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Original Article

A novel prognostic scoring system to predict portal vein tumor thrombosis in patients with hepatitis B virus-associated hepatocellular carcinoma

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Abstract: Purpose: Hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT) is associated with a poor prognosis for HCC patients. Herein we aimed to establish a scoring system to predict the risk of PVTT formation in hepatitis B virus (HBV)-associated HCC. Methods: A total of 848 patients from the Henan Province Traditional Chinese Medicine (TCM) Hospital with HCC were included in the study. Among them, 403 with and 445 without PVTT were retrospectively analyzed to identify the risk factors for PVTT formation, using a novel scoring system to predict the occurrence of PVTT in HBV-associated HCC patients. The scoring system was validated using clinical data from the First Affiliated Hospital of Henan University of TCM. Significant findings: The Cox proportional-hazard regression model revealed that gender, tumor size, the neutrophil-lymphocyte ratio, and alpha-fetoprotein and C-reactive protein concentrations were dependent clinical prognostic factors for PVTT, which were included in the final scoring model for PVTT prediction (AUC, 0.858; 95% CI: 0.832 to 0.881). The scoring model ranked HCC patients into 3 risk grades. A sensitivity analysis for validation of the scoring system was performed on 489 patients with HBV-related HCC. The proportion of patients in each grade was not significantly different. Conclusions: The study established a risk warning system for PVTT prediction in HCC patients. More substantial clinical data will be necessary to confirm these findings.

Keywords: Carcinoma, hepatitis B virus, hepatocellular, portal vein, thrombosis

Introduction

Hepatocellular carcinoma (HCC) is the third most commonly occurring cancer worldwide [1] and is most prevalent in Asia and Africa. Hepatitis B virus (HBV)-induced chronic hepatocyte damage contributes to HCC [1]. Due to widespread chronic HBV infection, HBV is responsible for half of the cases of HCC. When HCC cells invade the portal venous system, this can lead to the formation of a portal vein tumor thrombus (PVTT). PVTT is a sign of advanced-stage cancer and the median survival time of HCC patients with PVTT is circa 3 months without treatment [2].

According to the Barcelona Clinic Liver Cancer (BCLC) classification, which are widely adopted guidelines in Europe and America, HCC with PVTT is ranked as BCLC Stage C, with patients being recommended to receive treatment with the vascular endothelial growth factor (VEGF) inhibitor sorafenib, as well as other non-surgical treatments as first-line therapy [3]. However, a randomized controlled trial (RCT) reported that the median survival time after sorafenib treatment was only 6.5 months [4]. Thus, expert Chinese consensus recommended a more aggressive therapeutic approach such as hepatectomy for HCC patients with PVTT, which was found to prolong the median survival time to between 8 months and 22 months [4, 5].

It has been reported that the type of PVTT is one of the risk factors for mortality after surgical resection in HCC patients [6], and that

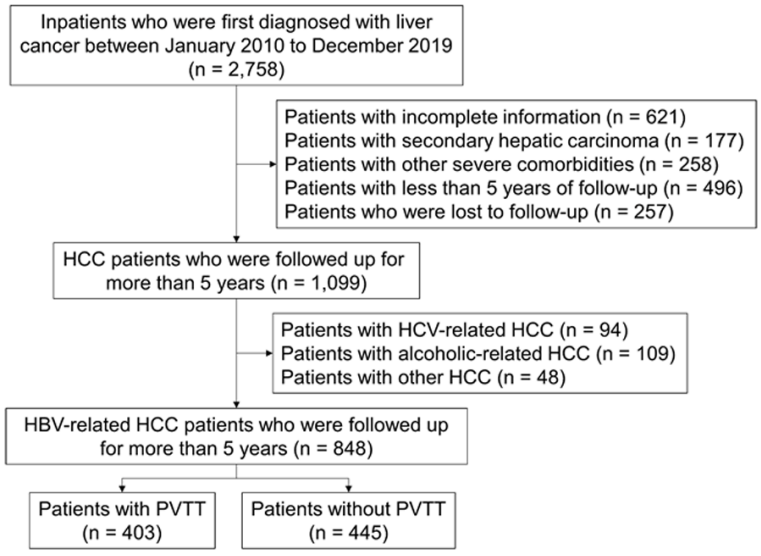

Figure 1. Flow chart of the study cohort. HCC, hepatocellular carcinoma; PVTT, portal vein tumor thrombus.

aggressive treatment could benefit selected HCC patients with PVTT. At present, only two classifications of PVTT are recognized, namely Cheng's and the Japanese V_p classifications [7]. However, no consensus has been reached on whether or not surgery should be conducted according to either classification standard. It should be noted that PVTT is asymptomatic and is always detected using imaging techniques [8]. Thus, more attention should be paid to potential early warning signs of PVTT.

