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The EZ-ALBI and PALBI scores contribute to the clinical application of ALBI in predicting postoperative recurrence of HCC

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This research intends to assess the variance between EZ-ALBI and PALBI in forecasting recurrence following the resection of hepatocellular carcinoma (HCC). A retrospective analysis was conducted using clinical data from 522 HCC patients across two medical institutions. The study analyzed albumin-bilirubin values (ALBI), along with the Easy albumin-bilirubin values (EZ-ALBI) and the Platelet-albumin-bilirubin values(PALBI), while assessing the clinical traits of patients across various grades. The analysis focused on the connections between ALBI, EZ-ALBI, and PALBI, as well as their variations in predicting the recurrence of HCC following surgical procedures. Notably, the clinical characteristics of patients exhibiting varying levels of PALBI differed from those categorized under ALBI and EZ-ALBI; however, the ALBI grade shared similar characteristics with the EZ-ALBI category. A strong correlation was found between ALBI and EZ-ALBI, with a coefficient of 0.862 (95% CI: 0.838–0.882, $p < 0.01$), whereas ALBI and PALBI yielded a coefficient of 0.760 (95% CI: 0.838–0.882, $p < 0.01$). The correlation coefficient between PALBI and EZ-ALBI was recorded at 0.571 (95% CI: 0.510–0.626, $p < 0.01$). There was a notable difference in survival outcomes among HCC patients classified with ALBI/EZ-ALBI/PALBI grade 1 compared to those with grade 2 or 3. Additionally, Cox regression analysis identified that maximum tumor diameter (MTD), microvascular invasion (MVI), pathological grade, as well as ALBI/EZ-ALBI/PALBI grades, among other factors, were tied to a decline in progression-free survival (PFS). The area under the curve (AUC) for the ALBI model at the 1, 2, and 3-year postoperative mark was 0.705, 0.652, and 0.694, respectively. In parallel, the AUC of the EZ-ALBI model during the same time intervals was 0.708, 0.659, and 0.694, respectively. For PALBI, the AUC values recorded at 1, 2, and 3 years following surgery were 0.748, 0.707, and 0.725, respectively. ALBI, EZ-ALBI, and PALBI served as predictive indicators for the recurrence of HCC in patients after surgery. Compared to ALBI, EZ-ALBI offers greater convenience in forecasting the prognosis of HCC patients, whereas PALBI demonstrates more accuracy than ALBI in predicting their prognosis.

Keywords ALBI, EZ-ALBI, PALBI, Hepatocellular carcinoma, Postoperative recurrence

Hepatocellular carcinoma (HCC) ranks as the sixth most prevalent malignant tumor and stands as the third primary cause of cancer-related deaths[1]. Surgical resection is considered the fundamental treatment for HCC. For those with HCC who qualify for surgical intervention, liver resection offers a chance for a potentially curative outcome. Nevertheless, the immediate and long-term effectiveness of liver resection in treating HCC still requires enhancement[2]. A significant number of patients with HCC who received surgical resection experience recurrence, with rates soaring as high as 50 to 70% within five years post-surgery[3]. Consequently, the prompt identification of risk factors linked to postoperative recurrence is vital to enhancing the long-term oncological prognosis for HCC patients who underwent hepatectomy.

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Individualized therapy for each patient is facilitated by a proper stratification of recurrence risk, which also enhances surveillance and promotes the use of adjuvant treatment for those at high risk. In recent years, researchers have devoted considerable effort to identifying effective monitoring strategies[4]. While several factors contribute to the decision-making for the ideal treatment plan, evaluating the initial recurrence risk plays a crucial role in determining the kind and timing of therapy. Research indicates that a range of preoperative elements can forecast the likelihood of recurrence following hepatectomy[5]. Beyond the tumor characteristics and treatment modalities, multiple patient-specific factors, including those related to existing liver conditions, have emerged as significant predictors of postoperative recurrence in patients with HCC. Numerous staging systems for liver cancer, such as the Barcelona Clinic Liver Cancer (BCLC) staging, integrate liver function metrics into the stratification of patients. Evidence suggests that the predictive accuracy of prognosis based on scoring systems like Child-Pugh or the Albumin to bilirubin ratio (ALBI) may be heightened in liver cancer patients[6–9]. Research indicates that the Child-Pugh score has not demonstrated significant predictive capability across various studies related to liver disease[10–11], furthermore, emerging alternative methods for assessing liver function may provide enhanced predictive effectiveness[12]. While the Child-Pugh classification is practical for clinical use, its predictive reliability is hindered by two subjective parameters. Conversely, ALBI serves as a completely objective measure for evaluating liver reserve function and has demonstrated significant predictive capability[13].

The ALBI score/grade was originally devised as a predictive framework for HCC, drawing from a cohort of 1313 Japanese patients[14]. Over several years of comprehensive study, multiple investigations have validated that ALBI, along with its liver function assessment criteria, has distinct independent impacts on factors related to HCC recurrence[15]. Nonetheless, certain research indicates that ALBI has yet to demonstrate optimal predictive effectiveness, and the intricate nature of its calculation poses challenges for its use in clinical settings. Consequently, various researchers have created improved systems that build on the ALBI framework. Notably, these variables, which are readily accessible, also prove to be more valuable than ALBI when different calculation approaches are employed[16]. This study's objective was to assess the efficacy of the Easy albumin-bilirubin index (EZ-ALBI) and the Platelet-albumin-bilirubin index (PALBI) in forecasting postoperative recurrence in HCC patients.

Materials and methods

Data collection and enrollment criteria

A retrospective analysis was conducted involving 522 patients with hepatocellular carcinoma (HCC) who were admitted to the First Affiliated Hospital of Zhengzhou University and the Second Affiliated Hospital of Henan University of Traditional Chinese Medicine from 2016 to 2019. At the time of diagnosis, baseline information was gathered, which included age, sex, body mass index (BMI), preoperative serum biochemistry results, tumor dimensions, presence of microvascular invasion, the BCLC tumor stage, and the Edmondson-Steiner grading. The criteria for inclusion were as follows: the China Liver Cancer (CNLC) staging system advocates for surgery as the primary treatment option; all patients underwent R0 curative hepatectomy; no recorded history of gastrointestinal bleeding; and all patients had reliable laboratory data available. Exclusion criteria included any of the following conditions occurring during follow-up: recurrence of HCC; ruptured HCC; preoperative antitumor therapies; esophagogastric variceal bleeding; discovery of other malignant tumors; and other life-threatening illnesses. Initially, 926 patients with hepatocellular carcinoma were identified. Based on the established inclusion and exclusion criteria, 31 cases were determined to be outside the indications for CNLC surgery. Additionally, 26 cases did not meet the criteria for radical resection, 156 cases had incomplete study data, 43 cases experienced recurrent HCC, and 11 cases involved ruptured liver cancer that required surgical intervention. Furthermore, 75 patients had a history of gastrointestinal bleeding either prior to or during follow-up, 49 patients underwent antitumor therapy before surgery, and 13 patients developed other life-threatening conditions during follow-up. Ultimately, 522 patients were included in the analysis.

The study received approval from the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (no. 2024-KY-0106-001) on February 15, 2024. Due to the retrospective nature of the study, the Ethics Committee of the First Affiliated Hospital of Zhengzhou University waived the need to obtain informed consent. All procedures involving human participants adhered to ethical standards set forth in the Helsinki Declaration (6th revision, 2008).

