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Development of a Nomogram Using the Inflammatory Risk Score for Prognostication in Moderate and Advanced Hepatocellular Carcinoma Associated with Hepatitis B Virus

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Background: The changes in risk scores of inflammatory markers among patients diagnosed with hepatocellular carcinoma (HCC) remain unknown.

Aims: To investigate the relationship between the inflammation risk score and other contributing factors and the prognostic outcomes in patients with moderate and advanced hepatitis B virus (HBV)-related HCC.

Study Design: A retrospective cohort study.

Methods: A total of 174 patients with moderate and advanced HBV related HCC were recruited to investigate the impact of stratified inflammatory risk scores and other associated risk factors on disease prognosis. Based on the optimal cut-off values calculated by the Youden index, the patients were divided into high-risk and low-risk groups based on their inflammation risk scores.

Results: The study found a significant difference in median survival time between the low-risk and high-risk groups based on the inflammation risk score. Furthermore, the inflammation risk score, alpha-fetoprotein levels, transarterial chemoembolization treatment, and Barcelona Clinic Liver Cancer stage were identified as independent prognostic factors. The four variables were used to construct a prognostic nomogram for HCC. Subsequent evaluations using time-dependent receiver operating characteristic analysis and calibration curve tests revealed the nomogram's commendable discriminatory ability. As a result, the nomogram proved to be an effective tool for predicting survival at 2- to 4-years.

Conclusion: The inflammation risk score has been identified as a significant prognostic factor for HBV-related HCC. The development of nomogram models has provided a practical and effective tool for determining the prognosis of patients affected by HBV-related HCC.

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignancies in the digestive system, accounting for one of the top five leading causes of cancer-related mortality in China. Notably, HCC accounts for over 75% of all liver tumors.[1] In terms of global cancer incidence rates for 2020, HCC ranks fifth in terms of patient prevalence, with a third-spot mortality rate. Furthermore, it is worth mentioning that the mortality rate among males is two to three times higher than females, indicating a significant gender disparity.[2] The prevalence of hepatitis B virus (HBV) infection is the primary etiological factor contributing to the development of HCC. Within the course of HCC disease progression, HBV infection combined with chronic inflammatory processes has the potential to result in the development of cirrhosis, paving the way for the appearance of malignant tumors. A fundamental work by Balkwill and Mantovani[3] and Singh et al.[4] revealed that a significant interplay exists between the host's immune response and the inflammatory environment,

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which is closely linked to the complex processes driving tumor cell development and metastasis. Their findings highlight a close relationship, indicating that the complex interplay between the host's immune system and the inflammatory condition significantly impacts the complex dynamics of tumor cell progression and dissemination.[3-5] The development and prognosis of HCC patients are closely related to inflammatory markers and the immune microenvironment.[6] Several scholarly investigations have been conducted to elucidate the complex relationship between inflammatory markers and their predictive value in prognosticating the fate of individuals with HCC. However, despite the amount of research, the characterization of inflammation markers and their relationship to HCC patients' prognoses remains a source of heated debate and conflicting viewpoints among the scientific community. This study aims to develop a clinical prognostic model for patients with moderate and advanced HBV-related HCC.[7-9] This model uses the inflammation risk score as a basic framework to comprehensively assess the disease's progression and prognosis.

MATERIALS AND METHODS

Case collection

Patients with moderate and advanced HBV-related HCC between January 2012 and 2022 were initially identified at a specific hospital. The inclusion criteria for this study were as follows: (a) the patient's diagnosis included the identification of moderate and advanced HBV-related HCC, categorized explicitly according to the Barcelona Clinic Liver Cancer (BCLC) staging system as stages B to D,[10] and (b) vigilant and consistent follow-up measures were implemented to ensure the accuracy and dependability of the patient's clinical status. The following criteria were used to exclude patients from the study: (a) patients with concurrent or additional malignancies; (b) patients with severe cardiovascular, neurological, pulmonary, or renal disorders; and (c) patients with incomplete or insufficient case information.

Our Institutional Review Board approved this study [Affiliated Hospital of Hunan Academy of Traditional Chinese Medicine; (approval number: 87, date: March 25, 2023)].