The present study aimed to identify the risk factors that contribute to the formation of PVTT, using clinical data of PVTT and non-PVTT HCC cohorts of patients and to establish an early risk and warning scoring system for PVTT using risk factors detected non-invasively to facilitate clinical diagnosis and treatment. As PVTT is a common complication of liver cancer, earlier diagnosis of PVTT is likely to improve the prognoses of HBV-related HCC patients.

Materials and methods

Study population

This retrospective study was conducted on the clinical data of HCC patients with or without PVTT who had been admitted to Henan Province TCM Hospital. The requirement of informed consent was waived because all personal identifiers were removed before data collection. The study was approved by the ethics committee of Henan TCM Hospital (approval number/date: 2021-12-08).

The flow chart of the study is shown in **Figure 1**. A total of 2,758 patients with HBV-related primary HCC were admitted to the Henan Province TCM Hospital from January 2010 to December 2019. HCC was diagnosed according to the diagnostic criteria for HCC of the American Association for the Study of Liver Diseases (AASLD) [9], and the diagnosis of PVTT in patients with HCC was based on combined imaging studies, including B ultrasound, color Doppler, enhanced computer tomography (CT) scans, magnetic resonance imaging (MRI) and Digital Subtraction Angiography (DSA) [10]. Further stratification showed that of the 2,758 patients, 613 underwent conservative medical therapy, 699 received transcatheter arterial chemoembolization (TACE), 152 received radiofrequency ablation (RFA), 951 received TACE combined with RFA, 128 underwent hepatectomy, 85 underwent hepatectomy combined with TACE + RFA, 89 underwent hepatectomy combined with TACE and 41 underwent hepatectomy combined with RFA.

The inclusion criteria were: (1) HBV-related HCC patients between the ages of 18 and 85 years; (2) male or female patients.

The exclusion criteria were: (1) patients with infection from another hepatotropic virus (hepatitis A, C, D, E) or non-hepatotropic virus co-infection; (2) patients with severe baseline diseases of the heart, lung, kidney, brain, blood and other important organs; (3) patients with mental illness; (4) metastatic liver cancer; (5) incomplete clinical data; and (6) patients not having complete 5-year follow-up data.

Based upon the inclusion and exclusion criteria, of 2,758 patients, 621 had incomplete clinical data, 177 had secondary hepatic carcinoma, 258 had severe comorbidities, 94 had HCV-related HCC, 109 had alcoholic hepatitis,

257 were lost to follow-up and 496 had follow-up periods < 5 years. Thus, a total number of 848 patients met the inclusion criteria, among whom 403 patients suffered with PVTT during the previous 5 years and 445 did not.

Population validation

To validate further the proposed scoring system, 489 patients with HBV-related HCC, diagnosed in the First Affiliated Hospital of Henan University of TCM from January 2012 to December 2019, were randomly selected for the prediction of the occurrence of PVTT.

R software was used to construct the nomogram model. The Hosmer-Lemeshow goodness-of-fit test, and the calibration curve were employed to evaluate the performance of the nomogram model.

Data collection

The clinical data at the time of diagnosis for all patients with HBV-related primary HCC were collected as follows: (1) baseline information including age, gender, smoker, alcohol drinker, past and family histories; (2) data from imaging studies of CT, ultrasonography and MRI; (3) laboratory indicators from routine blood tests (white blood cell [WBC], hemoglobin [HGB], the neutrophil-to-lymphocyte ratio [NLR], platelet [PLT]), liver and kidney functions (alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma-glutamyl transferase [GGT], total bilirubin [TBIL], albumin [ALB], albumin/globulin [A/G], creatinine [Cr]), fasting blood glucose (Glu), triglyceride (TC), coagulation function, inflammation index (C-reactive protein [CRP]), prothrombin activation (PTA), virological index (HBV-DNA) and tumor marker (alpha fetoprotein [AFP]).