Diagnosis and follow-up

The case of the newly diagnosed HCC patient was presented to a multidisciplinary committee in alignment with current guidelines prior to surgery, and the diagnosis was confirmed through postoperative pathological examination. The assessment focused on the first recurrence following the surgical procedure. In this study group, recurrence was characterized by the appearance of a tumor on imaging after surgical resection, independent of the tumor's location. Based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST), the initial recurrence post-surgery was identified as the presence of viable tumors detected after a period of 3 months. If a residual tumor was noted during the early postoperative phase, it was deemed a failure of the radical surgical approach. Consequently, such cases were omitted from this comparative analysis. Patients underwent follow-up examinations every 3 to 6 months until they either passed away or opted out of continued follow-up. The maximum duration of follow-up recorded was 60 months.

Calculation of ALBI, EZ-ALBI, and PALBI scores.

The ALBI score can be calculated using the formula: (log10 bilirubin (umol/L) × 0.66) - (albumin (g/L) × 0.085). The thresholds for ALBI grades are set at ≤ − 2.60 for grade 1/2 and > − 1.39 for grade 2/3[6]. Conversely, the EZ-ALBI score is determined by subtracting (9 × albumin (g/dL)) from total bilirubin (mg/dL). For this score, the

cut-off values for EZ-ALBI grades 1/2 and 2/3 are ≤ − 34.4 and > − 22.2, respectively[17]. The PALBI is calculated as follows: 2.02 × log10 (bilirubin) − 0.37 × (log10 bilirubin)^2 − 0.04 × (albumin) − 3.48 × log10 (platelets) + 1.01 × (log10 platelets)^2. The classification of PALBI grades is as follows: grade 1 (score ≤ − 2.53); grade 2 (score > − 2.53 and ≤ − 2.09); and grade 3 (score > − 2.09)[18].

Statistical analysis

Data analysis was performed using SPSS version 26.0 and GraphPad Prism version 10.1.2. Continuous variables were represented as mean ± standard deviation. To compare different groups, either the t-test or the Mann-Whitney U test was employed. Categorical variables were shown as counts and proportions, with comparisons between the two groups conducted via the chi-square test or Fisher's exact test. A two-sided P value below 0.05 was deemed statistically significant. For univariate analysis, the Kaplan-Meier method was utilized, while the Log-rank test was applied for survival analysis; significant factors were subsequently included in the Cox regression model for multivariate analysis. Nomograms were constructed based on the multivariable Cox regression analysis utilizing R version 4.1.2 software. Additionally, the receiver operating characteristic (ROC) curve for the model was generated, and the area under the ROC curve (AUC), along with sensitivity and specificity, was calculated to evaluate the predictive efficiency of recurrence across different models.

Results

Patient characteristics analysis

The characteristics at baseline for patients involved in this research are detailed in Table 1. A total of 522 individuals participated in the study, comprising 441 males and 81 females. The mean age was 53.89 ± 9.65 years, with an average BMI of 23.40 ± 3.73. Within the cohort of 522 patients, 462 had chronic infections due to hepatitis B and (or) C; this included 422 instances of HBV infection, 38 of HCV infection, and 2 cases of co-infection with both HBV and HCV. The mean largest tumor diameter was measured at 6.09 ± 4.14 cm. Microvascular invasion was absent in 346 patients, while 120 exhibited MV1, and 56 showed evidence of MV2. Using the Edmondson-Steiner classification, there were 12 patients classified as grade 1, 344 as grade 2, 159 as grade 3, and 7 as grade 4. In terms of BCLC staging, 37 patients were categorized as stage 0, 412 as stage A, and 73 as stage B. The mean total bilirubin level recorded was 14.31 ± 15.95 μmol/L, and the average albumin level was 40.02 ± 4.67 g/L. The average scores for ALBI, EZ-ALBI, and PALBI were − 2.69 ± 0.44, −35.18 ± 4.39, and − 2.67 ± 0.34, respectively. The average Aspartate aminotransferase level was noted at 43.59 ± 50.63 U/L, while the mean platelet count registered at 143.58 ± 64.16* 10^9/L. An average APRI of 0.98 ± 1.39 was observed, with 178 patients showing AFP levels exceeding 400 ng/mL. According to the ALBI, EZ-ALBI, and PALBI grading systems, 340 patients were classified as ALBI grade 1, 179 patients as ALBI grade 2, and 3 patients as ALBI grade 3. Additionally, 323 patients were classified as EZ-ALBI grade 1, 195 patients as EZ-ALBI grade 2, and 4 patients as EZ-ALBI grade 3. Furthermore, 370 patients were classified as PALBI grade 1, 125 patients as PALBI grade 2, and 27 patients as PALBI grade 3.

We also analyzed patient characteristics according to ALBI, EZ-ALBI, and PALBI grade. Table 2 presents the relationships between the ALBI, EZ-ALBI, and PALBI grading systems. The majority of patients in this cohort were categorized as grade 1 and grade 2. No significant differences were noted in sex, viral hepatitis status, MTD, MVI, Edmondson-Steiner grading, or AFP levels across the varying grades of ALBI and EZ-ALBI ($P > 0.05$). In contrast, significant differences were observed in age, BMI, BCLC stage, AST, PLT, and APRI when comparing patients with different ALBI and EZ-ALBI grades ($P < 0.05$). Additionally, patients exhibited significant variances in MTD, MVI, Edmondson-Steiner grading, AST, PLT, and APRI across the different PALBI grades ($P < 0.05$). However, no significant differences were found in sex, age, BMI, viral hepatitis status, BCLC stage, or AFP across the varying PALBI grades ($P > 0.05$).

Correlations between ALBI, EZ-ALBI, and PALBI scores

The correlation coefficients observed between the ALBI and EZ-ALBI scores stand at 0.862 (95% CI: 0.838–0.882, $p < 0.0001$) across all patients (see Fig. 1A). For the ALBI and PALBI scores, the correlation coefficient is 0.760 (95% CI: 0.722–0.794, $p < 0.0001$) for the entire patient cohort (refer to Fig. 1B). Furthermore, the correlation coefficient between the PALBI and EZ-ALBI scores registers at 0.571 (95% CI: 0.510–0.626, $p < 0.0001$) among all patients (illustrated in Fig. 1C).

Differences in survival between various groups

Figure 2D presents the survival curves for this patient cohort free from recurrence. By the conclusion of the follow-up period, 11 individuals were without recurrence, 88 were lost during the follow-up, and a total of 423 individuals experienced recurrence. The survival rates free from recurrence at 1 year, 2 years, and 3 years were 52.223%, 28.32%, and 15.30%, respectively. The average duration of follow-up recorded was 16.01 months.

