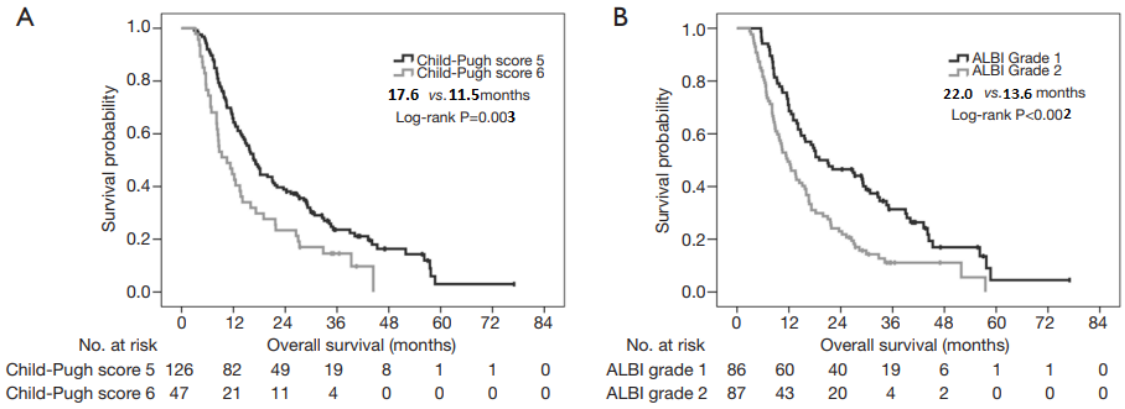

Figure 1: Over all Survival (OS) as determined by Kaplan -Meier curves. A) Comparative survival in patients having CTP 5 and CTP 6 scores. B) Comparative survival in patients having ALBI 1 and ALBI 2 grades

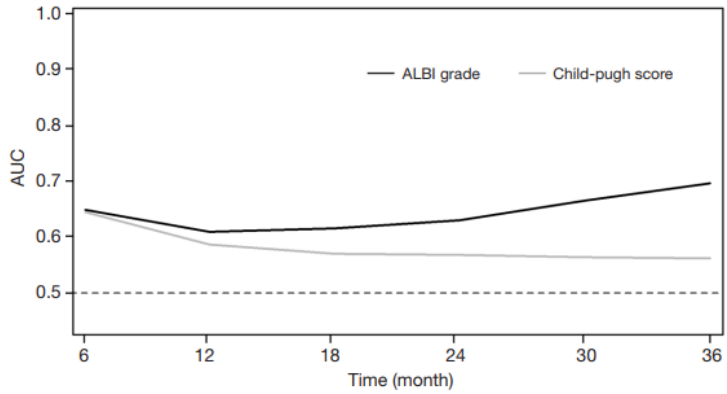

Figure 2: Reciever Operating curve (ROC) for CTP score and ALBI grade for predicting Overall Survival (OS)