Clinicopathologic variables

The study included 17 variables: age at the time of diagnosis, smoking status, presence of distant metastasis, vascular invasion, Child-Pugh stage, use of transarterial chemoembolization (TACE), platelet count, lymphocyte count, neutrophil count, monocyte count, levels of albumin (ALB), hemoglobin (Hb), total bilirubin (TBIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alpha-fetoprotein (AFP).

The inflammatory markers were derived using the following calculations: the neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the lymphocyte count, the platelet-to-lymphocyte ratio (PLR) by dividing the total platelet count by the lymphocyte count, and the lymphocyte-to-monocyte ratio (LMR) as the ratio of the absolute lymphocyte count to the monocyte count.

The primary outcome measure in this study was overall survival (OS), which was defined as the time from the diagnosis of HCC and the incidence of death or the last follow-up, with the final follow-up deadline set for July 1, 2022.

Statistical analysis

The statistical analysis was conducted using SPSS 25.0 and R 4.2.1 software. The R packages used were time-dependent ROC (0.4), survival (3.3.1), survminer (3.3.6), rms (6.3-0), and ggplot2 (3.3.6). The analysis examined the relationship between inflammation and the nomogram risk score of PLR, NLR, and LMR. The nomogram risk score was calculated using the following formula:

$$Risk\ score = \sum_{i=1}^{n} Coefficients \times Variable\ values(i).$$

The variable values represented numerical values for the three inflammatory markers (PLR, NLR, and LMR). The coefficients were obtained by a multivariate Cox regression analysis, in which inflammatory markers were used as variables, and OS was the outcome. The Youden index was used to calculate the optimal cut-off values for the inflammation risk score, platelet count, lymphocyte count, neutrophil count, monocyte count, ALB, Hb, TBIL, AST, ALT, and AFP. This analysis determines the coefficients for each inflammatory marker. We then used the time-dependent ROC package to calculate partial ROC-related information and data at the optimal cut-off. Based on these cut-off values, the 174 patients were divided into two groups: high-risk and low-risk. Kaplan-Meier survival curves were developed to assess the survival differences between these groups, and the significance of the differences was determined using log-rank analysis. The area under the curve (AUC) value of the inflammation risk score was calculated using time-dependent ROC analysis. Based on the optimal cut-off values, the patients were divided into high-risk and low-risk groups based on their inflammation risk scores. Cox univariate and multivariate analyses were performed on the 174 case data to obtain the risk ratio (hazard ratio) and 95% confidence interval (CI) (95% CI) for each variable. Independent risk factors were found and used to develop a nomogram. The nomogram risk score was then determined using a specific formula for risk score calculation. The time-dependent ROC analysis was used to determine the optimal cut-off values for the nomogram risk score. Based on these cut-off values, the 174 patients were divided into two groups: high-risk and low-risk. Kaplan-Meier survival curves were then constructed, and log-rank analysis was used to compare survival rates between the two risk groups. Furthermore, time-dependent ROC analysis was used to evaluate the discriminative ability of the nomogram risk score, and a calibration curve was used to assess its calibrating ability. In these analyses, $p < 0.05$ was considered statistically significant.

RESULTS

Patients' baseline characteristics

The study included 174 patients diagnosed with moderate and advanced HBV-related HCC, 87.9% of whom were male. According to the BCLC staging system, 56.9% of the patients were classified as stage D. Distant metastases were observed in 114 patients, and 134

TABLE 1. Baseline Clinicopathological Characteristics of the Patients.

Variables		All (n = 174)	Parameter	Value (mean ± SD)/IQR (25^{th}-75^{th} percentile)
Sexual	Female	21 (12.1%)	Platelet	124.00 (77-187.5)
	Male	153 (87.9%)	Neutrophil	4.29 (2.96-6.16)
Smoking	No	98 (56.3%)	Lymphocyte	1.06 (0.765-1.44)
	Yes	76 (43.7%)	Monocyte	0.5 (0.34-0.69)
Tumor size (cm)	< 5	70 (40.2%)	ALB	33.66 (29.29-38.66)
	≥ 5	104 (59.8%)	AFP	241.98 (50.39-2,392.40)
Child-Pugh stage	A	84 (48.3%)	Hb	118.18 ± 22.11
	B	81 (46.6%)	AST	76 (40.70-153.00)
	C	9 (5.2%)	ALT	43 (25.10-77.00)
BCLC stage	B	37 (21.3%)	TBIL	21.01 (12.13-37.20)
	C	38 (21.8%)	NLR	4.09 (2.43-6.59)
	D	99 (56.9%)	PLR	110.33 (69.639-207.86)
TACE	No	82 (47.1%)	LMR	2.04 (1.35-3.16)
	Yes	134 (77%)		
Distant metastasis	No	114 (65.5%)		
	Yes	60 (34.5%)		
Vascular invasion	No	85 (48.9%)		
	Yes	89 (51.1%)		
Age (years)	≥ 60	55 (31.6%)		
	< 60	119 (68.4%)		