A notable difference in survival rates exists between patients with HCC classified as ALBI grade 1 and those in grades 2 or 3 (Fig. 2A, $p < 0.05$). The rates of recurrence-free survival after 1, 2, and 3 years are 57.65%, 32.83%, and 17.35% for patients in ALBI grade 1, while for those in ALBI grades 2/3, the corresponding rates are 45.03%, 19.50%, and 11.42%. Patients classified as EZ-ALBI grade 1 exhibit superior recurrence-free survival rates when contrasted with those in EZ-ALBI grade 2/3 (Fig. 2B, $p < 0.05$). Specifically, the recurrence-free survival percentages at 1, 2, and 3 years stand at 57.57%, 33.00%, and 16.93% for EZ-ALBI grade 1, whereas for EZ-ALBI grade 2/3, the corresponding rates are 46.15%, 20.32%, and 12.89%. Similarly, PALBI grade 1 patients demonstrate more favorable recurrence-free survival rates in comparison to PALBI grade 2/3 individuals (Fig. 2C, $p < 0.05$). The respective recurrence-free survival rates for PALBI grade 1 at 1, 2, and 3 years are 57.75%, 33.06%, and 18.50%, while for PALBI grade 2/3, the figures are 42.30%, 16.12%, and 6.61%.

Variables	$n = 522$
Gender, Male (%)	441(84.48)
Age, years (Mean ± SD)	53.89 ± 9.65
BMI, Kg/m^2 (Mean ± SD)	23.40 ± 3.73
Viral Hepatitis (%)	462(88.51)
MTD, cm (Mean ± SD)	6.09 ± 4.14
MVI	
None (%)	346(66.28)
MV1 (%)	120(22.99)
MV2 (%)	56(10.73)
Edmondson-Steiner grade	
grade 1(%)	12 (2.30)
grade 2(%)	344(65.90)
grade 3(%)	159(30.46)
grade 4(%)	7(1.34)
BCLC Stage	
0	37(7.09)
A	412(78.93)
B	73(13.98)
TBIL, μmol/L (Mean ± SD)	14.31 ± 15.95
Alb, g/L (Mean ± SD)	40.02 ± 4.67
ALBI	−2.69 ± 0.44
EZ-ALBI	−35.18 ± 4.39
AST, U/L (Mean ± SD)	43.59 ± 50.63
PLT, 10^9/L (Mean ± SD)	143.58 ± 64.16
APRI (Mean ± SD)	0.98 ± 1.39
PALBI (Mean ± SD)	−2.67 ± 0.34
AFP > = 400ng/mL (%)	178(34.10)
ALBI grade	
grade 1(%)	340 (65.13)
grade 2(%)	179(34.29)
grade 3(%)	3(0.57)
EZ-ALBI grade	
grade 1(%)	323 (61.88)
grade 2(%)	195(37.36)
grade 3(%)	4(0.77)
PALBI grade	
grade 1(%)	370 (70.88)
grade 2(%)	125(23.95)
grade 3(%)	27(5.17)

Table 1. Baseline characteristics of 522 HCC patients who underwent curative resection. Note: BMI: Body Mass Index; MTD: Maximum tumor diameter; MVI: Microvascular invasion; TBIL: Total bilirubin; Alb: Albumin; ALBI: Albumin-Bilirubin score; EZ-ALBI: easy- Albumin-Bilirubin score; PALBI: Platelet-Albumin-Bilirubin score; AST: Aspartate aminotransferase; PLT: blood platelet count; APRI: Aspartateaminotransferase-to-Platelet Ratio Index; AFP: alpha-fetoprotein.

The establishment of postoperative recurrence prediction models of HCC

In the analysis involving the entire cohort ($n = 522$) using univariate methods, results indicated that MTD, MVI, Edmondson-Steiner grade, BCLC Stage, AFP, ALBI, EZ-ALBI, and PALBI were linked to progression-free survival with all p-values being less than 0.01. Conversely, factors such as gender, age, BMI, viral hepatitis, and APRI did not demonstrate significant relationships with PFS (all $p > 0.05$). These findings are illustrated in Table 3. We subsequently incorporated these variables into the Cox multivariate models, which were based on the grades of ALBI, EZ-ALBI, and PALBI (refer to Tables 4, 5 and 6). The outcomes were consistent across the three models, particularly between ALBI and EZ-ALBI.

The Cox analysis utilizing ALBI indicated that factors such as the maximum tumor diameter (MTD), microvascular invasion (MVI), pathological grade, and elevated ALBI or ALBI grade were linked to reduced progression-free survival (PFS), with all p-values being less than 0.01, as illustrated in Table 4. The C-index values for the ALBI model were calculated to be 0.648 (95% CI 0.621–0.675). Furthermore, the Cox analysis

Variables	ALBI grade		P	EZ-ALBI grade		P	PALBI grade		P
	grade 1(%)	grade 2 or 3(%)		grade 1(%)	grade 2 or 3 (%)		grade 1(%)	grade 2 or 3 (%)	
Sex, Male (%)	291(55.75)	150(28.74)	0.340	276(85.45)	165(31.61)	0.437	314(60.15)	127(24.33)	0.707
Age, years (Mean ± SD)	53.04 ± 9.72	55.46 ± 9.33	0.006	52.9 ± 9.77	55.48 ± 9.24	0.003	54.21 ± 9.76	53.09 ± 9.35	0.229
BMI, Kg/m^2 (Mean ± SD)	23.65 ± 3.59	22.93 ± 3.96	0.036	23.67 ± 3.67	22.96 ± 3.80	0.034	23.35 ± 3.69	23.52 ± 3.85	0.651
Viral Hepatitis (%)	301(57.66)	161(30.84)	0.982	288(55.17)	174(33.33)	0.548	325(62.26)	137(26.25)	0.445
MTD, cm (Mean ± SD)	5.84 ± 3.83	6.56 ± 4.64	0.071	5.85 ± 3.89	6.47 ± 4.50	0.109	5.73 ± 3.56	6.96 ± 5.21	0.009
MVI			0.571			0.504			0.029
None (%)	221(42.34)	125(23.95)		208(39.85)	138(26.44)		241(46.17)	105(20.11)	
MV1 (%)	83(15.9)	37(7.09)		78(14.94)	42(8.05)		95(18.20)	25(4.79)	
MV2 (%)	36(6.90)	20(3.83)		37(7.09)	19(3.64)		34(6.51)	22(4.21)	
Edmondson-Steiner grade			0.730			0.698			0.002
grade 1(%)	6(1.15)	6(1.15)		6(1.15)	6(1.15)		6(1.15)	6(1.15)	
grade 2(%)	225(43.10)	119(22.80)		210(40.23)	134(25.67)		261(50.00)	83(15.9)	
grade 3(%)	104(19.92)	55(10.54)		102(19.54)	57(10.92)		97(18.58)	62(11.88)	
grade 4(%)	5(0.96)	2(0.38)		5(0.96)	2(0.38)		6(1.15)	1(0.19)	
BCLC Stage			0.016			0.005			0.248
0	30(5.75)	7(1.34)		30(5.75)	7(1.34)		29(5.56)	8(1.53)	
A	256(49.04)	156(29.89)		241(46.17)	171(32.76)		285(54.60)	127(24.33)	
B	54(10.34)	19(3.64)		52(9.96)	21(4.02)		56(10.73)	17(3.26)	
AST, U/L (Mean ± SD)	34.94 ± 20.76	59.74 ± 78.54	0.000	35.85 ± 21.81	56.14 ± 75.60	0.000	36.07 ± 22.64	61.88 ± 84.37	0.000
PLT, 10^9/L (Mean ± SD)	149.26 ± 60.83	132.97 ± 68.88	0.008	149.14 ± 59.98	134.56 ± 69.62	0.015	138.15 ± 56.24	156.80 ± 78.90	0.009
APRI	0.67 ± 0.53	1.54 ± 2.13	0.000	0.69 ± 0.54	1.45 ± 2.06	0.000	0.79 ± 0.68	1.42 ± 2.29	0.001
AFP ng/mL (%)			0.179			0.328			0.210
< 400	231(44.25)	113(21.65)		218(41.76)	126(24.14)		250(47.89)	94(18.01)	
>= 400	109(20.88)	69(13.22)		105(20.11)	73(13.98)		120(22.99)	58(11.11)	

