

NLR-PALBI Score and Its Grading: Predicting Overall Survival of Patients with Primary Liver Cancer Undergoing Transcatheter Arterial Chemoembolisation

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Background: Transcatheter arterial chemoembolisation (TACE) is the main first-line treatment regimen for advanced unresectable primary liver cancer (PLC), yet there is significant heterogeneity in patient prognosis. The postoperative platelet-albumin-bilirubin (PALBI) score can assess liver reserve function, and the neutrophil-to-lymphocyte ratio (NLR) reflects systemic inflammatory status. At present, there are insufficient studies on the predictive value of the combined NLR-PALBI score and its grading for overall survival (OS) in PLC patients after TACE.

Aim of the Study: To investigate the prognostic performance of postoperative NLR-PALBI score and grading for OS in PLC patients treated with TACE.

Patients and Methods: This was a retrospective cohort study enrolling 112 PLC patients who received TACE in our hospital from March 2017 to October 2019 and met the inclusion and exclusion criteria. Among them, 97 were male (86.61%) and 15 were female (13.39%), with a mean age of 54.26 years. The optimal cut-off values of postoperative NLR (6.97) and PALBI score (−1.65) were determined via receiver operating characteristic (ROC) curve, and the NLR-PALBI score and grading system (Grade I: 0 points, Grade II: 1 point, Grade III: 2 points) were constructed. ROC curve, Kaplan-Meier survival analysis and Cox proportional hazards regression model were applied to evaluate the prognostic value of each indicator and screen independent influencing factors of OS.

Results: ROC curve analysis showed that the NLR-PALBI score had an AUC of 0.776, which was significantly higher than that of single NLR (AUC=0.741) and PALBI score (AUC=0.709) ($P<0.01$), with a sensitivity of 66.7% and a specificity of 89.1%. Multivariate Cox regression analysis confirmed that postoperative NLR (HR=1.573, 95% CI 1.011–2.446, $P=0.005$) and NLR-PALBI score (HR=1.656, 95% CI 1.398–1.961, $P=0.044$) were independent risk factors for poor prognosis in PLC patients. Kaplan-Meier analysis revealed that patients with NLR-PALBI Grade III had the shortest OS, with 1-year, 3-year and 5-year OS rates of 71.43%, 4.76% and 0%, respectively ($P<0.01$).

Conclusion: Both postoperative NLR and NLR-PALBI score are independent risk factors for OS in PLC patients treated with TACE. The NLR-PALBI score has superior prognostic predictive value to single indicators, and patients with NLR-PALBI Grade III have the worst prognosis.

Keywords: primary liver cancer, transcatheter arterial chemoembolization, neutrophil-to-lymphocyte ratio, platelet-albumin-bilirubin score, overall survival

Introduction

Primary liver cancer (PLC) is a highly malignant tumour that ranks 6th in global incidence and 3rd in cancer-related mortality worldwide.¹ It has an insidious onset and rapid progression, with approximately 60–70% of patients diagnosed at the intermediate or advanced stage and losing the opportunity for curative surgery.¹ Existing data show that around 700,000

people die from PLC each year.² The World Health Organization estimates that more than 1 million patients will die from liver cancer by 2030.³ For patients with unresectable intermediate and advanced PLC, TACE has become the core treatment modality.⁴ TACE blocks the blood supply of the tumour while locally infusing chemotherapeutic agents, with the advantages of minimal invasiveness, high targeting and repeatability.^{5,6} It can not only significantly shrink the tumour and prolong patients' survival, but also downstage the tumour in some patients to provide an opportunity for secondary curative treatment. However, there is significant heterogeneity in the prognosis of patients receiving standard TACE treatment, and some patients experience liver function deterioration and accelerated tumour progression after the procedure. Therefore, reliable prognostic assessment tools are urgently needed to screen the population who can benefit from TACE.

Accumulated studies have confirmed that liver reserve function and systemic inflammatory and immune status are closely associated with postoperative recurrence and mortality in TACE-treated patients.⁷⁻⁹ Among these, the PALBI score is an assessment method for liver reserve function proposed in recent years. Based on three indicators: platelet count, albumin and bilirubin, it comprehensively reflects the synthetic function, excretory function of the liver and the risk of portal hypertension, and has more objective and accurate prognostic value than the Child-Pugh score.¹⁰ The NLR is a commonly used inflammatory indicator, which can sensitively reflect the progression of inflammation and the tendency of the body's immune response, and is also associated with the prognosis of PLC patients.¹¹ Our team's previous study¹² confirmed that the preoperative systemic immune-inflammation index (SII) combined with NLR has prognostic value for patients' postoperative overall survival, which laid a foundation for the prognostic significance of preoperative inflammatory indicators.