Statistical analysis

Quantitative variables are presented as the median and 25% percentile and 75% percentile ([Q1, Q3] 25th, 75th percentile) and were compared using the Wilcoxon rank sum test. For comparisons between data presented as frequencies, a χ^2 test was employed.

Cox regression analysis was used to analyze multiple risk factors for survival. Multiple factors with a single factor $P < 0.05$ were included in the multifactorial regression model. Hazard ratio (HR) values were converted into integers to score and accumulate. Excel was used to plot a heat map and risk groupings. MedCalc was used to draw the receiver operating characteristic (ROC) curve of the model and to evaluate it, and Graphpad was used to construct the Kaplan-Meier curve of tumor thrombus in the different groups of patients. The survival times were followed-up and the survival curves of different risk groups were plotted and compared with the log-rank test results. SPSS ver. 22.0 was used for all statistical analyses. A *P*-value < 0.05 was considered to be a significant finding.

Results

Baseline

The baseline characteristics of the model cohort are shown in **Table 1**. Of note, the PVTT group had a significantly higher proportion of males (83.87 vs. 68.76%, $P < 0.001$) and also exhibited significantly higher levels of NLR (3.08 vs. 1.83, $P < 0.001$), CRP (13.00 vs. 3.20 mg/L, $P < 0.001$) and GGT (70.90 vs. 42.70 U/L, $P < 0.001$) than the non-PVTT group. The PVTT group had lower levels of ALB (34.30 vs. 37.00 g/L, $P < 0.001$), TC (0.77 vs. 0.80 mmol/L, $P = 0.002$), the proportion of patients with AFP ≤ 350 ng/mL (68.98 vs. 90.11%, $P < 0.001$) and a lower proportion of patients with tumor size < 5 cm (56.58 vs. 84.94%, $P < 0.001$) than the non-PVTT group.

Univariate and multivariate analysis of PVTT predictors in HBV-related primary hepatic carcinoma

Predictors of PVTT were assessed using forward stepwise Cox proportional hazards regression analysis. The baseline variables with significance between two groups, included gender, NLR, tumor size, AFP and CRP, which were screened as prognostic factors using univariate analysis, which identified gender ($P < 0.001$), alcohol history ($P = 0.006$), smoking history ($P = 0.007$), the Child-Pugh score ($P < 0.001$), single/multiple tumors ($P = 0.001$), tumor size ($P < 0.001$), treatment ($P = 0.001$), WBC ($P = 0.005$), HGB ($P = 0.010$), PLT ($P = 0.005$), NLR ($P < 0.001$), Glu ($P = 0.001$), ALT ($P = 0.009$), AST ($P < 0.001$), ALB ($P < 0.001$), A/G ($P = 0.001$), GGT

Table 1. Baseline of characteristics of patients with and without PVTT in HBV related HCC