Table 2. Patient characteristics according to ALBI, EZ-ALBI, and PALBI grade.

employing EZ-ALBI demonstrated that MTD, MVI, pathological grade, and high EZ-ALBI or EZ-ALBI grade correlated with decreased PFS, also with all p-values under 0.01, as detailed in Table 5. The C-index for the EZ-ALBI model was found to be 0.652 (95% CI 0.625–0.679). Additionally, the Cox analysis based on PALBI revealed that the MTD, MVI, pathological grade, and elevated PALBI or PALBI grade were associated with lower PFS, with p-values consistently below 0.01, as shown in Table 6. The C-index for the PALBI model was recorded at 0.675 (95% CI 0.647–0.703).

Comparison of different clinical prognostic nomograms

Utilizing the aforementioned predictive factors, we developed three prognostic nomograms, illustrated in Figs. 3, 4 and 5. The first prognostic nomogram, illustrated in Fig. 3, was created using predictive factors derived from the ALBI score, which carries the most weight in this model. The factors of MTD, MVI, and pathological grade also contribute to varying weights. Similarly, the second prognostic nomogram presented in Fig. 4 was generated based on the EZ-ALBI score, where the weights of MTD, MVI, and pathological grade have been reduced to varying degrees. Lastly, the third prognostic nomogram, displayed in Fig. 5, was formulated using predictive factors associated with the PALBI score, where the reduction in the weights of MTD, MVI, and pathological grade is more pronounced.

Evaluation of the predictability of the different prediction models

In order to assess the predictive capabilities of the ALBI model and the EZ-ALBI model in patients with HCC, ROC curves were constructed (see Fig. 6). The AUC values for both ALBI and EZ-ALBI were found to be similar, while the AUC for PALBI surpassed those of EZ-ALBI and ALBI. This indicates that EZ-ALBI and ALBI exhibit comparable performance in predicting PFS following curative hepatectomy for HCC patients, whereas PALBI demonstrates superior predictive capability compared to the other two models. The area under the curve (AUC) values were 0.705, 0.652, and 0.694 for the ALBI model at one year, two years, and three years post-operation, respectively. For the EZ-ALBI model, the AUC values were 0.708, 0.659, and 0.694 at one year, two years, and three years following surgery. Finally, the PALBI model showed AUC values of 0.748, 0.707, and 0.725 for the same time points after the procedure. In the ALBI model, the sensitivity at 1, 2, and 3 years was 0.526, 0.348, and 0.418, respectively. The specificity for the same periods was 0.833, 0.920, and 0.904, while the Yoden index values were 0.348, 0.268, and 0.322. In the EZ-ALBI model, the sensitivity at 1, 2, and 3 years was 0.508, 0.362, and 0.581, respectively. The specificity for these time points was 0.856, 0.920, and 0.750, with the Jordon index values being 0.364, 0.282, and 0.331. In the PALBI model, the sensitivity at 1, 2, and 3 years was 0.519, 0.384, and 0.549, respectively. The specificity for these years was 0.900, 0.945, and 0.863, and the Yoden index values were 0.420, 0.329, and 0.412.

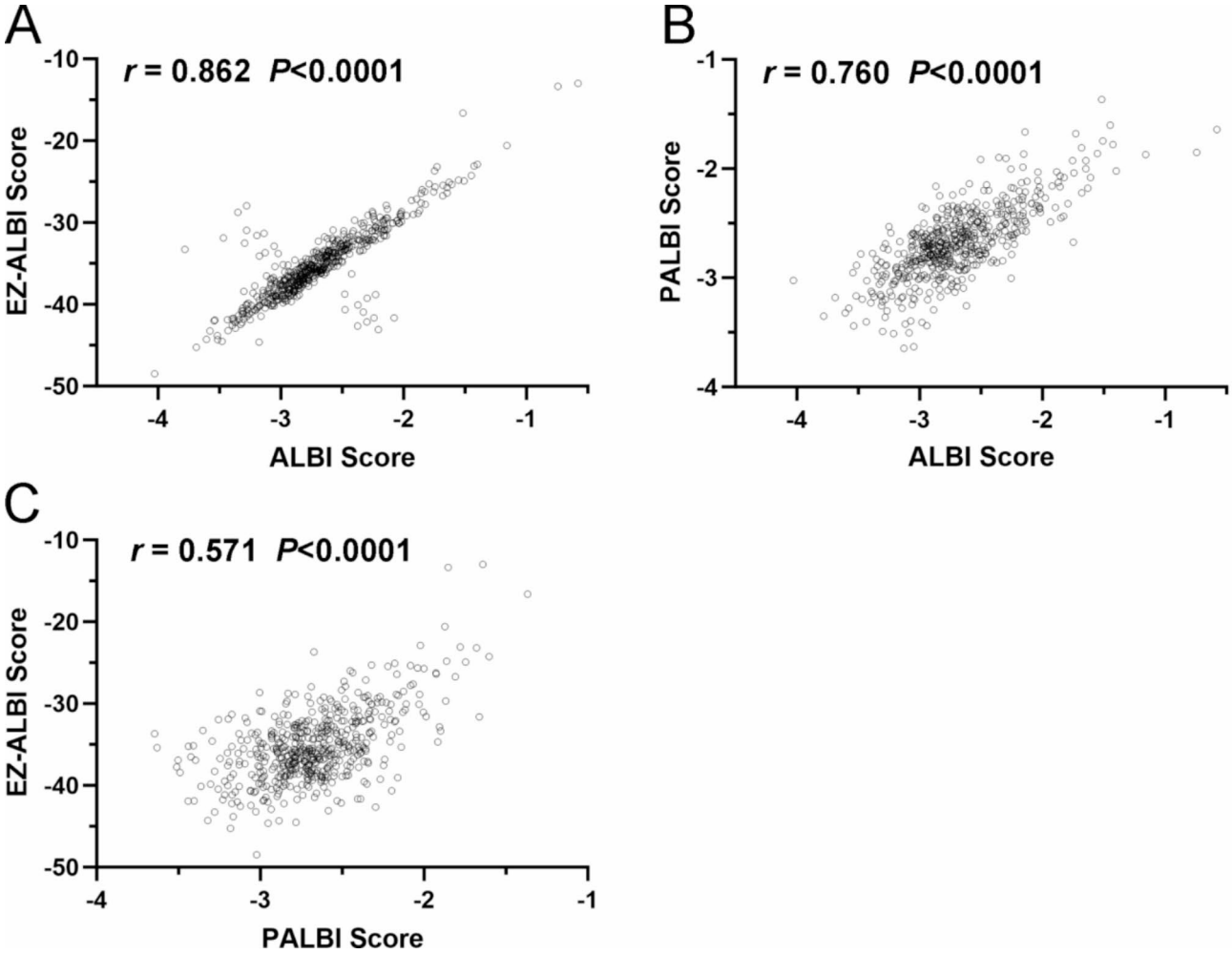

Fig. 1. Scatter plot representations for the three scoring systems alongside the recurrence-free survival curve for the full cohort. (**a**) Scatter plot comparisons between the EZ-ALBI and ALBI scores. (**b**) Scatter plot comparisons of the PALBI and ALBI scores. (**c**) Scatter plot comparisons between EZ-ALBI and PALBI scores.