AFP, alpha-fetoprotein; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BCLC, Barcelona Clinic Liver Cancer; Hb, hemoglobin; IQR, interquartile range; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SD, standard deviation; TACE, transarterial chemoembolization; TBIL, total bilirubin.

patients underwent TACE treatment. Table 1 shows a comprehensive overview of the patients' baseline characteristics. Hb conforms to the normal distribution and is summarized as a value (mean ± standard deviation), whereas other variables do not conform to the normal distribution and are expressed as an interquartile range (25^{th}-75^{th} percentile).

Cut-off values of the inflammation risk score, ALB, AFP, Hb, AST, ALT, and TBIL for predicting the OS

The Youden index was used to calculate the optimal cut-off values for the inflammation risk score, platelet count, lymphocyte count, neutrophil count, monocyte count, ALB, Hb, TBIL, AST, ALT, and AFP. Table 2 shows the particular cut-off values, AUC, sensitivity, and specificity values for these variables.

Inflammation risk score

The inflammation risk score for PLR, NLR, and LMR was determined using a precise formula:

$$Risk\ score = \sum_{i=1}^{n} Coefficients \times Variable\ values\ (i).$$

The variable values represent the numerical values of the PLR, NLR, and LMR inflammatory markers. The coefficients were obtained by multivariate Cox regression analysis, with inflammatory markers as variables and OS as the outcome. The cohort of 174 patients was divided into high-risk and low-risk groups using a predetermined cut-off value of -0.033. Patients in the high-risk group had a risk score equal to or more than -0.033, whereas those in the low-risk group had a risk score less than -0.033. Log-rank statistical analysis was used to determine the survival differences between these two

TABLE 2. Cut-off Values of the Variables for Predicting Overall Survival.

Variables	Cut-off values	AUC	Sensitivity	Specificity
Inflammation risk score	-0.033	60.2	60.2	63.2
ALB (g/l)	32.1	67.5	54.1	77.6
AFP (ng/ml)	69.11	59.7	79.6	38.2
ALT (U/l)	39.5	60.3	65.3	55.3
AST (U/l)	57	66.1	70.4	59.2
TBIL (μmol/l)	16.66	62.3	72.4	51.3
Hb (g/l)	114	62.0	54.1	69.7

AUC, area under the curve; ALB, albumin; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; Hb, hemoglobin.

groups. Kaplan-Meier survival curves were then plotted to show the survival rates of the high-risk and low-risk patient groups. The analysis yielded notable findings. The median survival time for the low-risk group was 431 days (95% CI: 294-669), whereas for the high-risk group, it was 201 days (95% CI: 148-271). The difference in survival outcomes was statistically significant ($p = 0.001$), as shown in Figure 1. Using the time-dependent ROC analysis, the AUC values for the inflammation risk score were calculated at various time intervals. Specifically, the AUC values for 2- to 4-years were 0.621, 0.629, and 0.612, respectively. These values, shown in Figure 2, show the predictive capability of the inflammation risk score throughout the indicated time periods.

Univariate and multivariate Cox analyses of factors for the prediction of OS of moderate and advanced HBV-related HCC patients

The Cox analysis revealed significant relationships ($p < 0.05$) between OS and various factors, including the inflammation risk score, ABL, AFP, BCLC stage, AST, Child-Pugh stage, TACE treatment, distant metastasis, and vascular invasion. These findings, shown in Figure 3, highlight the prognostic relevance of these factors in HBV-related HCC patients.

Furthermore, the multivariate analysis identified independent prognostic factors for HBV-related HCC patients. The inflammation risk score, BCLC stage, AFP, and TACE treatment were significant independent OS predictors ($p < 0.05$). These results highlight the importance of these factors in determining the prognosis of HBV-related HCC patients and the potential clinical implications.