However, studies focusing on dynamic indicators after TACE, especially the prognostic value of postoperative NLR and PALBI score, are still relatively limited, and the validation of their combined application is even more scarce. Studies have shown that liver function and inflammatory indicators after TACE can stably reflect treatment-related injury and the body's compensatory status, with better predictive value than preoperative static indicators.¹³⁻¹⁶

Therefore, taking postoperative dynamic indicators as the core, this study aims to further analyse the correlation between NLR, PALBI score and the clinical characteristics of PLC patients treated with TACE, construct the NLR-PALBI score and grading system by combining the two indicators, and finally verify the prognostic predictive performance of this new grading system for PLC patients after TACE.

Materials and Methods

Approval

This study was approved by the Medical Ethics Committee of Liuzhou Hospital of Traditional Chinese Medicine (Liuzhou, China). All procedures involving human participants complied with the principles outlined in the Declaration of Helsinki, and all methods were performed in accordance with relevant guidelines and regulations.

Patient Selection

A retrospective analysis was performed on the clinical data of 311 PLC patients who underwent TACE in our hospital from March 2017 to October 2019. A total of 112 PLC patients met the inclusion and exclusion criteria and had complete follow-up data. Among them, 97 were male (86.61%) and 15 were female (13.39%), with an age range of 28 to 79 years and a mean age of 54.26 years. All patients had no hematological diseases to ensure that the platelet count represented the normal baseline value.

The inclusion criteria were as follows: i) According to the relevant criteria in the Diagnostic Criteria for Primary Liver Cancer,¹⁷ the diagnosis was confirmed clinically, and the tumor was confirmed to be unresectable PLC by imaging; ii) the tumor diameter was ≤ 10 cm, and the number of tumors was ≤ 3 ;^{18,19} iii) there was no extra-hepatic metastasis; iv) the patients underwent percutaneous hepatic arterial chemoembolization and did not succumb during the perioperative period; v) the data on preoperative SII, NLR and clinicopathological features were complete; vi) the patient could be followed up normally for at least 3 months after the surgery with no omission of clinical data.

The exclusion criteria were as follows: i) Previous liver surgery; ii) a combination of malignant tumors other than PLC; iii) a combination of other acute or chronic diseases or immune system disorders; iv) long-term use of anti-inflammatory medications; v) an estimated survival time of < 6 months; and vi) patients with incomplete or lost follow-up information.

Clinical Data and Calculations

The collected clinical data included gender, age, smoking history, drinking history, total bilirubin (TBIL), platelet (PLT), neutrophil (NEUT), lymphocyte (LYM), albumin (ALB), aspartate transaminase (AST), alanine aminotransferase (ALT), systemic immunoinflammatory index (SII), platelet-to-lymphocyte ratio (PLR), prognostic nutritional index (PNI), AST to platelet ratio index (APRI), NLR, albumin-bilirubin (ALBI) score, PALBI score, NLR-PALBI score, and overall survival (OS). The calculation formulas were: $NLR = N/L$; $PALBI = [2.02 \times \log_{10}(TBIL) - 0.37 \times (\log_{10}(TBIL))^2 - 0.04 \times ALB - 3.48 \times \log_{10}(PLT) + 1.01 \times \log_{10}(PLT)^2]$. Among them, PLT, NEUT, and LYM were the platelet count, absolute neutrophil count, and absolute lymphocyte count in routine blood tests (3–5 weeks after surgery), respectively. TBIL and ALB were the serum total bilirubin and albumin in liver function tests (3–5 weeks after surgery), respectively.

NLR-PALBI Grading

First, the optimal cut-off values of NLR and PALBI grading were determined by receiver operating characteristic curve (the optimal cut-off value of NLR in this study was 6.97, and that of PALBI grading was -1.65). Subsequently, 5-fold cross-validation was performed, which confirmed that the optimal cut-off values of NLR and PALBI grade were 6.95 and -1.64 , respectively, which were highly consistent with the critical values determined from the original dataset. Next, an independent dichotomous collinearity test was conducted for NLR and PALBI score. The results showed that the variance inflation factor (VIF) values of both dichotomised indicators were <5 , indicating no significant collinearity. Therefore, we combined NLR and PALBI score using a combination of equal-weight dichotomous assignment method and linear addition, to construct a novel prognostic grading system—the NLR-PALBI grade. The calculation method of NLR-PALBI grading was as follows: patients with $NLR \geq 6.97$ and $PALBI \text{ score} \geq -1.65$ received 2 points; patients with $NLR < 6.97$ and $PALBI \text{ score} \geq -1.65$, or $NLR \geq 6.97$ and $PALBI \text{ score} < -1.65$ received 1 point; patients with $NLR < 6.97$ and $PALBI \text{ score} < -1.65$ received 0 points. The NLR-PALBI grading system achieved a mean area under the curve (AUC) of 0.771 (95% confidence interval [CI]: 0.678–0.858) in the test set, with a sensitivity of 65.2% and a specificity of 87.8%, confirming that the prediction model has favourable stability.

