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Original Article

Development and verification of a nomogram for predicting portal vein tumor thrombosis in hepatocellular carcinoma

Guanghua Liu[1], Jiangwen Long[1], Chaoshui Liu[2], Jie Chen[3]

[1]Department of Blood Transfusion, Laboratory of Hematology, Hunan Provincial People's Hospital (The First Affiliated Hospital of Hunan Normal University), Changsha 410002, Hunan, China; [2]Hunan Provincial Key Laboratory of The Research and Development of Novel Pharmaceutical Preparations, The "Double-First Class" Application Characteristic Discipline of Hunan Province (Pharmaceutical Science), Changsha Medical University, Changsha 410219, Hunan, China; [3]Department of Clinical Laboratory, Hunan Provincial People's Hospital (The First Affiliated Hospital of Hunan Normal University), Changsha 410002, Hunan, China

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Abstract: Objective: To develop a nomogram to predict the risk of portal vein tumor thrombosis (PVTT) in hepatocellular carcinoma (HCC) patients. Methods: Patients diagnosed with HCC at Hunan Provincial People's Hospital between January 2010 and January 2022 were enrolled. Data on demographic characteristics, comorbidities, and laboratory tests were collected. Multivariate logistic regression was used to identify independent risk factors for PVTT, which were then incorporated into a predictive nomogram. The nomogram's discriminative ability was evaluated using the area under the receiver operating characteristic (AUC) curve. Clinical utility was assessed through decision curve analysis (DCA). Results: Being male (OR 1.991, 95% CI 1.314-3.017, P = 0.001), Barcelona Clinic Liver Cancer (BCLC) staging (stage C: OR 8.043, 95% CI 4.334-14.926, P<0.001; stage D: OR 7.977, 95% CI 3.532-18.017, P<0.001), tumor size >5 cm (OR 1.792, 95% CI 1.116-2.876, P = 0.016), and D-dimer (OR 1.126, 95% CI 1.083-1.171, P<0.001) were identified as independent risk factors for PVTT. The nomogram formula is: Logit = -2.8961 + 0.6586 (male) + BCLC staging (-0.1922 for B, 1.9251 for C, or 1.7938 for D) + 0.5418 (tumor size >5 cm) + 0.1051 DDi. The nomogram achieved an AUC of 0.798 (95% CI 0.774-0.822) in the training set and 0.822 (95% CI 0.782-0.862) in the validation set. Sensitivities were 86.6% and 90.7%, while specificities were 68.2% and 71.8% in the training and validation sets, respectively, demonstrating strong discrimination and predictive accuracy. DCA indicated a favorable risk threshold probability. Conclusion: A nomogram incorporating male sex, BCLC staging, tumor size, and D-dimer demonstrated good predictive performance for PVTT. This tool may aid in the early comprehensive assessment of PVTT risk in HCC patients.

Keywords: Portal vein tumor thrombosis, hepatocellular carcinoma, nomogram

Introduction

Hepatocellular carcinoma (HCC) is a common malignant solid tumor [1] with a 5-year relative survival rate of 18% [2], resulting in more than 600,000 deaths annually [3]. Due to the absence of typical symptoms or signs at early stages, most cases are diagnosed at intermediate or advanced stages. Portal vein tumor thrombosis (PVTT) is one of the most frequent complications of HCC, occurring in 10%-60% of cases [4], and is a hallmark of advanced HCC. HCC with PVTT is characterized by limited hepatic reserve function, high susceptibility to blood metastasis, complications related to portal hypertension, and poor tolerance to treatment. When tumor thrombi extend to the first branch or main trunk of the portal vein, the disease is typically considered terminal. Long-term survival for HCC patients with PVTT remains poor, despite advancements in systemic therapy, hepatic artery infusion chemotherapy, and transcatheter arterial chemoembolization [5].

Given the poor prognosis of HCC with PVTT, identifying biomarkers for PVTT is crucial for

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early diagnosis and treatment. Non-invasive biomarkers such as albumin-to-alkaline phosphatase ratio ≤0.49, glutamic oxalacetic transaminase-to-platelet ratio index >0.48, male sex, extrahepatic metastasis, and multiple tumors have been identified as independent risk factors for PVTT [6]. Immune-related genes may regulate extracellular matrix components, facilitating PVTT formation [7]. Erythroid-transdifferentiated myeloid cells can promote PVTT by damaging vascular endothelium and enhancing coagulation [8]. S100P has been proposed as a novel biomarker for PVTT [9], while elevated protein induced by vitamin K absence II (PIVKA-II) levels is also a significant independent risk factor [10]. Moreover, alterations in ascitic microbiota have been associated with PVTT development in HCC [11].