Development of the nomogram

Based on the results of the multivariate analysis, the inflammatory risk score stratification, AFP, BCLC staging, and TACE treatment were selected as crucial factors for constructing a nomogram. This nomogram aims to precisely predict the 2- to 4-years survival probability for patients with moderate and advanced HBV-related HCC. By integrating these variables, the nomogram provides an effective tool for clinicians to estimate survival probabilities and make informed decisions about patient management. Figure 4 shows the nomogram, which may be used for prognostic evaluation in clinical practice.

Stratification of nomogram risk score

The nomogram risk score was determined using a risk score calculation formula. The risk score is calculated using the following formula:

$$Risk\ score = \sum_{i=1}^{n} Coefficients \times Variable\ values(i).$$

where the variables include AFP, BCLC staging, and TACE treatment. The coefficients are the coefficients of the last three variables identified using a multivariate Cox proportional hazards model. The 174 patients were classified as high-risk (cut-off value of more than or equal to -0.720) and low-risk (cut-off value of less than -0.720). The log-rank statistical analysis was used to assess the survival rates between groups, and Kaplan-Meier survival curves were plotted.

The survival time analysis of the high-risk and low-risk stratified groups yielded compelling results. The median survival time for the low-risk group was 524 days (95% CI: 380-629), whereas the high-risk group had 102 days (95% CI: 77-142). The difference in survival outcomes was statistically significant ($p < 0.001$). Notably, the risk stratification based on the nomogram risk score performed better than the single inflammation risk score stratification

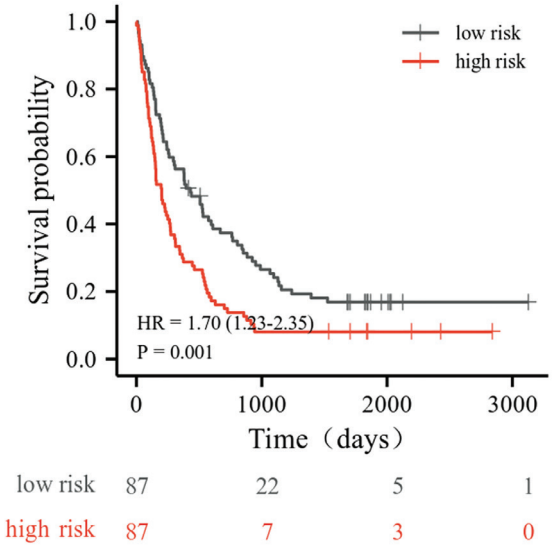

FIG. 1. Kaplan-Meier survival curve of the inflammation risk score.

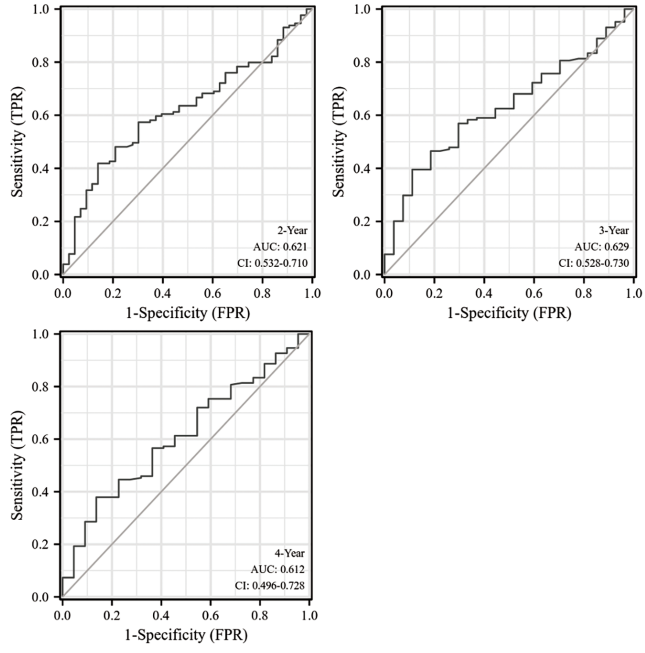

FIG. 2. Time-dependent area under the curve of the inflammation risk score.