Discussion

The primary approach for treating HCC is radical resection, but the significance of ALBI, EZ-ALBI, and PALBI systems in these patients has not been extensively documented. Research involving HCC patients undergoing TACE revealed that ALBI grading, together with EZ-ALBI and PALBI, can effectively stratify patients according to prognosis[18], although the relationships among ALBI, EZ-ALBI, and PALBI were not examined in detail in that investigation, it was noted that individuals classified in the poorer liver function category exhibited elevated ALBI, EZ-ALBI, and PALBI values, whereas those in the superior liver function category showed lower values. Many studies have shown that PALBI can predict the prognosis of HCC patients well, demonstrating certain value[19–21].In a separate study, an analysis of baseline data from 3,794 patients newly diagnosed with HCC revealed a strong linear correlation between the EZ-ALBI and ALBI scores across the entire population, with a correlation coefficient of 0.965[16]. The EZ-ALBI scoring method is straightforward and practical for evaluating liver reserve capacity and effectively differentiates between the survival rates of patients with early-stage and advanced HCC. Could such findings be observed in a group of patients with HCC who are undergoing curative surgical procedures?

In our bi-center analysis involving 522 HCC patients who received curative resection, it was noted that the characteristics of the cohort were comparable among patients with varying ALBI and EZ-ALBI classifications, while PALBI demonstrated discrepancies when compared to the two aforementioned grading systems. A detailed analysis of the traits of cases categorized by different ALBI and EZ-ALBI ratings indicated no significant differences with respect to gender, viral hepatitis status, MTD, MVI, Edmondson-Steiner grade, and AFP between ALBI and EZ-ALBI. However, notable differences were identified in terms of age, BMI, BCLC stage, AST, PLT, and APRI. We conducted a correlation analysis of ALBI, EZ-ALBI, and PALBI and found that ALBI was highly consistent with EZ-ALBI, while EZ-ALBI was poorly consistent with PALBI.

Given the favorable consistency of EZ-ALBI with ALBI, can EZ-ALBI serve as a substitute for ALBI in postoperative HCC patients? A comparison of the predictive power of the two may give us the answer. In terms of the survival curve, The rates of recurrence-free survival after 1, 2, and 3 years are 57.65%, 32.83%, and 17.35%

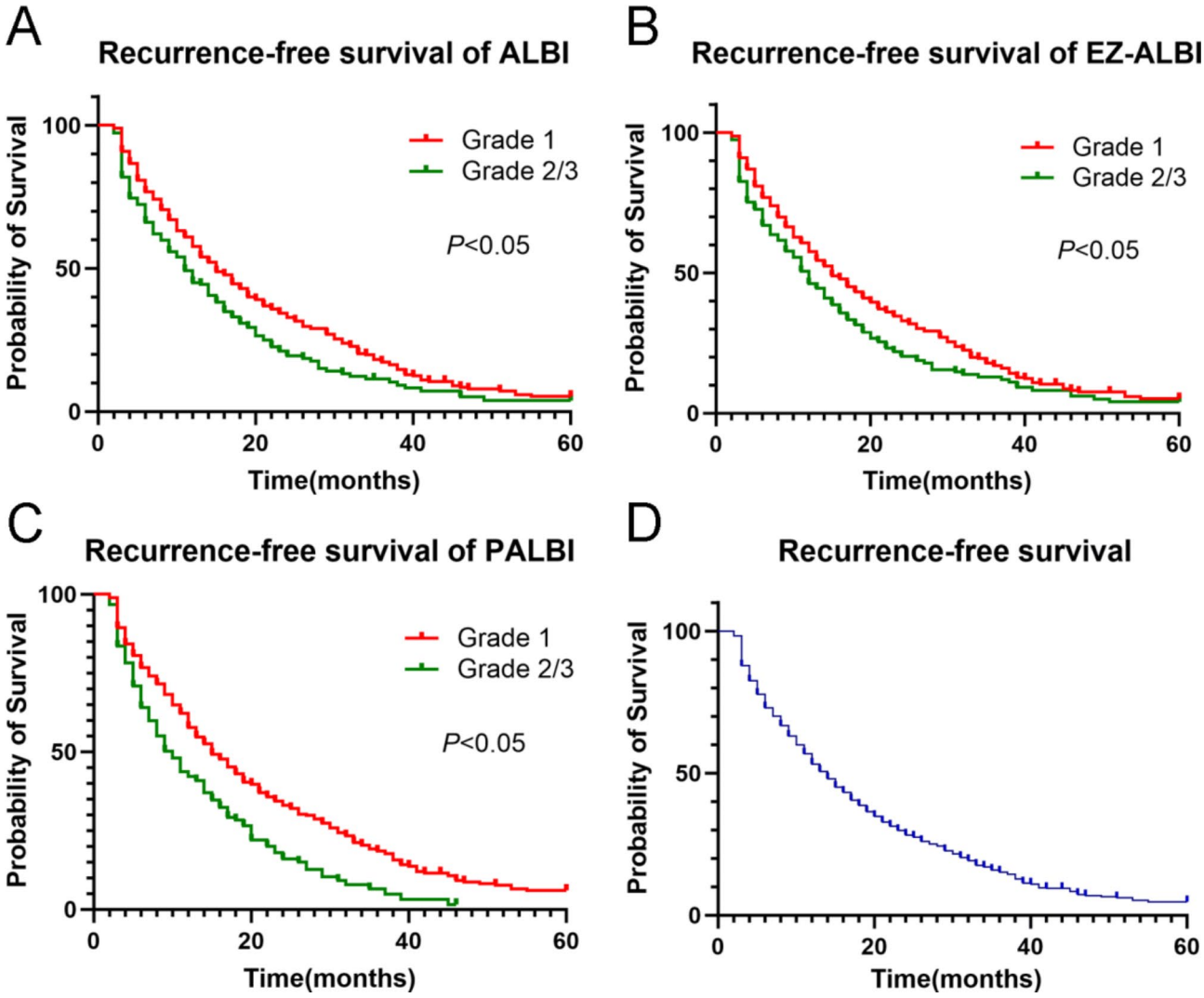

Fig. 2. The analysis of survival distribution among patients across various grades in the three scoring systems was conducted. (**a**) Survival distribution corresponds to the different ALBI grades. (**b**) Survival distribution relating to the various EZ-ALBI grades. (**c**) Survival distribution for the different PALBI grades. (**d**) The recurrence-free survival curve for the full cohort.