Despite these findings, studies on PVTT formation and risk biomarkers remain limited, often focusing on genetic or laboratory indices. However, genetic testing has limitations in clinical applications due to high cost. Therefore, early and comprehensive assessment of PVTT risk is vital for timely treatment and improving prognosis in HCC patients.

This study collected demographic, clinical, laboratory, and imaging data from HCC patients to identify independent risk factors for PVTT. Based on these factors, we aimed to develop a predictive nomogram for assessing PVTT risk in HCC patients and validate its predictive performance through internal validation.

Materials and methods

Study population

Patients with HCC diagnosed at Hunan Provincial People's Hospital between January 2010 and January 2022 were retrospectively reviewed. The diagnosis of HCC was based on the Standardization for Diagnosis of HCC (2022 edition) [12], confirmed through histologic and radiologic examinations. Radiological diagnostic criteria included liver lesions with typical features of liver cancer and nodule diameters >2 cm on imaging. HCC was classified according to the Barcelona Clinic Liver Cancer (BCLC) classification [13].

Portal vein tumor thrombosis (PVTT) was diagnosed based on the Consensus of Chinese Experts on Multidisciplinary Diagnosis and Treatment of HCC with PVTT (2021 edition) [14], with at least one of the following imaging features: 1) Hypoechoic intravascular embolus echoes similar to the primary tumor on ultrasound. 2) Low-density filling defects in vessels on contrast-enhanced computed tomography (CT). 3) Intravascular filling defects observed on magnetic resonance imaging (MRI) enhancement.

Exclusion criteria: 1) Age <18 years. 2) Presence of malignancy other than HCC. 3) PVTT confirmed by color Doppler ultrasound or multislice spiral CT. 4) Incomplete clinical data.

Patients with HCC were randomly assigned to the training or validation sets in a 3:1 ratio to develop and validate the nomogram. Clinical features of both sets were comared to enhance model prediction. HCC patients with PVTT during hospitalization were categorized into the PVTT group, while those without were included in the non-PVTT group. This study was approved by the Medical Ethics Committee of Hunan Provincial People's Hospital. All procedures adhered to institutional ethical standards.

Data collection

Demographic data, including sex, age, drinking history, smoking history, comorbidities (hypertension, diabetes, heart disease), and complications (portal hypertension, splenomegaly, ascites, esophagogastric varices, encephalopathy), were recorded. Laboratory data included white blood cell count (WBC), lymphocyte count (L), neutrophil count (N), monocyte count (M), platelet count (PLT), mean platelet volume (MPV), hemoglobin (Hb), mean corpuscular volume (MCV), hematocrit (HCT), total bile acid (TBA), total bilirubin (TB), alanine transaminase (ALT), albumin (ALB), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), activated partial thromboplastin time (APTT), prothrombin time (PT), international normalized ratio (INR), D-dimer (DDi), platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR).

Statistical analysis

Categorical variables were expressed as numbers (percentages) and compared using Chi-