Postoperative Follow-Up and Survival Recording

All 112 patients were followed up through outpatient visits, telephone interviews, or re-admission until death or the cut-off date (5 years after surgery [1800 days]). The median follow-up period, longest follow-up period, and shortest follow-up period were 1230 days, 1800 days, and 60 days, respectively. The follow-up period ended on October 18, 2024. During the follow-up period, a total of 66 subjects (58.93%) died. The median survival time was 1230 days (HR: 146.534; 95% CI: 942.794–1517.206). The 1-year, 3-year, and 5-year OS rates were 88.39%, 57.14%, and 41.07%, respectively.

Statistical Analysis

Statistical software SPSS 29.0 and Excel 2024 were used for data processing and analysis. Measurement data were expressed as $\bar{x} \pm s$, and comparison of count data was performed using χ^2 test or Fisher's exact test. The area under the ROC curve (AUC) was calculated by plotting the receiver operating characteristic (ROC) curve to determine the optimal cut-off values of NLR and PALBI grading. Kaplan-Meier (K-M) survival curve was used to analyze the impact of SII and NLR on the survival time of PLC patients. ROC curve and Cox proportional hazards regression model were used to analyze the predictive value of SII and NLR for patient prognosis. $P < 0.05$ was considered statistically significant.

Results

Patient Characteristics

Among the included patients, 97 were male (86.61%) and 15 were female (13.39%), with an average age of 54.26 years. Among them, 57 patients were <55 years old and 55 patients were ≥ 55 years old. There were 65 patients with a smoking history (58.04%) and 47 patients without (41.96%). There were 60 patients with a drinking history (53.57%) and 52

patients without (46.43%). In the NLR-PALBI score, 47 patients (41.96%) scored 0, 44 patients (39.29%) scored 1, and 21 patients (18.75%) scored 2. The baseline characteristics of PLC patients are listed in Table 1.

ROC Curve Analysis of NLR, PALBI Score, and NLR-PALBI Score

According to the ROC curve, the optimal cut-off value of NLR was 6.97 (Figure 1A), and that of the PALBI score was -1.65 (Figure 1B). Patients were thus divided into high NLR group ($\text{NLR} \geq 6.97$) and low NLR group ($\text{NLR} < 6.97$), high PALBI score group ($\text{PALBI} \geq -1.65$) and low PALBI score group ($\text{PALBI} < -1.65$). ROC curve was used to evaluate the sensitivity, specificity, and AUC of NLR, PALBI score, and NLR-PALBI score. The results showed that the predictive efficacy of the NLR-PALBI score ($\text{AUC} = 0.776$) was higher than that of NLR ($\text{AUC} = 0.741$) or PALBI score ($\text{AUC} = 0.709$). All the above indicators had good prognostic predictive effects (Table 2 and Figure 1C).

Table 1 Clinical Characteristics of PLC Patients

Clinical Characteristic	Value
Sex, n (%)	
Female	15(13.39%)
Male	97(86.61%)
Age (years)	54.260±12.084
Smoking history, n (%)	
Yes	65(58.04%)
No	47(41.96%)
Drinking history, n (%)	
Yes	60(53.57%)
No	52(46.43%)
TBIL(umol/L)	40.073±34.474
PLT($10^9/\text{L}$)	151.366±93.932
NEUT($10^9/\text{L}$)	6.279±3.358
LYM($10^9/\text{L}$)	0.854±0.387
ALB(g/L)	31.902±5.841
AST(U/L)	194.375±184.992
ALT(U/L)	147.804±192.885
SII	1379.671±1364.235
PLR	202.481±150.208
PNI	36.173±6.543
APRI	1.550±1.500
NLR	8.800±6.728
ALBI score	-1.719±0.564
PALBI score	-1.885±0.395
NLR-PALBI score, n (%)	0.589±0.203
Score 0 (Grade I)	47(41.96%)
Score 1 (Grade II)	44(39.29%)
Score 2 (Grade III)	21(18.75%)

Notes: Data are presented as mean ± standard deviation unless indicated.