for patients in ALBI grade 1, the recurrence-free survival percentages at 1, 2, and 3 years stand at 57.57%, 33.00%, and 16.93% for EZ-ALBI grade 1, while for those in ALBI grades 2/3, the corresponding rates are 45.03%, 19.50%, and 11.42%, for EZ-ALBI grade 2/3, the corresponding rates are 46.15%, 20.32%, and 12.89%. The ALBI grade and EZ-ALBI grade share similar prognostic characteristics. The Normogram shows the prognostic prediction models based on ALBI, EZ-ALBI, and PALBI respectively. As shown in the figure, among the models based on ALBI and EZ-ALBI, ALBI and EZ-ALBI have the highest weights, while the weights of MTD, MVI, and pathological degree are not significantly different. In the evaluation of model prediction efficiency, The area under the curve (AUC) values were 0.705, 0.652, and 0.694 for the ALBI model at one year, two years, and three years post-operation, respectively. For the EZ-ALBI model, the AUC values were 0.708, 0.659, and 0.694, Their Predictive effectiveness was similar at 1, 2, and 3 years after surgery. Despite some differences in sensitivity and specificity, their predicted Jorden indexes at 1, 2, and 3 years after surgery were similar. Therefore, we believe that there is high consistency between the ALBI and EZ-ALBI grading systems in distinguishing clinical and prognostic characteristics of patients. Considering the simple calculation method of EZ-ALBI, EZ-ALBI can replace ALBI in predicting the prognosis of postoperative HCC patients.

The characteristics of patients differentiated by PALBI grading were significantly different from those of ALBI and EZ-ALBI. 29.12% of patients were classified as grade 2/3 by PALBI, and 27 of them were classified as grade 3. Age, BMI, MTD, MVI, Edmondson-Steiner grade, and BCLC Stage were distinguished by PALBI grades in the cohort differently from ALBI and EZ-ALBI. In terms of correlation analysis, the correlation coefficient for PALBI compared to ALBI was 0.762, indicating lower consistency. The correlation between PALBI and EZ-ALBI was even weaker, with a coefficient of 0.571. Although the correlation between PALBI and ALBI is limited, numerous studies have indicated that PALBI outperforms ALBI regarding the prediction of patient outcomes[18–24]. The

Variables	HR(95%CI)	pValue
Gender, (Male vs. Female)	0.92(0.71–1.20)	0.562
Age, years(≥ 65 vs. < 65)	0.84(0.63–1.11)	0.176
BMI, Kg/m^2	0.99(0.96–1.02)	0.520
Viral Hepatitis	1.08(0.86–1.15)	0.654
MTD, cm	1.08(1.06–1.10)	0.000
MVI	1.79(1.55–2.07)	0.000
Edmondson-Steiner grade	1.49(1.26–1.76)	0.000
BCLC Stage	1.36(1.09–1.68)	0.007
APRI	1.05(0.99–1.11)	0.155
AFP ng/mL (≥ 400 vs. < 400)	1.51(1.24–1.85)	0.000
ALBI	1.89(1.52–2.34)	0.000
EZ-ALBI	1.04(1.02–1.07)	0.002
PALBI	2.27(1.70–3.03)	0.000
ALBI grade (1 vs. 2/3)	1.35(1.11–1.65)	0.005
EZ-ALBI grade (1 vs. 2/3)	1.31(1.07–1.59)	0.005
PALBI grade (1 vs. 2/3)	1.60(1.29–1.97)	0.000

Table 3. Univariate Cox analysis of variables associated with HCC recurrence.

	ALBI		ALBI grade	
Variables	HR(95%CI)	pValue	HR(95%CI)	pValue
MTD, cm	1.05(1.02–1.07)	0.000	1.06(1.03–1.08)	0.000
MVI	1.62(1.39–1.88)	0.000	1.57(1.35–1.83)	0.000
Edmondson-Steiner grade	1.36(1.13–1.63)	0.001	1.32(1.10–1.59)	0.003
ALBI	2.06(1.64–2.57)	0.000		
ALBI grade			1.38(1.13–1.69)	0.001

Table 4. Multivariate Cox analysis of variables associated with HCC recurrence based on ALBI and ALBI grade.

	PALBI		PALBI grade	
Variables	HR(95%CI)	pValue	HR(95%CI)	pValue
MTD, cm	1.04(1.02–1.07)	0.000	1.05(1.03–1.07)	0.000
MVI	1.60(1.37–1.86)	0.000	1.61(1.39–1.88)	0.000
Edmondson-Steiner grade	1.28(1.07–1.53)	0.002	1.24(1.04–1.50)	0.020
PALBI	2.14(1.58–2.90)	0.000		
PALBI grade			1.55(1.24–1.93)	0.003

Table 6. Multivariate Cox analysis of variables associated with HCC recurrence based on PALBI and PALBI grade.

	EZ-ALBI		EZ-ALBI grade	
Variables	HR(95%CI)	pValue	HR(95%CI)	pValue
MTD, cm	1.05(1.03–1.08)	0.000	1.06(1.03–1.08)	0.000
MVI	1.58(1.36–1.83)	0.000	1.57(1.35–1.82)	0.000
Edmondson-Steiner grade	1.35(1.12–1.63)	0.002	1.33(1.10–1.60)	0.002
EZ-ALBI	1.05(1.02–1.07)	0.000		
EZ-ALBI grade			1.33(1.09–1.63)	0.003

Table 5. Multivariate Cox analysis of variables associated with HCC Recurrence-Based on EZ-ALBI and EZ-ALBI grade.

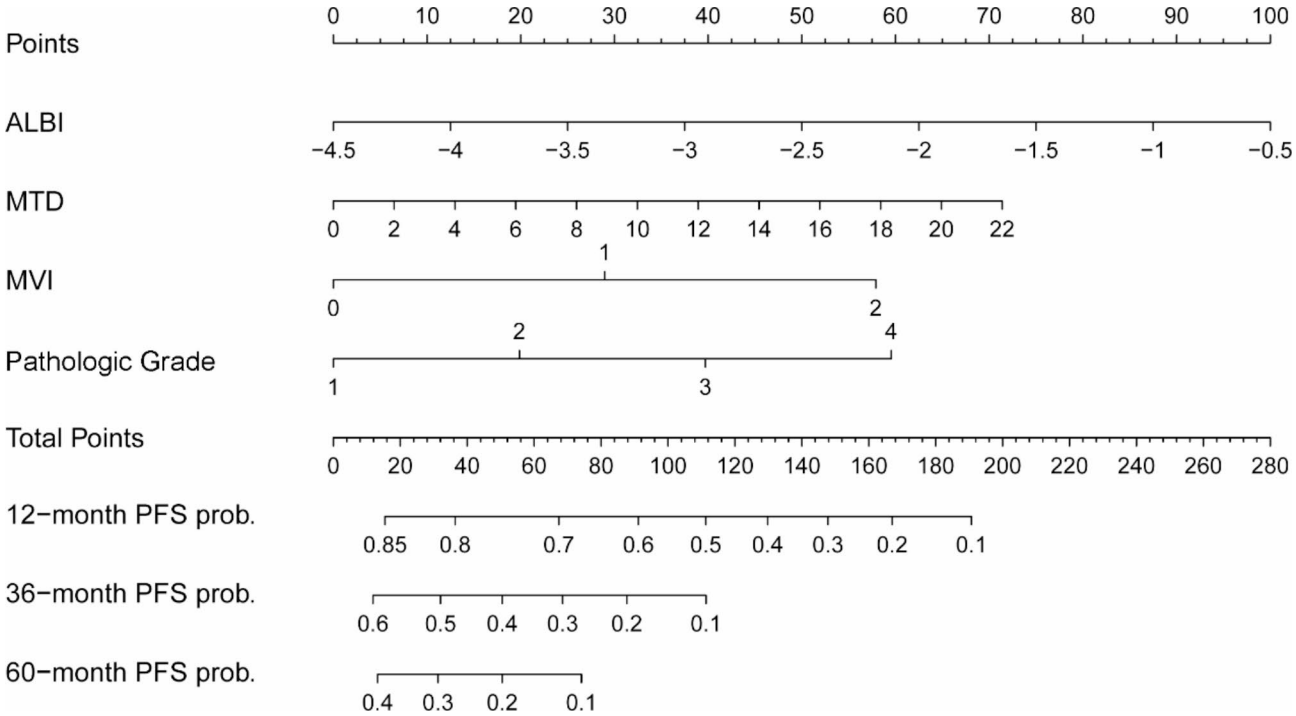

Fig. 3. The nomogram plot was built based on ALBI.