Table 1. Demographics, clinical and laboratory data of patients with HCC

Variable	All patients n = 1752	Training set n = 1314	Validation set n = 438
Age (year)	57 (50-65)	57 (50-65)	57 (49-66)
Sex (male/female)	1466/286	1100/214	366/72
Smoking history	211 (12.0%)	163 (12.4%)	48 (11.0%)
Drinking history	244 (13.9%)	188 (14.3%)	56 (12.8%)
Comorbidities			
Hypertension	302 (17.2%)	216 (16.4%)	86 (19.6%)
Diabetes	233 (13.3%)	165 (12.6%)	68 (15.5%)
Heart disease	70 (4.0%)	52 (4.0%)	18 (4.1%)
Complications			
Splenomegaly	1139 (65.0%)	855 (65.1%)	284 (64.8%)
Portal hypertension	1295 (73.9%)	978 (74.4%)	317 (72.4%)
Esophagogastric varices	581 (33.2%)	445 (33.9%)	136 (31.1%)
Ascites	896 (51.1%)	678 (51.6%)	218 (49.8%)
Encephalopathy	32 (1.8%)	28 (2.1%)	4 (0.9%)
BCLC stage			
A	421 (24.0%)	308 (23.4%)	113 (25.8%)
B	569 (32.5%)	426 (32.4%)	143 (32.6%)
C	667 (38.1%)	513 (39.0%)	154 (35.2%)
D	95 (5.4%)	67 (5.1%)	28 (6.4%)
Tumor size			
≤5 cm	778 (44.4%)	587 (44.7%)	191 (43.6%)
>5 cm	974 (55.6%)	727 (55.3%)	247 (56.4%)
Satellite opacities	412 (23.5%)	316 (24.0%)	96 (21.9%)
WBC ($\times 10^9$/L)	5.19 (3.70-7.17)	5.19 (3.68-7.15)	5.22 (3.74-7.21)
N ($\times 10^9$/L)	3.33 (2.16-5.13)	3.33 (2.15-5.13)	3.33 (2.17-5.10)
L ($\times 10^9$/L)	1.01 (0.71-1.41)	1.01 (0.71-1.41)	1.05 (0.72-1.41)
M ($\times 10^9$/L)	0.45 (0.30-0.65)	0.45 (0.30-0.65)	0.47 (0.31-0.65)
HB (g/L)	120 (101-134)	119 (100-135)	120 (102-133)
HCT	36.1 (30.8-40.8)	36.0 (30.5-40.9)	36.1 (31.3-40.2)
MCV (fL)	94.7 (90.1-99.6)	94.5 (90.0-99.3)	95.0 (90.4-100.0)
PLT ($\times 10^9$/L)	116 (72-179)	114 (71-178)	120 (73-182)
MPV (fL)	11.0 (9.9-11.9)	11.0 (9.9-11.9)	11.0 (9.9-11.9)
TB (μmol/L)	24.1 (15.4-43.4)	24.0 (15.6-43.6)	24.1 (15.0-42.9)
TBA (μmol/L)	21.0 (7.7-48.1)	20.6 (7.7-48.0)	21.7 (7.6-48.6)
ALB (g/L)	33.2 (28.8-37.7)	33.0 (28.9-37.7)	33.5 (28.5-38.0)
ALT (U/L)	44.2 (27.8-70.1)	44.0 (27.5-71.6)	45.6 (28.1-74.7)
AST (U/L)	65.9 (40.8-118.4)	65.8 (40.1-118.3)	66.7 (41.9-119.4)
ALP (U/L)	142.2 (98.0-217.9)	141.6 (97.0-219.5)	145.0 (101.9-213.0)
GGT (U/L)	131.4 (61.8-274.1)	130.5 (62.6-270.1)	134.0 (60.4-283.2)
BUN (mmol/L)	5.16 (4.03-6.65)	5.19 (4.06-6.67)	5.08 (3.98-6.61)
CR (μmol/L)	67.1 (56.5-80.2)	67.2 (57.0-80.4)	66.69 (54.99-79.90)
PT (s)	13.1 (11.8-14.8)	13.0 (11.8-14.8)	13.2 (11.8-14.6)
INR	1.14 (1.03-1.30)	1.14 (1.03-1.30)	1.15 (1.03-1.28)
FIB (g/L)	2.35 (1.69-3.26)	2.35 (1.69-3.25)	2.35 (1.68-3.29)
DDi (mg/L)	1.50 (0.56-3.81)	1.49 (0.57-3.78)	1.54 (0.56-3.86)
NLR	3.25 (2.08-5.39)	3.29 (2.08-5.37)	3.14 (2.08-5.48)

PLR	111.22 (75.00-173.15)	110.80 (75.00-172.64)	112.10 (75.14-177.31)
PVTT	580 (33.1%)	440 (33.5%)	140 (32.0%)

WBC, white blood cell count; N, neutrophil count; L, lymphocyte count; M, monocyte; HB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; PLT, platelet count; MPV, mean platelet volume; TB, total bilirubin; TBA, total bile acid; ALB, albumin; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; PT, prothrombin time; INR, international normalized ratio; DDi, D-dimer; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PVTT, portal vein tumor thrombus; HCC, hepatocellular carcinoma.

square tests. Continuous variables were presented as medians (interquartile ranges [IQR]) and analyzed using the Mann-Whitney U test. Variables with *P*-values <0.05 were considered significant. Multivariate logistic regression was performed to identify independent risk factors for PVTT and construct a predictive nomogram.