Characteristics	HR(95% CI) Univariate analysis	P value Univariate analysis	HR(95% CI) Multivariate analysis	P value Multivariate analysis
Inflammation Risk Score		0.008		0.005
high risk	1.546 (1.121-2.133)		1.655 (1.165-2.352)	
low risk	0.647 (0.469-0.892)		0.604 (0.425-0.858)	
Albumin(g/L)		<0.001		0.213
<32.1	1.757 (1.266-2.438)		1.335 (0.847-2.105)	
>32.1	0.569 (0.410-0.790)		0.749 (0.475-1.180)	
AFP(ng/ml)		0.007		0.042
>69.11	1.662 (1.145-2.412)		1.494 (1.015-2.199)	
<69.11	0.602 (0.415-0.873)		0.669 (0.455-0.985)	
BCLC stage		<0.001		
B	0.256(0.161-0.407)		0.395 (0.228-0.685)	<0.001
C	2.698 (1.563-4.656)		1.657 (0.891-3.079)	0.110
D	4.665 (2.902-7.500)		3.292 (1.850-5.858)	<0.001
ALT(U/L)		0.345		
>39.5	1.168 (0.846-1.611)			
<39.5	0.856 (0.621-1.181)			
AST(U/L)		0.007		0.251
>57	1.560 (1.126-2.162)		1.247 (0.856-1.818)	
<57	0.641 (0.462-0.888)		0.802 (0.550-1.169)	
TBIL(umol/L)		0.009		0.786
>16.66	1.565 (1.120-2.188)		1.055 (0.718-1.549)	
<16.66	0.639 (0.457-0.893)		0.948 (0.646-1.392)	
Hb(g/L)		0.022		0.982
>114	0.687 (0.497-0.948)		1.005 (0.667-1.513)	
<114	1.456 (1.055-2.011)		0.995 (0.661-1.499)	
Age		0.631		
<60	1.087 (0.772-1.532)			
>60	0.920 (0.653-1.295)			
Smoking		0.459		
no	1.130 (0.817-1.563)			
yes	0.885 (0.640-1.224)			
Sexual		0.405		
male	1.233 (0.753-2.019)			
female	0.811 (0.495-1.328)			
Tumor size		0.647		
>5cm	0.927 (0.669-1.284)			
<5cm	1.079 (0.779-1.495)			
Child-Pugh stage				
A	0.693 (0.503-0.955)	0.025	1.166 (0.799-1.701)	0.425
B	1.348 (0.969-1.874)	0.076	0.776 (0.529-1.139)	0.195
C	3.630 (1.779-7.404)	<0.001	1.227 (0.542-2.776)	0.624
TACE		0.001		0.046
no	1.702 (1.234-2.346)		1.443 (1.007-2.067)	
yes	0.588 (0.426-0.810)		0.693 (0.484-0.993)	
Distant metastasis		<0.001		0.174
no	0.518 (0.370-0.725)		0.768 (0.524-1.124)	
yes	1.930 (1.378-2.702)		1.303 (0.890-1.908)	
Vascular invasion		<0.001		0.226
no	0.465 (0.334-0.647)		0.787 (0.534-1.160)	
yes	2.152 (1.546-2.995)		1.271 (0.862-1.874)	

FIG. 3. Forest graph of the univariate analysis.
HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; ALB, albumin; BCLC, Barcelona Clinic Liver Cancer; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; Hb, hemoglobin; TACE, transarterial chemoembolization

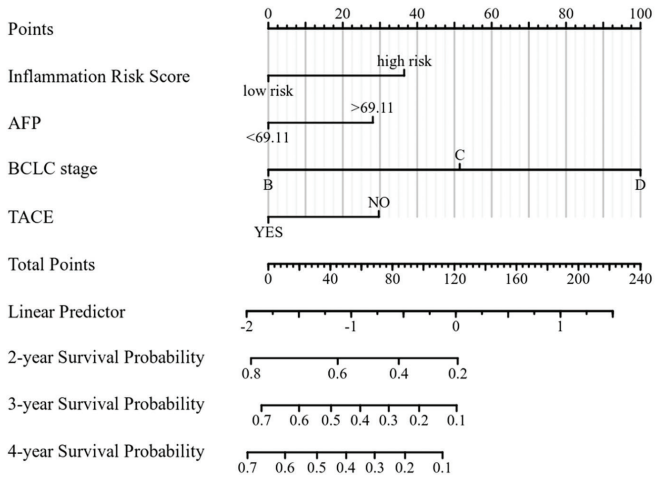

FIG. 4. Nomogram of the 2- to 4-years survival probabilities for patients diagnosed with moderate and advanced hepatitis B virus-related hepatocellular carcinoma.
AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; TACE, transarterial chemoembolization