Abbreviations: TBIL, total bilirubin; PLT, platelet; NEUT, neutrophil; LYM, lymphocyte; ALB, albumin; AST, aspartate transaminase; ALT, alanine aminotransferase; SII, systemic immunoinflammatory index; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; APRI, AST to platelet ratio index; NLR, neutrophil-to-lymphocyte ratio; ALBI score, albumin-bilirubin score; PALBI score, platelet-albumin-bilirubin score; NLR-PALBI score, neutrophil-lymphocyte ratio-platelet-albumin-bilirubin score.

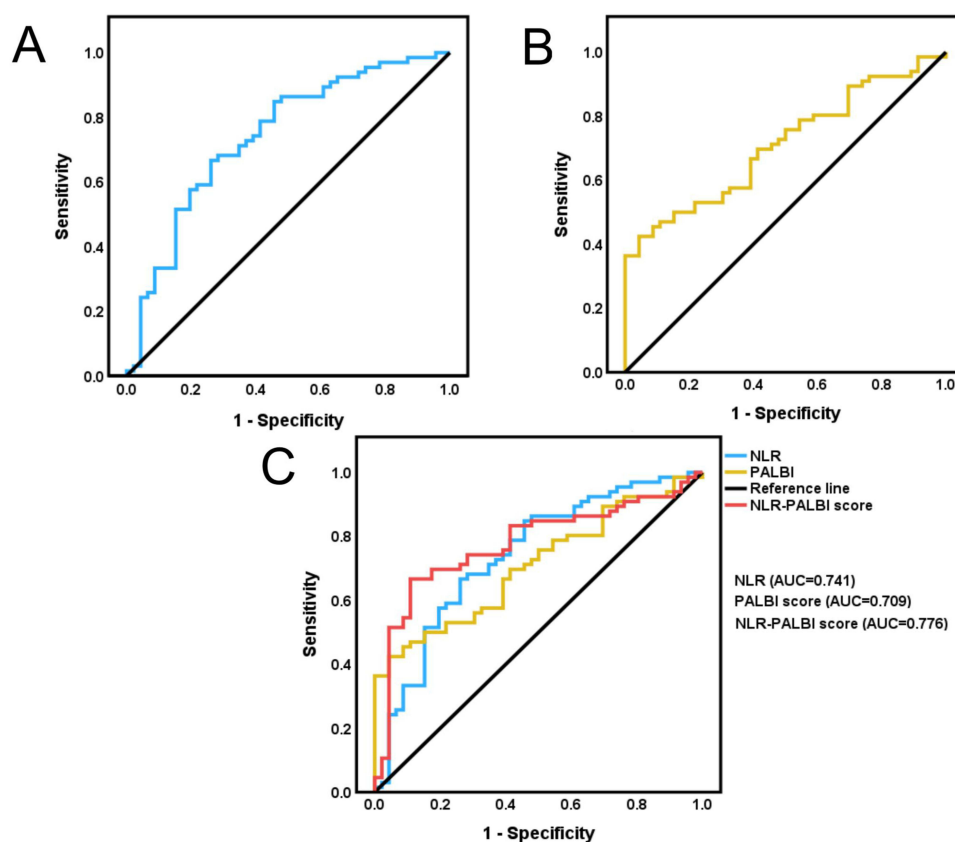


Figure 1 ROC curves of NLR, PALBI score and NLR-PALBI score.

Notes: (A–C) ROC analysis: ROC curves of NLR (A), PALBI score (B), and comparative ROC curves of NLR, PALBI score and NLR-PALBI score with corresponding AUC values (C).

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PALBI score, platelet- albumin- bilirubin score; NLR-PALBI score, neutrophil-lymphocyte ratio-platelet-albumin-bilirubin score; AUC, area under the curve; ROC, receiver operating characteristic.

Comparison of Clinical Data

Patients were divided into Grade I (NLR<6.97 and PALBI<-1.65, score 0), Grade II (NLR<6.97 and PALBI $\geq$ -1.65, NLR $\geq$ 6.97 and PALBI<-1.65, score 1), and Grade III (NLR $\geq$ 6.97 and PALBI $\geq$ -1.65, score 2) according to the NLR-PALBI score. The differences in clinical characteristics among patients with NLR-PALBI Grade I, II, and III were compared. The results showed that there were statistically significant differences in the NLR-PALBI score among drinking history, TBIL, PLT, NEUT, ALB, AST, SII, PNI, PLR, NLR, ALBI score, and PALBI score ($P<0.05$), while there were no statistically significant differences in other clinical indicators.