Variable		None-PVTT (*n* = 445)	PVTT (*n* = 403)	*P*-value
Gender	n			0.001*
Male		306	338	
Female		139	65	
Age (years)	Median [Q1, Q3]	56 [50-61]	55 [49-61]	0.393
Alcohol history	n			0.018*
Yes		120	139	
No		325	264	
Smoking history	n			0.006*
Yes		142	165	
No		303	238	
WBC (× 10^9/L)	Median [Q1, Q3]	4.07 [2.92-5.22]	4.54 [3.13-6.39]	< 0.001
HGB (g/L)	Median [Q1, Q3]	129.90 [111.70-142.40]	122.50 [106.95-139.05]	0.002*
NLR	Median [Q1, Q3]	1.83 [1.36-2.66]	3.08 [2.07-5.12]	< 0.001*
PLT (× 10^9/L)	Median [Q1, Q3]	79.00 [54.00-124.30]	90.40 [56.20-146.70]	0.020*
Cr (μmol/L)	Median [Q1, Q3]	66.00 [55.00-76.70]	65.10 [58.00-76.10]	0.313
Glu (mmol/L)	Median [Q1, Q3]	5.42 [4.91-6.51]	5.81 [5.07-7.49]	< 0.001
ALT (U/L)	Median [Q1, Q3]	31.10 [21.60-45.90]	34.50 [24.05-59.10]	0.002*
AST (U/L)	Median [Q1, Q3]	36.00 [26.80-55.30]	46.00 [31.30-73.35]	0.001*
TBIL (μmol/L)	Median [Q1, Q3]	17.80 [12.70-29.40]	20.70 [14.20-36.20]	0.001*
ALB (g/L)	Median [Q1, Q3]	37.00 [31.50-40.90]	34.30 [30.30-38.80]	< 0.001*
A/G	Median [Q1, Q3]	1.20 [1.00-1.40]	1.10 [0.80-1.30]	< 0.001
GGT (U/L)	Median [Q1, Q3]	42.70 [25.10-74.30]	70.90 [39.00-138.25]	< 0.001*
TC (mmol/L)	Median [Q1, Q3]	0.80 [0.64-1.05]	0.77 [0.59-0.92]	0.002*
PTA (%)	Median [Q1, Q3]	76.00 [63.50-91.00]	72.00 [59.50-84.60]	< 0.001*
CRP (mg/L)	Median [Q1, Q3]	3.20 [3.20-8.10]	13.00 [3.20-17.70]	< 0.001*
AFP (ng/mL)	n			< 0.001*
≤ 350		401	278	
> 350		44	125	
Single/multiple tumor	n			0.001*
Single		287	217	
Multiple		158	186	
Child-Pugh score	n			< 0.001*
A		247	169	
B		146	162	
C		52	72	
Tumor size (cm)	n			< 0.001*
< 5		378	228	
≥ 5		67	175	
HBV-DNA (IU/mL)	n			0.059
< 500		187	181	
≥ 500		258	222	

AFP, alpha fetoprotein; A/G, albumin/globulin; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; Glu, fasting blood glucose; HBV, hepatitis B virus; HGB, hemoglobin; [Q1, Q3], [25% percentile, 75% percentile]; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; PTA, prothrombin activation; PVTT, portal vein tumor thrombus; TBIL, total bilirubin; TC, triglyceride; WBC, white blood cell. *P-value < 0.05.

(P < 0.001), PTA (P = 0.024), TC (P < 0.001), AFP (P < 0.001), HBV-DNA (P = 0.008) and CRP (P < 0.001) as significant prognostic factors (**Table 2**).

Table 2. Univariate and multivariate Cox regression analysis of PVTT in HBV-related HCC

Variable		Univariate analysis			Multivariate analysis		
		HR	95% CI	*P*-value	Adjusted HR	95% CI	*P*-value
Gender	Male/female	1.901	[1.458-2.481]	< 0.001*	2.151	[1.592-2.909]	< 0.001*
Age (years)	≥ 50	0.995	[0.985-1.005]	0.321			
Alcohol history	Yes/no	1.333	[1.086-1.638]	0.006*			
Smoking history	Yes/no	1.316	[1.079-1.605]	0.007*			
Hypertension	Yes/no	0.868	[0.687-1.096]	0.235			
Diabetes	Yes/no	1.036	[0.826-1.300]	0.760			
Child-Pugh score	A/B/C	1.279	[1.124-1.455]	< 0.001*			
Single/multiple tumor	Single/multiple	1.381	[1.134-1.682]	0.001*			
Tumor size (cm)	≥ 5	2.865	[2.349-3.493]	< 0.001*	2.520	[2.013-3.153]	< 0.001*
Treatment	Conservative treatment/minimally invasive surgery/ resection/minimally invasive surgery + resection	0.735	[0.639-0.847]	0.001*			
WBC (× 10^9/L)		1.331	[1.091-1.624]	0.005*			
NLR	≥ 1.91	3.410	[2.648-4.391]	< 0.001*	2.400	[1.831-3.145]	< 0.001*
HGB (g/L)	> 120	0.773	[0.635-0.940]	0.010*			
PLT (× 10^9/L)	> 130	1.329	[1.091-1.617]	0.005*			
Cr (μmol/L)	> 88.2	1.190	[0.885-1.600]	0.250			
Glu (mmol/L)	> 6.1	1.396	[1.145-1.702]	0.001*			
ALT (U/L)	> 40	1.301	[1.067-1.585]	0.009*			
AST (U/L)	> 40	1.747	[1.431-2.133]	< 0.001*			
TBIL (μmol/L)	> 17.1	1.201	[0.983-1.468]	0.073			
ALB (g/L)	> 35	0.686	[0.564-0.835]	< 0.001*			
A/G	> 1	0.714	[0.586-0.869]	0.001*			
GGT (U/L)	> 45	1.947	[1.583-2.394]	< 0.001*			
TC (mmol/L)	> 0.78	0.619	[0.476-0.806]	< 0.001*			
PTA (%)	> 70	0.797	[0.655-0.970]	0.024*			
AFP (ng/mL)	> 350	2.875	[2.324-3.555]	< 0.001*	2.304	[1.810-2.934]	< 0.001*
CRP (mg/L)	> 5	5.024	[4.101-6.155]	< 0.001*	4.136	[3.278-5.219]	< 0.001*
HBV-DNA (IU/mL)	> 500	1.340	[1.079-1.644]	0.008*			