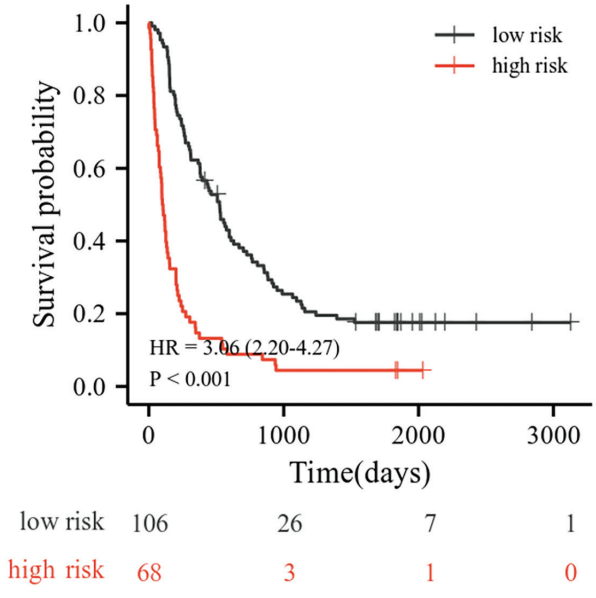

FIG. 5. Kaplan-Meier survival curve of the nomogram risk score.

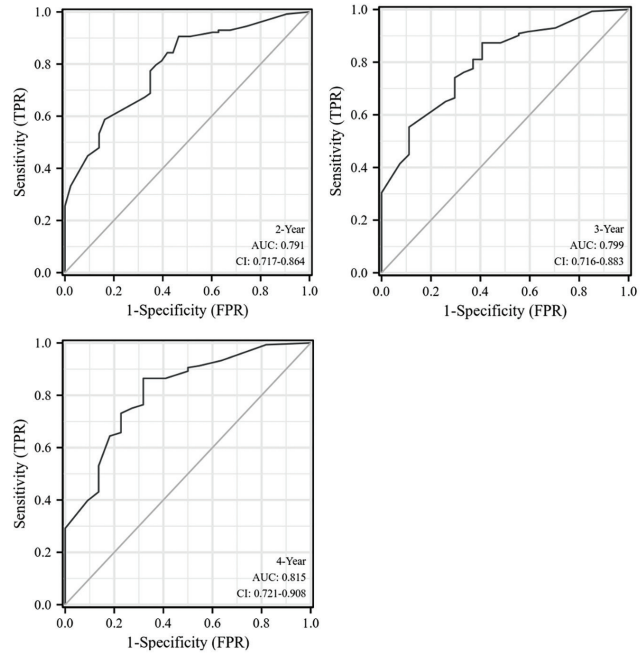

FIG. 6. Time-dependent area under the curve.

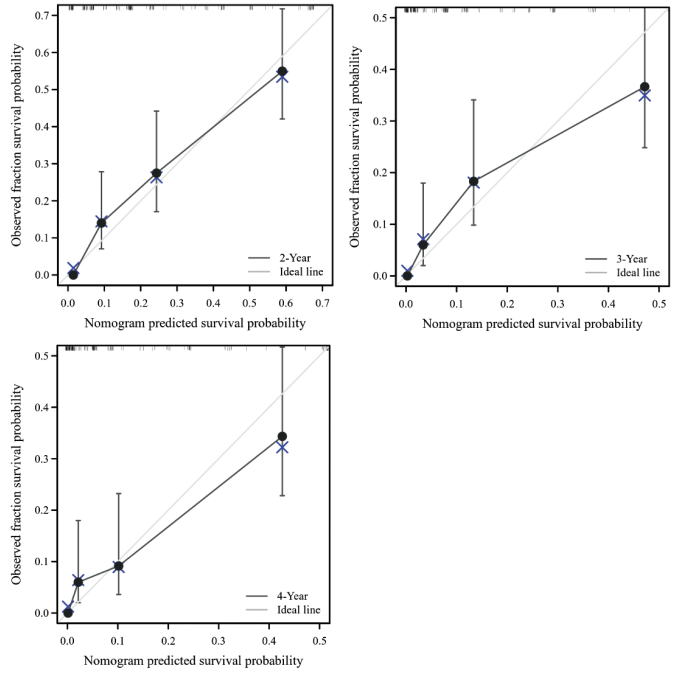

FIG. 7. Calibration curve.