Prognostic Value of NLR, PALBI Score, and NLR-PALBI Grade

K-M survival curve analysis showed that the survival time of patients in the high NLR group was significantly shorter than that in the low NLR subgroup ($P<0.01$; Figure 2A). The survival time of patients in the high PALBI score group was significantly

Table 2 Effect of Postoperative NLR, PALBI Score and NLR - PALBI Score on the Prognosis of Patients with Primary Liver Cancer

Indicators	AUC	SE	P-value	Cut-Off Value	Sensitivity,%	Specificity,%	Youden Index	95% CI
NLR	0.741	0.048	<0.001	6.97	66.7	73.9	0.406	0.646–0.836
PALBI score	0.709	0.048	<0.001	-1.65	42.4	95.7	0.381	0.615–0.803
NLR-PALBI score	0.776	0.045	<0.001	0.62	66.7	89.1	0.558	0.687–0.865

Abbreviations: NLR, neutrophil- to- lymphocyte ratio; PALBI score, platelet- albumin- bilirubin score; NLR-PALBI score, neutrophil-lymphocyte ratio-platelet-albumin-bilirubin score; CI, confidence interval; AUC, area under the curve; SE, standard error.

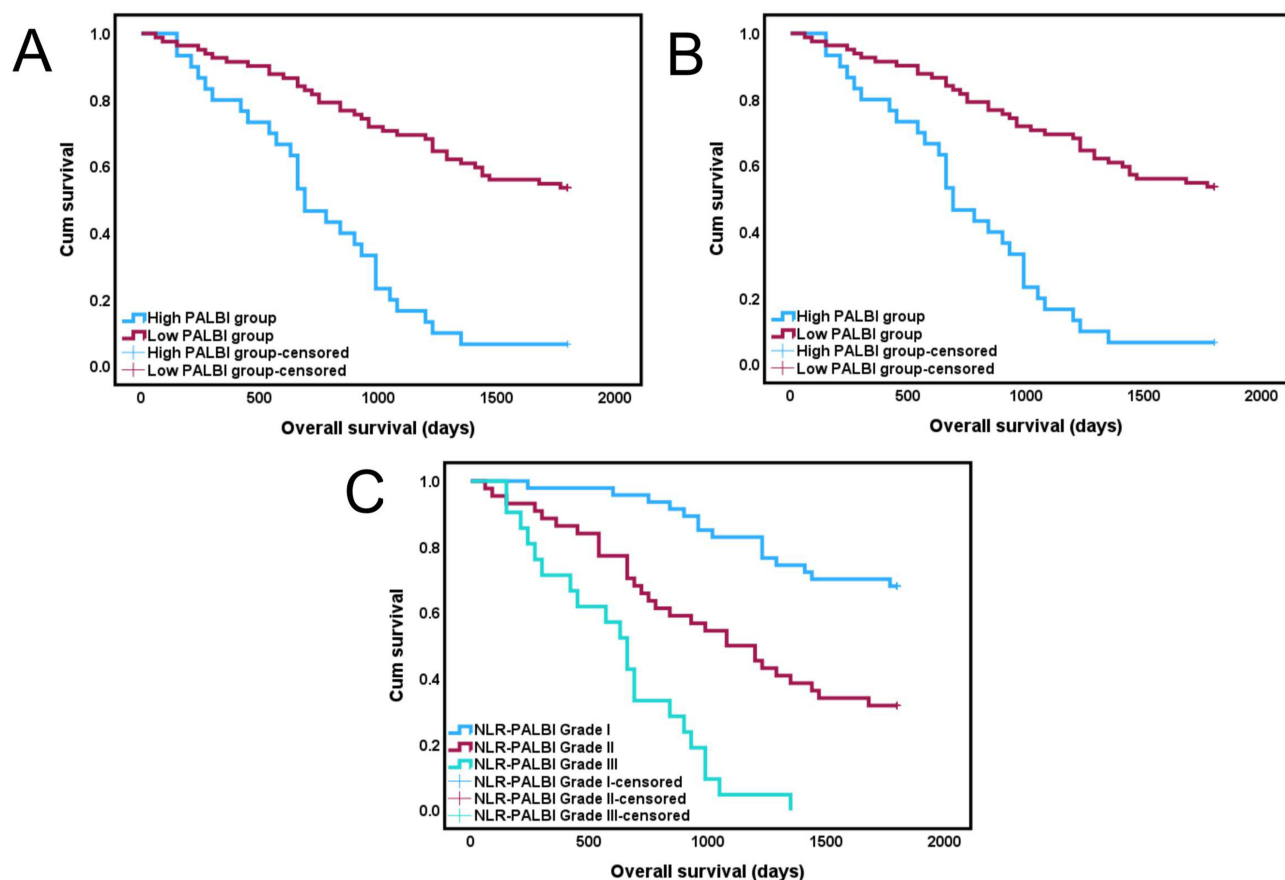


Figure 2 Kaplan-Meier survival curves for NLR (A), PALBI score (B), and NLR-PALBI grade (C).