AFP, alpha fetoprotein; A/G, albumin/globulin; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; Glu, fasting blood glucose; HBV, hepatitis B virus; HGB, hemoglobin; HR, hazard ratio; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; PTA, prothrombin activation; PVTT, portal vein tumor thrombus; TBIL, total bilirubin; TC, triglyceride; WBC, white blood cell. *P-value < 0.05.

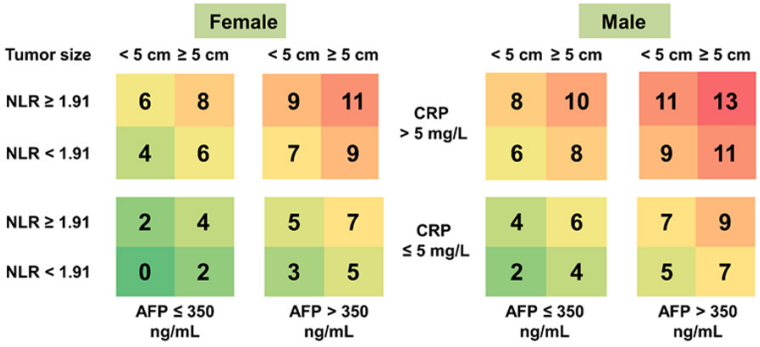

Figure 2. Definition of scoring system of PVTT prediction. AFP, alpha fetoprotein; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PVTT, portal vein tumor thrombus.

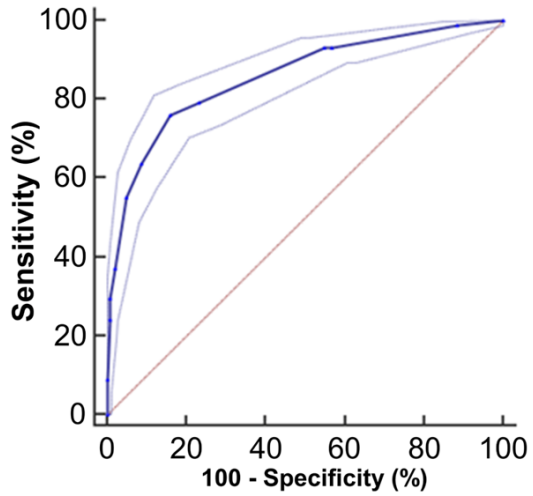

Figure 3. Receiver-operating characteristic curve of the prediction model.

Next, multivariate analysis was conducted, which confirmed that only gender ($P < 0.001$, HR: 2.151, 95% CI: [1.592-2.909]), tumor size ($P < 0.001$, HR: 2.520, 95% CI: [2.013-3.153]), NLR ($P < 0.001$, HR: 2.400, 95% CI: [1.831-3.145]), AFP ($P < 0.001$, HR: 2.304, 95% CI: [1.810-2.934]) and CRP ($P < 0.001$, HR: 4.136, 95% CI: [3.278-5.219]) remained as predictors of PVTT.