(Figure 5). These findings show the improved predictive ability of the nomogram risk score in patient stratification and survival outcomes.

Validation of nomogram

The time-dependent ROC analysis yielded notable results. The AUC values for the nomogram risk score at 2- to 4-years were 0.791, 0.799, and 0.815, respectively. These values show the predictive effectiveness of the nomogram in anticipating survival outcomes at various time intervals. The nomogram outperformed the single inflammation risk score (Figure 6).

The calibration curve of the nomogram confirmed its reliability in prognosticating patient survival at 2- to 4-years. The curve indicated a high level of concordance between predicted and observed survival probabilities, demonstrating the accurate predictive ability of the nomogram. Figure 7 shows the calibration curve, demonstrating its usefulness in predicting patient survival outcomes. These findings highlight the improved predictive ability of the nomogram, making it a valuable tool for clinicians in assessing and forecasting patient survival over varying time frames.

DISCUSSION

HCC is a highly prevalent and fatal cancer worldwide. The primary cause of HCC is HBV infection. At present, HCC treatment options include surgical resection, liver transplantation, TACE, chemotherapy, radiotherapy, targeted therapy, and immunotherapy. Early-stage HCC patients are typically treated with surgical resection or liver transplantation, whereas those with moderate or advanced HCC are treated with other treatment methods. Despite the diversity of available treatments, HCC continues to have high rates of recurrence and mortality. Existing worldwide prognostic systems, such as the BCLC and tumor, node, and metastasis (TNM) stages, provide valuable prognostic information, but their clinical application is limited. It is important to use biomarkers to predict patient prognosis to provide prompt medical interventions to high-risk HCC patients and reduce mortality rates. Using biomarkers, clinicians may be able to identify patients at high-risk of disease progression and change treatment strategies appropriately. The use of reliable prognostic biomarkers provides significant potential for improving patient outcomes and directing tailored therapeutic interventions for HCC.

Several patients develop tumors as a result of persistent chronic inflammatory stimulation. Within the complex environment of the tumor microenvironment, inflammatory cells emerge as vital contributors, controlling tumor survival, persistent proliferation, and insidious metastasis.[11] Furthermore, during the complex process of tumor growth, the body continually produces a dynamic array of immune responses intrinsically linked to cancer development.[12] Thus, the inflammatory response plays a critical role in the progression of HCC.[13] NLR, PLR, and LMR are easily accessible markers of inflammation that may be obtained during routine blood tests. NLR is the ratio of neutrophils to lymphocytes. Previous studies have shown that neutrophils could initiate and develop the tumor microenvironment, but lymphocytes can inhibit tumor cell proliferation and migration.[14] Thus, an increased NLR indicates tumor progression. NLR is an independent risk factor for patients with HCC, with an increase in NLR indicating poorer OS for HCC, consistent with previous study.[15] The NLR has been extensively validated as a predictor of recurrence and prognosis for HCC.[16-19] The PLR represents the ratio of platelets to lymphocytes. Platelets have crucial roles in sensing, monitoring, and transmitting information, and they are closely linked to the development and progression of neoplasms. Platelets can selectively bind to proteins released by cancer cells and integrate tumor-derived microvesicles containing RNA, which promotes tumorigenesis and progression.[20] Tumor cells and platelets interact bidirectionally: first, tumor cells can damage the vascular endothelium, activate platelets, trigger the coagulation system, and cause thrombus formation; second, the tripartite interaction among platelets, vascular walls, and tumor cells results in tumor cell adhesion to the vascular wall and an increase in malignant tumor marrow proliferation. Tumor cells produce thrombopoietin, which causes an increase in platelets. Increased platelet counts and PLR indicate a hypercoagulable condition in the blood, which can promote tumor thrombosis.[21] LMR is the ratio of lymphocytes to monocytes. According to research, an excess of circulating monocytes congregates and differentiates into tumor-associated macrophages within the tumor stroma, promoting tumor invasion and metastasis and inhibiting the function of anti-tumor immune cells. Therefore, a decrease in lymphocytes, an increase in monocytes, and a reduction in LMR promote tumor cell invasion and metastasis.[22] Rungsakulkij et al.[23] showed the significant prognostic value of NLR, PLR, and LMR in predicting microvascular invasion in histopathological evaluations.[24] Furthermore, these markers have received widespread recognition and substantial validation as reliable predictors of recurrence and survival in HCC.[25-29] Thus, it is crucial to monitor changes in inflammatory markers of NLR, PLR, and LMR during patient management and actively address and modulate the inflammatory microenvironment and immune responses in patients, as such interventions show promise for improving patient survival outcomes. As is widely known, TACE plays an essential role in treating HCC. Our findings revealed that TACE treatment is an important prognostic factor. Therefore, it is highly recommended to consider TACE treatment, unless contraindications exist, due to its potential impact on improving patient prognosis. AFP is a remarkably sensitive biomarker for the diagnosis of HCC. Higher serum AFP levels were associated with shorter survival periods in HCC patients, indicating a prognostic relationship with patient outcomes. Patients with short survival periods had higher levels of AFP than their longer-surviving counterparts, and increased AFP is an independent risk factor for shorter survival in such patients.[30] In line with our study, Yang et al.[2] identified AFP as an independent prognostic factor for HCC, reinforcing its significance in our findings. Therefore, it is imperative to conduct regular AFP re-evaluations during the treatment period, which not only evaluates the efficacy of the interventions but also provides indications of potential improvement in patient prognosis.