Notes: Kaplan-Meier survival curves for (A) low vs. high NLR groups, (B) low vs. high PALBI score groups and (C) NLR-PALBI grades.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PALBI score, platelet-albumin-bilirubin score; NLR-PALBI grade, neutrophil-lymphocyte ratio-platelet-albumin-bilirubin grade; OS, overall survival; cum, cumulative.

shorter than that in the low PALBI score group ($P < 0.01$; Figure 2B). The 1-year, 3-year, and 5-year OS rates of patients with NLR-PALBI Grade I (0 points) were 97.87%, 82.98%, and 46.68%, respectively; those of patients with NLR-PALBI Grade II (1 point) were 86.36%, 50%, and 22.73%, respectively; those of patients with NLR-PALBI Grade III (2 points) were 71.43%, 4.76%, and 0%, respectively. Patients with NLR-PALBI Grade III (2 points) had the shortest OS time ($P < 0.01$; Figure 2C).

Univariate and Multivariate Analyses of Prognostic Factors

In this study, 19 variables were selected for univariate Cox proportional hazards regression analysis. The results showed that drinking history, TBIL, PLT, NEUT, LYM, AST, SII, PLR, NLR, ALBI score, PALBI score, and NLR-PALBI score had significant effects on the OS of PLC patients ($P < 0.05$; Table 3), while other clinical variables had no significant impact on OS. To avoid the influence of multicollinearity on the results, TBIL, PLT, NEUT, LYM, and AST (direct constituent indicators of NLR, ALBI score, and PLR) were first excluded. Subsequently, the variance inflation factor (VIF) was used for collinearity diagnosis of the remaining variables (drinking history, SII, PLR, NLR, ALBI score, PALBI score, NLR-PALBI score), with $VIF < 10$ indicating no severe multicollinearity. The highly correlated variable PALBI score ($VIF = 14.505$) was eliminated. The VIF values of the remaining variables (Drinking history=1.228, SII=4.670, PLR=2.522, NLR=3.679, ALBI score=2.628, NLR-PALBI score=5.792) were all < 10 , confirming a low risk of multicollinearity. Then, SII, PLR, NLR, ALBI score, PALBI score, and NLR-PALBI score were included in the multivariate Cox proportional hazards regression analysis. However, the analysis revealed that only drinking history (HR: 2.339; 95% CI: 1.306–4.190; $P = 0.004$), SII (HR: 1.001; 95% CI: 1.000–1.001; $P < 0.001$), NLR (HR: 0.885; 95% CI: 0.793–0.988; $P = 0.005$), and NLR-PALBI score (HR: 1.656; 95% CI: 1.398–1.961; $P = 0.044$) were independent risk factors for OS (Table 3).

Table 3 Univariate and Multivariate Cox Regression Analysis of Overall Survival

Variable	Univariate Analysis HR (95% CI)	P	Multivariate Analysis HR (95% CI)	P
Sex	0.417 (0.167–1.038)	0.060	2.319 (1.293–4.156)	0.005 ^a
Age	0.991 (0.970–1.013)	0.433		
Smoking history	0.984 (0.604–1.604)	0.949		
Drinking history	3.245 (1.896–5.554)	<0.001 ^a		
TBIL	1.007 (1.002–1.012)	0.011 ^a		
PLT	1.003 (1.001–1.005)	0.002 ^a		
NEUT	1.192 (1.115–1.275)	<0.001 ^a		
LYM	0.701 (0.357–1.375)	0.031 ^a		
ALB	0.955 (0.907–1.005)	0.077		
AST	1.002 (1.001–1.004)	<0.001 ^a		
ALT	1.000 (0.999–1.001)	0.538	1.001 (1.000–1.001)	0.002 ^a
SII	1.000 (1.000–1.001)	<0.001 ^a		
PLR	1.002 (1.001–1.003)	<0.001 ^a	0.999 (0.996–1.001)	0.373
PNI	0.958 (0.917–1.001)	0.056	1.573 (1.011–2.446)	0.029 ^a
APRI	1.082 (0.942–1.243)	0.262		
NLR	1.731 (1.122–2.669)	<0.001 ^a		
ALBI score	1.833 (1.123–2.991)	0.015 ^a	1.500 (0.445–5.062)	0.513
PALBI score	5.274 (2.597–10.709)	<0.001 ^a	1.656 (1.398–1.961)	0.045 ^a
NLR-PALBI score	2.027 (1.586–2.590)	<0.001 ^a		

Note: ^aP<0.05.