Establishment of an early risk and warning scoring system for PVTT in HBV-related primary HCC

The scoring system proposed for PVTT was based on the results of multivariate regression shown in **Figure 2**, which are detailed as male and NLR ≥ 1.91. Tumor sizes ≥ 5 cm were each assigned a value of 2; AFP > 350 ng/mL was given the value 3; CRP > 5 mg/L 4 and other variables including female, tumors < 5 cm, NLR < 1.91, AFP < 350 ng/mL and CRP < 5 mg/L values of 0. Based on this scoring system, the PVTT risk was stratified as low-risk: total score 0-4, medium-risk: total score 5-8 and high-risk: total score 9-13. The AUC of the model was 0.858 (95% CI: 0.832 to 0.881, **Figure 3**).

Prediction of survival in HCC patients with PVTT using the scoring system

K-M survival analysis with a log-rank test was performed for the cohort of patients with PVTT. As shown in **Figure 4**, the high-risk group exhibited a significantly higher incidence of PVTT formation, with the low-risk group tended to have the lowest incidence of PVTT. The total rank score was significantly associated with the incidence of PVTT formation in HCC patients (log-rank *P*-value < 0.001), and a higher total score indicated a higher probability of PVTT formation. Taken together, these results indicated that the scoring system could potentially serve as a prediction method for PVTT formation.

Since all included cohorts were followed up for at least 5-years, the 1-year progression-free survival (PFS) curve was first plotted using the Kaplan-Meier method. Patients in the high-risk group had shorter 1-year PFS times (**Figure 5A**) and 1-year all-cause survival (**Figure 5B**) than the medium-risk and low-risk groups ($P < 0.001$). On the other hand, patients in the low-risk group had higher 1-year PFS times and a 1-year all-cause survival times than those in the medium-risk and high-risk groups ($P \leq 0.001$). The 1-year PFS and the 1-year all-cause survival were significantly different among patients in the three groups ($P < 0.001$).

Similarly, patients in the high-risk group had shorter 5-year PFS times (**Figure 5C**) and 5-year all-cause survival (**Figure 5D**) than those in the medium-risk and low-risk groups ($P < 0.001$). In contrast, patients in the low-risk group had longer 5-year PFS times and a 5-year all-cause survival than those in the medium-risk and high-risk groups ($P < 0.001$). The 5-year PFS and the 5-year all-cause survival times were significantly different among patients in the

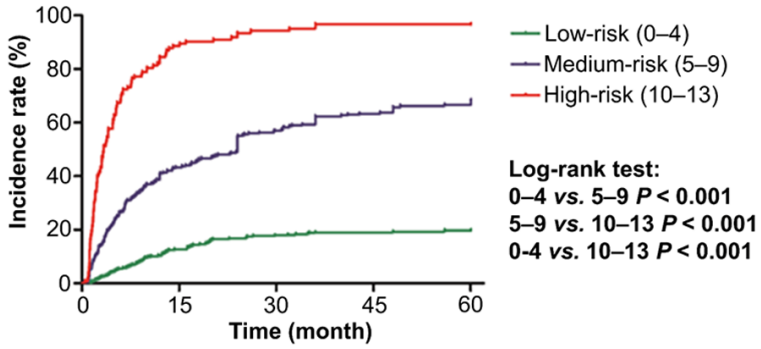

Figure 4. Kaplan-Meier analyses for the incidence of PVTT in patients with different risk. PVTT, portal vein tumor thrombus.

three groups ($P < 0.001$). These results indicated good discrimination of survival times among the different risk groups of patients.

Performance of the scoring system for PVTT prediction

The effectiveness of the scoring system was tested in a validation cohort of 489 patients with HBV-related primary HCC diagnosed in the First Affiliated Hospital of Henan University of TCM from January 2012 to December 2019. The calibration curves for the probability of occurrence of PVTT displayed high consistency between the predicted values and the actual observations in the validation set (**Figure 6**). As expected, the prediction efficiency of the scoring system delivered a better performance in the HCC cohort enrolled in the present study.