The study focused on the inflammatory risk scores of NLR, PLR, and LMR to construct a prognosis model for the survival prediction of patients with moderate and advanced HBV-related HCC. Initially, a dataset of 174 patients was obtained from the particular hospital. The inflammatory risk scores of NLR, PLR, and LMR were then calculated using the collected data. The cohort of 174 patients was divided into two groups: high-risk and low-risk, with a median survival period of 431 days for the low-risk group and 201 days for the high-risk group. Furthermore, the time-dependent ROC analysis AUC values were 0.621, 0.629, and 0.612 for the 2- to 4-years periods, respectively. Further analysis using univariate and multivariate Cox regression revealed independent prognostic factors, such as the inflammation risk score, AFP, BCLC stage, and TACE treatment.

A prognostic model was then developed by constructing a nomogram using these factors. The nomogram is a valuable tool for predicting patient prognosis, providing tailored risk assessments, and facilitating better decision-making in clinical practice. The cohort of 174 patients was divided into high-risk and low-risk groups, resulting in a significant difference in median survival periods, with the low-risk group having a median survival period of 524 days and the high-risk group having 102 days. Furthermore, AUC values showed that the nomogram risk score outperformed the single inflammation risk score in terms of predictive ability. The AUC values for the nomogram risk score were 0.791, 0.799, and 0.815 for the 2- to 4-years intervals, respectively. These findings support the superior discrimination and prognostic efficacy of the nomogram risk score over the single inflammation risk score.

The calibration curve validates the predictive efficacy of the constructed model. In this case, the calibration curve showed that the model effectively predicts the survival prognosis at 2- to 4-years intervals. Traditionally, the globally recognized BCLC and TNM stage systems have been the dominant methods for prognostic prediction in HCC. However, clinical observations have revealed that patients with the same stage often have different survival prognoses. This discrepancy might be due to the absence of some factors, including age, gender, and the inflammatory microenvironment, in the BCLC and TNM stage systems. As a result, the present study combined inflammatory risk scores and additional variables to construct a comprehensive prognosis nomogram. This nomogram aims to improve the prediction of survival prognosis for patients with HCC by considering a wide variety of significant factors, providing clinicians with tools for prognosis evaluation.

In conclusion, our study identified significant prognostic factors for patients with moderate and advanced HBV-related HCC, such as the inflammation risk score, AFP, BCLC stage, and TACE treatment. The nomogram developed using these factors shows promising predictive efficiency. However, it is important to emphasize that the model could not be validated due to a lack of an adequate sample size. Therefore, further external validation is necessary to assess and confirm the effectiveness of the developed model in our study.

Ethics Committee Approval: OOur Institutional Review Board approved this study [Affiliated Hospital of Hunan Academy of Traditional Chinese Medicine; (approval number: 87, date: March 25, 2023)].

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authorship Contributions: Concept- X.Y., Design- R.Y., Data Collection or Processing- H.C., Analysis or Interpretation- R.Y., Literature Search- W.P., P.Z.; Writing- K.L., P.X.

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