Abbreviations: TBIL, total bilirubin; PLT, platelet; NEUT, neutrophil; LYM, lymphocyte; ALB, albumin; AST, aspartate transaminase; ALT, alanine aminotransferase; SII, systemic immunoinflammatory index; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; APRI, AST to platelet ratio index; NLR, neutrophil-to-lymphocyte ratio; ALBI score, albumin-bilirubin score; PALBI score, platelet-albumin-bilirubin score; NLR-PALBI score, neutrophil-lymphocyte ratio-platelet-albumin-bilirubin score.

Discussion

TACE is the standard first-line treatment regimen for patients with unresectable intermediate and advanced PLC.¹⁷ However, the high heterogeneity among patients leads to significant differences in their prognosis. Therefore, on the basis of our team's previous study,¹² we combined NLR and PALBI score to innovatively construct the NLR-PALBI grading system. Compared with existing combined models, most previous studies focused on preoperative indicators (such as preoperative NLR and preoperative PALBI score), mostly explored inflammatory or liver reserve indicators alone, and ignored the synergistic effect of the two.^{20–23} Although our team's previous study¹² confirmed the prognostic value of preoperative SII combined with NLR, it did not include liver reserve function, a core influencing factor. TACE treatment can induce transient liver function fluctuations and inflammatory stress responses,^{24,25} meaning preoperative static indicators cannot reflect patients' immediate response to treatment and compensatory capacity, and may easily overestimate or underestimate the actual prognostic risk.^{12,13} In contrast, this study takes postoperative dynamic indicators as the core. It dynamically captures the balance of systemic inflammation and immunity after treatment through NLR, and comprehensively evaluates liver synthetic function, excretory function and the risk of portal hypertension through PALBI. The AUC of the NLR-PALBI score (0.776) was not only significantly higher than that of NLR alone (0.741) and PALBI score alone (0.709), but also had a high specificity of 89.1%, which can more accurately identify high-risk patients and thus optimize subsequent treatment strategies for patients.

In terms of individual indicators, as a core indicator reflecting systemic inflammatory and immune status, the value of NLR lies in its ability to simultaneously capture the degree of inflammatory activation (neutrophils) and anti-tumor immune capacity (lymphocytes) of the body.^{26,27} In this study, the optimal cut-off value of NLR was 6.97, and the OS of patients in the high NLR group (NLR≥6.97) was significantly shortened (P<0.01), which was consistent with the results of the study published by Wang C.²⁸ This study enrolled 380 PLC patients treated with TACE, and confirmed that NLR (HR=1.34, 95% CI: 1.03–1.75, P<0.05) was an independent risk factor for OS. The results of the multicenter study by Minici R²⁹ further verified the adverse prognostic value of high NLR in PLC patients. Notably, the optimal cut-off value

of NLR in this study (6.97) was higher than that in the study by Wang et al. In-depth analysis revealed that this may be due to the significant difference in the degree of liver function injury between the two study populations. The mean serum TBIL of patients in this study reached 40.07 $\mu\text{mol/L}$, which was not only far beyond the normal reference range, but also significantly higher than the TBIL level of PLC patients in the study by Wang et al (16.9 $\mu\text{mol/L}$), suggesting that the study population had more severe hepatocyte injury and worse bile excretion function. In the case of severe liver function injury, hepatocyte necrosis will release inflammatory factors such as IL-6 and TNF- α , stimulate neutrophil proliferation and enhance their anti-inflammatory and immunosuppressive effects. Meanwhile, the disorder of the immune micro-environment will accelerate lymphocyte apoptosis, leading to an overall increase in the baseline level of NLR, which in turn shifts the optimal cut-off value for distinguishing prognostic risk upward accordingly.^{30,31} In addition, the small sample size may also have a certain impact on the cut-off value.

The PALBI score is based on three objective indicators: platelet count, albumin and bilirubin, which is more comprehensive than the traditional Child-Pugh score and albumin-bilirubin (ALBI) score.³² In this study, the optimal cut-off value of the PALBI score was -1.65 , and the OS of patients in the high PALBI score group (PALBI score ≥ -1.65) was significantly shortened ($P < 0.01$), which was highly consistent with the conclusion of the study by Wu F.³³ This study compared the predictive value of PALBI (AUC=0.619, 95% CI: 1.071–1.742, $P < 0.05$) and ALBI (AUC=0.550, 95% CI: 0.457–0.642, $P < 0.05$) in 151 cirrhotic patients with BCLC stage C PLC receiving conventional transcatheter arterial chemoembolisation (c-TACE), and found that the PALBI grade (HR=1.366, 95% CI: 1.071–1.742, $P < 0.05$) had better prognostic predictive performance. Ho SY³⁴ further confirmed the unique advantage of the PALBI grade in the assessment of liver reserve function.