Discussion

Portal metastasis has been reported to occur in 30-100% of HCC cases [11]. The present retrospective study first employed univariate combined with multivariate analyses to identify 5 different variables as independent risk factors for PVTT formation and then established a novel PVTT prediction scoring system with further validation. First, an HBV-related HCC sex disparity was found, evidenced by HCC being more frequently and more aggressive in males than in females, suggesting a correlation between gender and PVTT. It has been shown that estrogen can not only can protect females infected with HBV from having a high-risk of developing HCC [12] but can also slow down HCC-related HCC progression in female HCC. Conversely, androgens may promote HCC-related hepatocarcinogenesis as the androgen-androgen receptor complex can activate transcription of the HBV genome, and the male gender has been reported to be an independent risk factor for poor HCC outcomes. Thus, the gender of HCC patients can be taken as a potential parameter for predicting the occurrence of PVTT.

Tumor size has long been recognized as an important predictor of HCC prognosis and also an independent risk factor for the recurrence of HCC. A recent study suggested that tumor size was a risk factor for the formation of PVTT [13], and other research has confirmed that a tumor size > 8 cm is an independent predictor for the occurrence of PVTT in HCC [14]. More importantly, HCC cells in tumors > 5 cm exhibited a higher probability of migrating into the portal vein [15]. Therefore, we adapted a cutoff tumor size > 5 cm to evaluate the probability of PVTT formation in the scoring system.

AFP, a glycoprotein, is a diagnostic tool for HCC as it is secreted from HCC cells into the serum [16], and has been accepted as a prognosis marker, with a cut-off concentration ≥ 400 ng/mL indicating a poor prognosis. A serum AFP concentration between 20 and 400 ng/mL has been reported to be a feasible cutoff for long-term outcome prediction in unselected HCC patients [17]. According to previous studies, the concentration of AFP in the serum is positively correlated with tumor size [17, 18]. Although the use of AFP as a prognosis marker has been challenged, a retrospective study revealed that AFP is still a significant diagnosis and prognosis marker of HBV-related HCC, rather than non-HBV-related HCC [19].

CRP, an inflammation marker synthesized by hepatocytes under the control of cytokines IL-6, is associated with the poor prognosis of several types of cancer and can be considered as a useful marker when AFP presents negative in HBV-related HCC patients. Thus, CRP carries diagnostic and prognosis potential in HBV-related HCC.

NLR was identified as another independent predictor of PVTT. A previous study reported