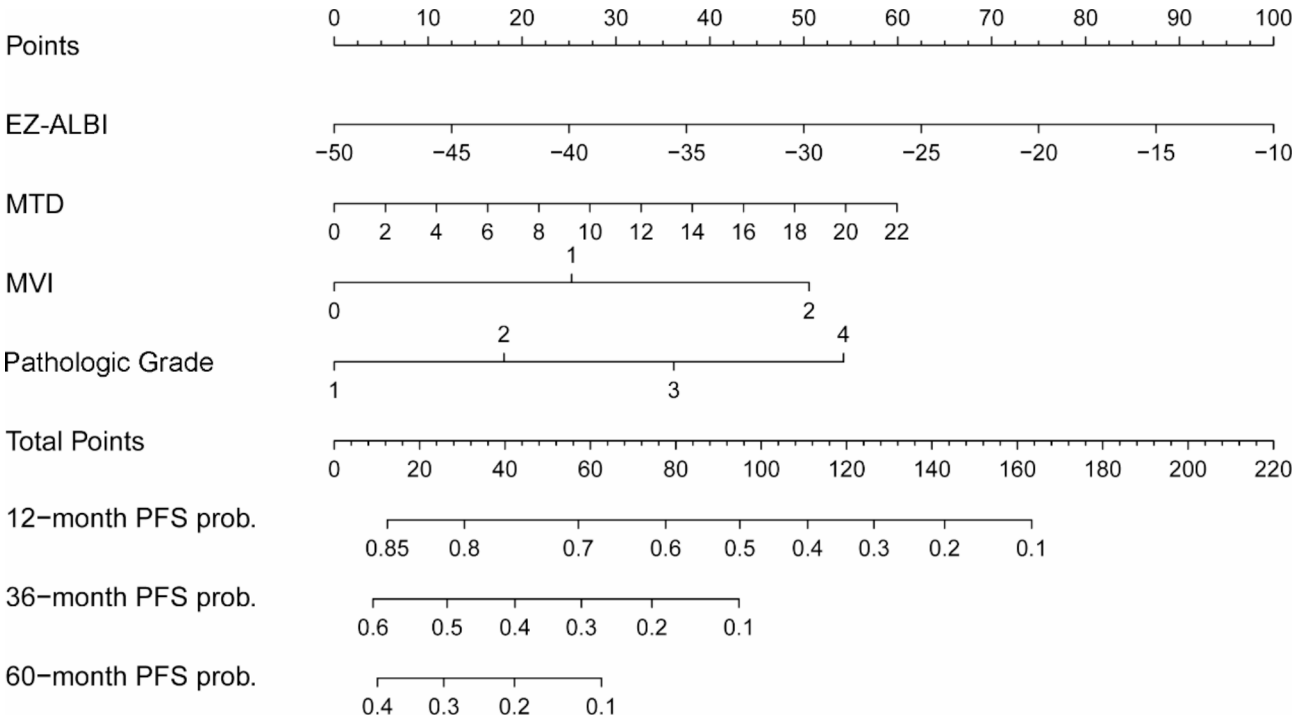

Fig. 4. The nomogram plot was built based on EZ-ALBI.

postoperative recurrence rate of HCC patients based on PALBI grading was also significantly different from that of ALBI and EZ-ALBI. The respective recurrence-free survival rates for PALBI grade 1 at 1, 2, and 3 years are 57.75%, 33.06%, and 18.50%, while for PALBI grade 2/3, the figures are 42.30%, 16.12%, and 6.61%. Patients with PALBI grade 2/3 had a higher risk of recurrence than patients with ALBI grade 2/3 and EZ-ALBI grade 2/3. Compared with ALBI and EZ-ALBI models, the weights of MTD, MVI, and pathological degree have the lowest weight in the recurrence prediction model developed by PALBI. Additional studies on liver cancer have shown

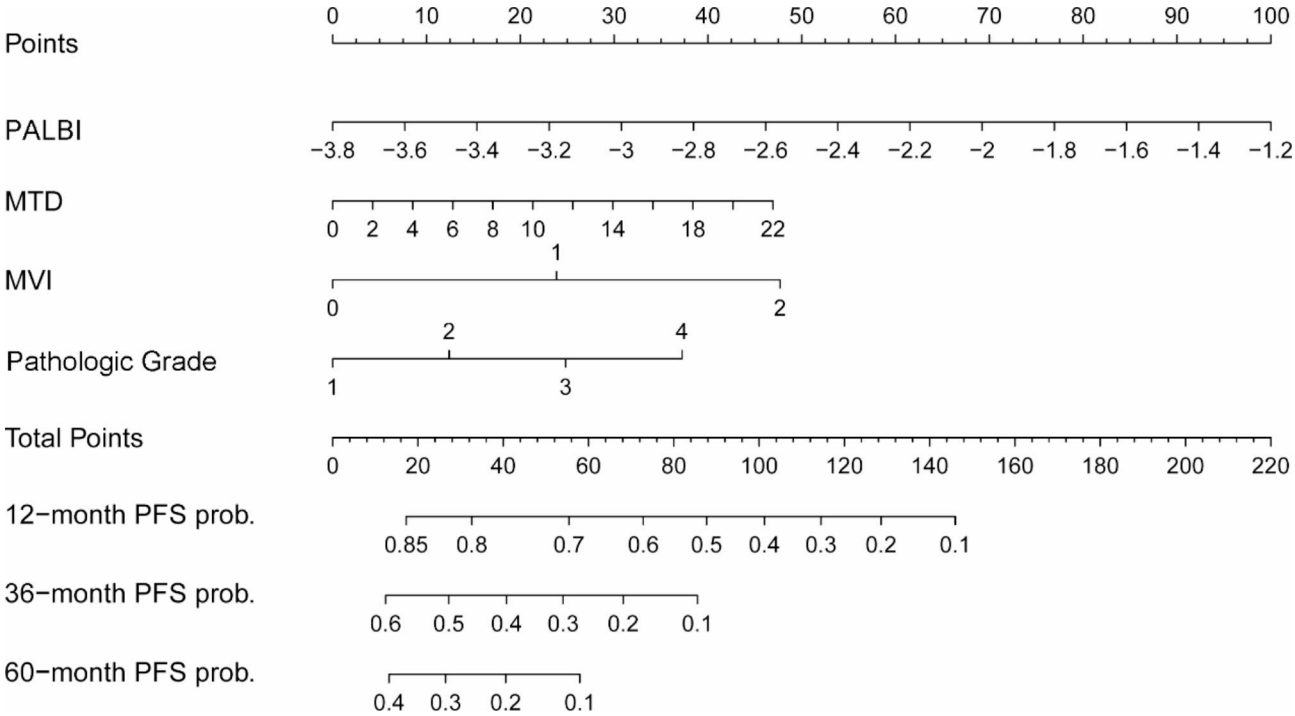

Fig. 5. The nomogram plot was built based on PALBI.