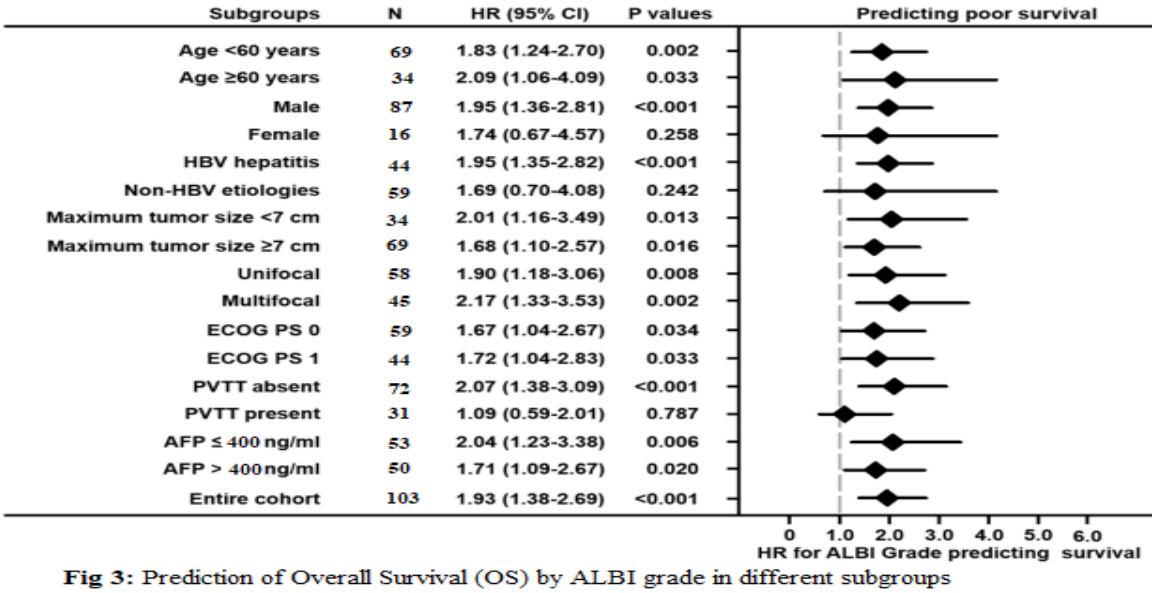

Fig 3: Prediction of Overall Survival (OS) by ALBI grade in different subgroups

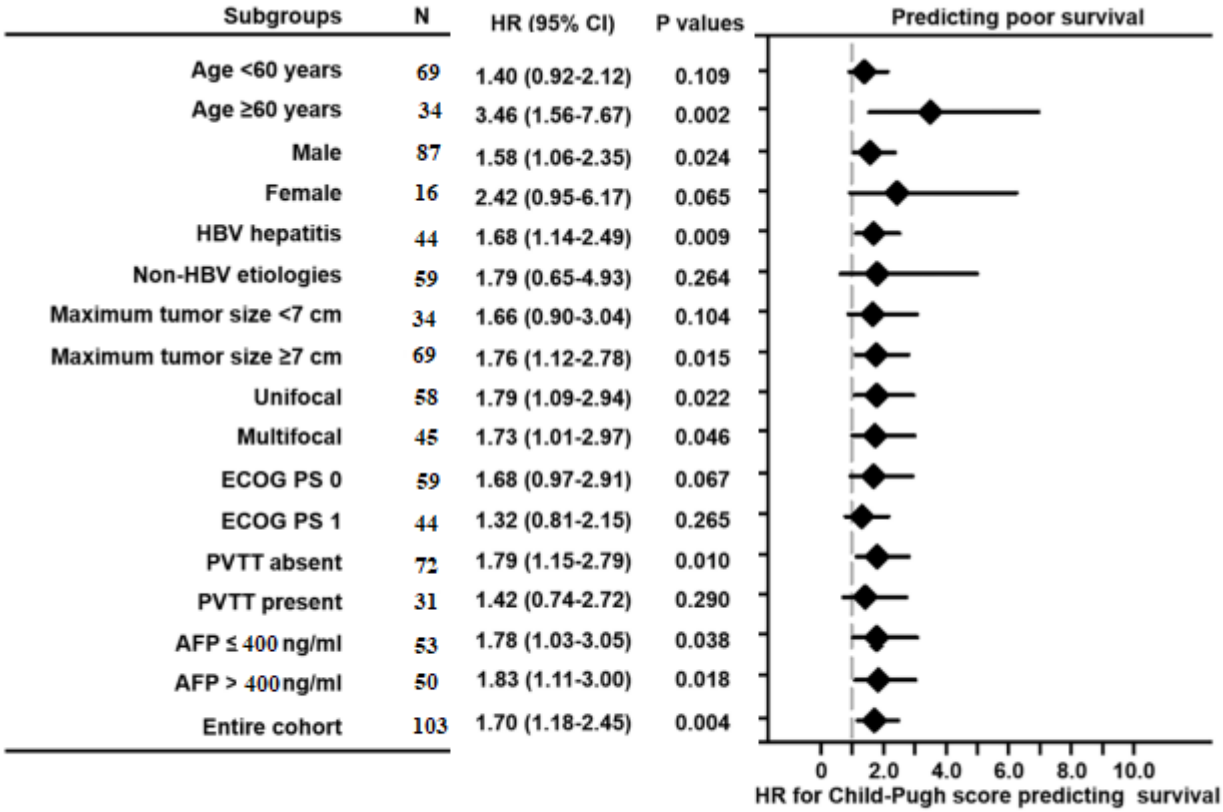

Fig 4: Prediction of Overall Survival (OS) by CTP score in different subgroups

DISCUSSION

Tumor size, liver functional reserves, and performance status significantly influence survival rates in patients diagnosed with hepatocellular carcinoma (HCC). The Child-Pugh (CTP) score, despite its widespread use, introduces subjectivity and has notable limitations (6). In contrast, the Albumin-Bilirubin (ALBI) grade, developed by Johnson et al., provides an objective and straightforward method to classify patients with distinctly different prognoses and has shown potential to outperform the CTP classification (7, 16-18). This grade has been validated across various therapeutic settings including curative treatments, locoregional therapies, and systemic treatments such as sorafenib. However, its efficacy in distinguishing overall survival (OS) among patients receiving TACE combined with sorafenib had not been explored until this study (20-22).

The findings from this research demonstrate that the ALBI grade offers a clearer and more significant differentiation of prognosis in patients with preserved hepatic functions (CTP class A) compared to the CTP score. These observations are consistent with previous studies recommending the ALBI grade for stratifying patients within the Child-Pugh A category (19, 23). Moreover, ROC analyses confirmed that the ALBI grade surpasses the CTP score in long-term prediction of OS. Given the variability in patient characteristics within intermediate stage HCC, the ALBI grade may be more suitable for stratification in these patients, many of whom retain intact liver function. This assertion is supported by Hiraoka et al., who developed an ALBI grade-based subgrouping for intermediate HCC that proved superior to Bolondi et al.'s liver function substage classification (26).

Nonetheless, this study is not without its limitations. The retrospective design and the fact that it was conducted at only two centers might introduce biases. Additionally, the predictive power of both the CTP score and the ALBI grade decreased in certain patient subgroups, possibly due to their small sizes. Despite these issues, the ALBI grade was found to be a more suitable prognostic tool than the CTP score in the majority of patient subgroups. It is also crucial to note that as all participants were from Punjab, the generalizability of these findings may be limited, and further research is necessary to validate these results in more diverse populations. This study underscores the importance of selecting an appropriate liver function classification system to improve prognostic accuracy in patients undergoing treatment for HCC.

CONCLUSION

This study indicates that the ALBI grade is potentially a superior prognostic tool compared to the CTP score for predicting outcomes in hepatocellular carcinoma (HCC) patients with stable hepatic function (CTP class A) who are treated with combination therapy involving sorafenib. The clearer stratification offered by the ALBI grade could significantly influence the clinical management and staging of HCC, leading to more tailored treatment approaches. These results advocate for the inclusion of the ALBI grade in future

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clinical trials and therapeutic strategies, potentially refining patient selection for specific treatments and enhancing overall survival outcomes. Further research is needed to confirm these findings across broader and more varied patient populations.

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