In this retrospective study, we analysed the clinical data of 112 patients with PLC who underwent TACE. Cox proportional hazards regression analysis showed that postoperative NLR, PALBI score, and NLR-PALBI score were all significantly associated with patient prognosis. Among these, NLR (HR: 1.573; 95% CI: 1.011–2.446; $P = 0.005$) and NLR-PALBI score (HR: 1.656; 95% CI: 1.398–1.961; $P = 0.044$) were independent risk factors for poor prognosis in PLC patients. ROC curve analysis revealed that the NLR-PALBI score had an AUC of 0.776, which was significantly higher than that of NLR alone (0.741) and PALBI score alone (0.709), with a specificity of 89.1%. In addition, K-M survival curve analysis demonstrated that patients with NLR-PALBI Grade III had the shortest OS ($P < 0.01$). Based on the above findings, in combination with the Guidelines for the Diagnosis and Treatment of Primary Liver Cancer¹⁷ and relevant clinical studies,^{5,35} we put forward the following clinical recommendations: For patients with NLR-PALBI Grade III, repeated TACE treatment should be avoided in clinical practice, and targeted therapy (such as sorafenib and lenvatinib) or immunotherapy (such as PD-1 inhibitors) should be prioritised to maximally preserve patients' liver reserve function while controlling tumour progression. For patients with NLR-PALBI Grade I and Grade II, who have relatively favourable postoperative liver reserve function and systemic inflammatory and immune status and can tolerate the local therapeutic effects of TACE, conventional TACE treatment can be administered with prolonged follow-up intervals.

In addition, this study also analysed PNI and APRI,^{36,37} which have been reported to be associated with PLC prognosis in previous studies. However, the results showed that PNI (AUC=0.378; HR=0.958; 95% CI: 0.917–1.001; $P = 0.056$) and APRI (AUC=0.570; HR=1.082; 95% CI: 0.942–1.243; $P = 0.262$) had no significant correlation with the prognosis of PLC patients treated with TACE. We speculate that this is related to factors such as severe overall liver function injury (mean AST: 194.38 U/L, mean ALT: 147.80 U/L, mean TBIL: 40.07 $\mu\text{mol/L}$) and poor nutritional status (mean albumin: 31.90 g/L) in the study population, which masked the potential impact on prognosis.

This study still has several limitations. First, as a retrospective study, all data were collected from a single centre, which may introduce selection bias. In future research, large cohorts of patients from different regions and hospitals can be included to further verify the reliability and stability of the study results. Second, we set the inclusion criteria of "tumour diameter ≤ 10 cm and number of tumours ≤ 3 ", and only included patients with moderate tumour load treated with TACE. Although this effectively controlled the confounding effect of tumour load, a key prognostic factor, on the study results, it also limited the generalisability of the findings to a certain extent. For patients with high tumour load (tumour diameter > 10 cm and number of tumours > 3), the prognostic performance of the NLR-PALBI grading system constructed in this study still needs to be further verified in large-sample, multi-centre clinical studies. In addition, there are still many potential influencing factors in our model, such as the inaccurate recording of the number of TACE

sessions. These factors may be intertwined with the immune-inflammatory response during tumour onset and progression, and jointly affect patient prognosis. Therefore, in future studies, factors including postoperative recurrence time, number of TACE sessions and tumour stage should be accurately recorded to ensure the accuracy of the prognostic model. Meanwhile, more precise multimodal prognostic models can be constructed by combining postoperative imaging indicators, molecular markers and other relevant factors.

Conclusion

This study confirms that in PLC patients undergoing TACE, the higher the postoperative NLR and PALBI score, the worse the prognosis; the NLR-PALBI grading can effectively distinguish populations with different prognostic risks, and the predictive value of the NLR-PALBI score is superior to that of any individual indicator. The combination of the two can provide a more accurate basis for clinical decision-making in such patients.

Data Sharing Statement

The data generated in the present study may be requested from the corresponding author.

Ethics Approval and Consent to Participate

This study was performed in accordance with the Declaration of Helsinki Declaration of Helsinki and was approved by the Medical Ethics Committee of Liuzhou Hospital of Traditional Chinese Medicine (Liuzhou, China; initial review approval no. 2023JUL-KY-059-01; follow-up review approval no. 2023JUL-KY-059-02). Given the observational non-interference nature of this study, the Ethics Committee waived the requirement for informed consent. To strictly protect patient privacy and data security, the clinical medical record data of all enrolled patients were anonymised prior to extraction and analysis. Only de-identified clinical indicator data were used for statistical analysis throughout the research process. The storage and use of data strictly complied with relevant regulations on medical data confidentiality, and no patients' personal privacy information was disclosed at any stage of the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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