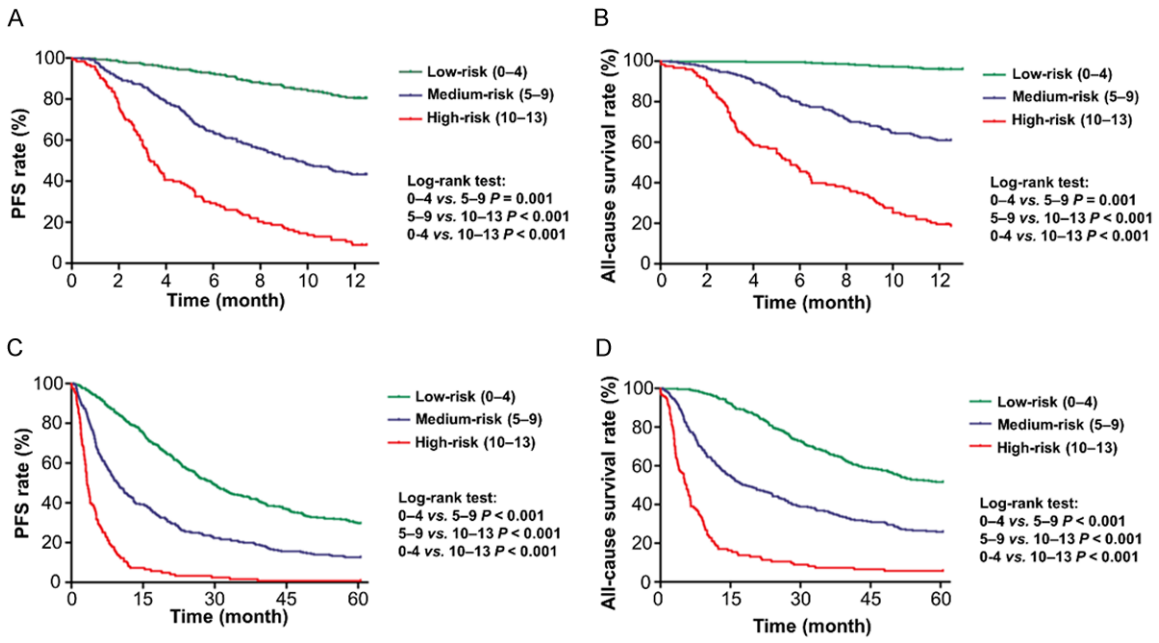

Figure 5. Kaplan-Meier analyses for the 1-year PFS rate (A), 1-year all-cause survival rate (B), 5-year PFS rate (C) and 5-year all-cause survival rate (D) in patients with different risk factors. PFS, progression-free survival.

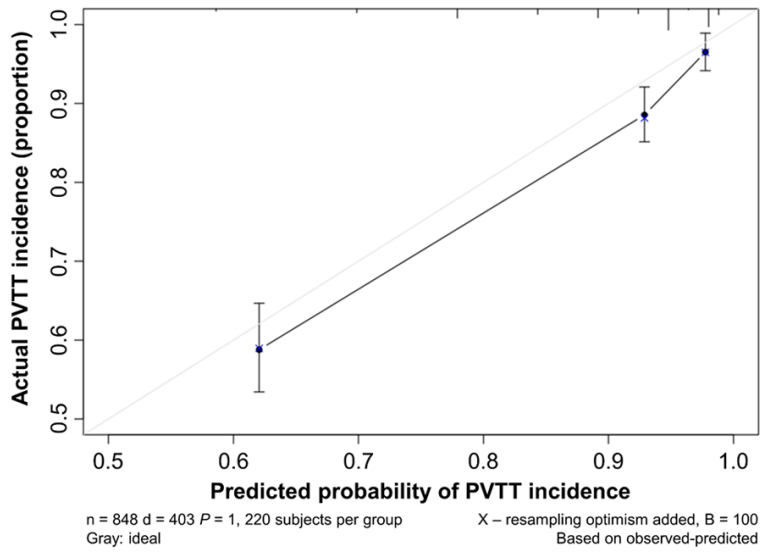

Figure 6. Calibration curves for the PVTT prediction model. PVTT, portal vein tumor thrombus.

that an increased NLR in HCC patients was associated with poor prognosis in primary HCC patients [20] and could predict the surgical outcomes of HCC patients [21]. More importantly, the preoperative NLR has been reported to be a prognostic factor after hepatectomy for HCC patients with PVTT [22]. Thus, we included NLR in the predictive scoring system for PVTT formation.

Previously, two retrospective studies revealed that the presence of cirrhosis is one of the risk factors for the development of PVTT [13, 14]. Cirrhosis has been proven to be important in the fundamental pathogenesis of HCC, which can be graded using the Child-Pugh score for prognostically assessing the overall survival of HCC patients. However, in the present study, a relationship between the grade of cirrhosis and PVTT prognosis was not found, with the proportion of each cirrhosis grade being similar between PVTT and non-PVTT patients. Thus, the cirrhosis grade was not used as a prognosis marker for PVTT formation in the present study.

The serum HBV load, also, was not significantly related to PVTT formation in HBV-associated HCC in the present study. A previous study reported that HBV infection could induce the

alteration of the TGF-β-miR-34a-CCL22 axis, and thus abnormality of the liver microenvironment, which may induce the formation of PVTT [23]. A retrospective study also revealed that active HBV replication might contribute to vascular invasion in HCC patients [24]. That is, positive HBsAg or a certain level of HBsAg might be a more accurate clinical marker to predict the occurrence of PVTT.

The limitation of the present study is rooted in its retrospective case-control single-center nature, which not only carries recall and selection bias but also can only be considered as level III evidence. Thus, further investigations with randomized control trials and long-term, large-scale analyses of clinical data are required to confirm this scoring system and its prediction capability.

In conclusion, gender, tumor size, NLR, AFP and CRP concentrations are reliable factors that can predict the likelihood of PVTT formation in HBV-related HCC patients, and indirectly indicate the prognosis and long-term consequences for HCC patients.

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Disclosure of conflict of interest

None.

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