that the predictive framework utilizing ALBI and PALPI exhibits strong predictive performance[25–27]. In the evaluation of model prediction efficiency, The area under the curve (AUC) values were 0.748, 0.707, and 0.725 for the PALBI model at one year, two years, and three years post-operation, respectively, which were greater than that of the ALBI model and EZ-ALBI. In the PALBI model, the sensitivity at 1, 2, and 3 years was 0.519, 0.384, and 0.549, respectively and the specificity for these years was 0.900, 0.945, and 0.863, and the Yoden index values were 0.420, 0.329, and 0.412. Although its sensitivity and specificity did not show an overwhelming advantage over ALBI and EZ-ALBI, the PALBI model always had the largest Jorden index, which suggests its relatively good predictive power. Thus, PALBI offers a superior predictive value for the recurrence of HCC following surgery.

The EZ-ALBI grading system serves as an effective counterpart to the ALBI grading system in forecasting the postoperative recurrence of HCC patients, with its calculation being less complex. While PALBI requires more intricate calculations, it offers greater precision in predicting the outcomes for patients following liver cancer surgery. Naturally, our research presents certain limitations. To begin with, a significant proportion of the patients had a background of viral hepatitis, predominantly hepatitis B. Additionally, since this investigation was conducted at a large hospital as a bi-center study, further external validation of the EZ-ALBI and PALBI classifications is still necessary.

Conclusion

ALBI, EZ-ALBI, and PALBI have all been identified as predictors for postoperative recurrence in individuals with HCC. A recurrence model that incorporates these factors offers enhanced predictive capabilities for HCC patients following surgical intervention. When it comes to forecasting the prognosis of HCC patients post-surgery, EZ-ALBI is considered more convenient than ALBI, whereas PALBI demonstrates greater accuracy than ALBI. Therefore, both the EZ-ALBI and PALBI scoring systems may serve as viable alternatives to the ALBI score in clinical applications.

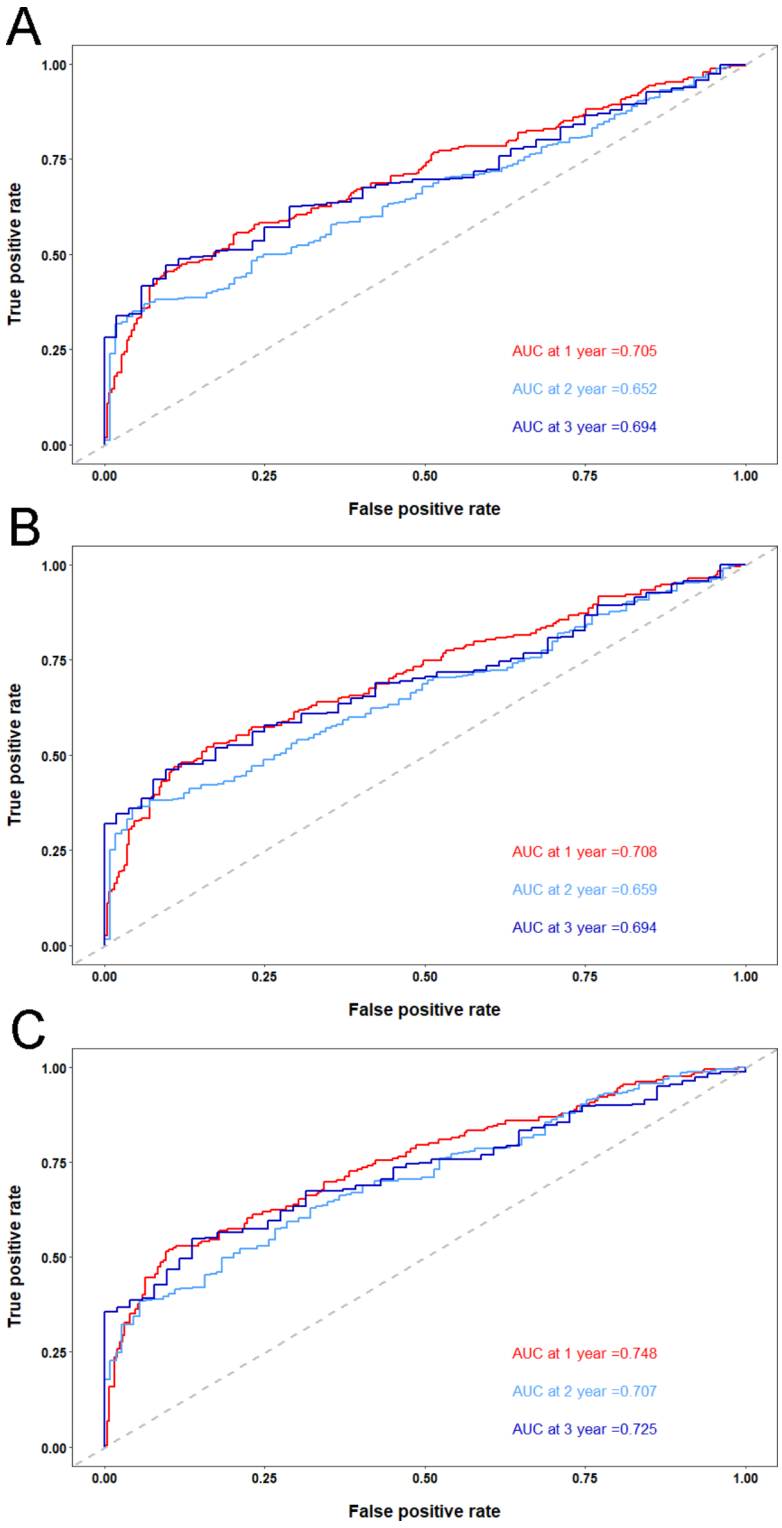

Fig. 6. The receiver operating characteristic (ROC) curves along with their respective area under the curve (AUC) for progression-free survival (PFS) at 1, 2, and 3 years, are derived from the three different scoring systems. (**a**) ROC curves together with the AUC for PFS calculated using the ALBI scoring system. (**b**) ROC curves and AUC pertaining to PFS based on the EZ-ALBI system. (**c**) ROC curves and AUC related to PFS were determined by the PALBI scoring method.

Data availability

The research data that support this publication can be obtained from the corresponding author upon reasonable request.

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Author contributions

The study was designed by Tao Sun and Xinguang Qiu, while the data analysis was conducted by Tao Sun and Xiangkun Wang. Clinical data collection and oversight of the entire study process were carried out by Tao Sun, Guangcan Zhu, Jinfu Zhang, Juan Huang, and Renfeng Li. The writing was directed by Xinguang Qiu, and the manuscript was both written and revised by Tao Sun.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
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