The calibration performance of the nomogram was assessed using calibration curves comparing observed outcomes and predicted probabilities. The discriminative ability of the nomogram was evaluated using the area under the receiver operating characteristic curve (AUC). Decision curve analysis (DCA) was performed to assess the clinical utility of the nomogram.

All analyses were conducted using SPSS software (IBM, Chicago, IL, USA, version 23.0) and R software (version 4.2.1).

Results

Comparison of baseline characteristics

A total of 1,752 patients with HCC were included in this retrospective study, and their baseline characteristics are summarized in **Table 1**. The median age was 57 years (range: 50-65 years), and most patients were male. PVTT was identified in 580 patients (33.1%). Of the total cohort, 1,314 patients were assigned to the training set, and 438 were assigned to the validation set. PVTT was observed in 440 patients (33.5%) in the training set and 140 patients (32.0%) in the validation set.

In the training set, 874 patients were categorized as non-PVTT and 440 as PVTT. The median age of the PVTT group was significantly lower than that of the non-PVTT group (55 vs. 59, P<0.05). Male patients were more likely to develop PVTT. Compared to the non-PVTT group, the PVTT group showed higher rates of diabetes, splenomegaly, portal hypertension, esophagogastric varices, and ascites (all P<0.05). Patients in the PVTT group also had more advanced BCLC stages and larger tumor sizes (all P<0.05). Satellite opacities were more frequently observed in the PVTT group (P<0.05).

Laboratory findings revealed higher levels of WBC, N, PLT, TB, ALT, AST, ALP, GGT, PT, INR, FIB, DDi, PLR, and NLR in the PVTT group, while lymphocyte count and MCV levels were lower compared to the non-PVTT group (**Table 2**).

Construction of the nomogram

Multivariate logistic regression analysis identified four independent risk factors for PVTT: male sex (OR 1.991, 95% CI 1.314-3.017, P = 0.001), BCLC staging (stage C: OR 8.043, 95% CI 4.334-14.926, P<0.001; stage D: OR 7.977, 95% CI 3.532-18.017, P<0.001), tumor size >5 cm (OR 1.792, 95% CI 1.116-2.876, P = 0.016), and DDi (OR 1.126, 95% CI 1.083-1.171, P<0.001) (**Table 3**).

A nomogram model was developed based on these factors to predict PVTT risk (**Figure 1**). The model formula is as follows: Logit = -2.8961 + 0.6586 (sex: male) + BCLC staging (-0.1922 for stage B, 1.9251 for stage C, 1.7938 for stage D) + 0.5418 (tumor size >5 cm) + 0.1051 (DDi).

The probability of PVTT can be calculated by summing the scores of each predictor on the point scale and mapping the total score to the probability axis.

Validation of the nomogram

The calibration curve demonstrated good agreement between the predicted and actual probabilities of PVTT in the training set using the bootstrap resampling method with 1,000 repetitions (**Figure 2**).

ROC curves indicated satisfactory predictive performance of the nomogram, with AUC values of 0.798 (95% CI 0.774-0.822) in the train-

Table 2. Comparison of demographics, clinical and laboratory data between the PVTT group and non-PVTT group in the training set

Variable	PVTT group n = 440	Non-PVTT group n = 874	P
Age (year)	55 (50-63)	59 (50-66)	0.009
Sex (male/female)	394/46	706/168	<0.001
Smoking history	55 (12.5%)	108 (12.4%)	0.930
Drinking history	68 (15.5%)	120 (13.7%)	0.405
Comorbidities			
Hypertension	60 (13.6%)	156 (17.8%)	0.058
Diabetes	39 (8.9%)	126 (14.4%)	0.005
Heart disease	12 (2.7%)	40 (4.6%)	0.133
Complications			
Splenomegaly	310 (70.5%)	545 (62.4%)	0.004
Portal hypertension	353 (80.2%)	625 (71.5%)	0.001
Esophagogastric varices	166 (37.7%)	279 (31.9%)	0.041
Ascites	271 (61.6%)	407 (46.6%)	<0.001
Encephalopathy	9 (2.0%)	19 (2.2%)	1.000
BCLC stage			<0.001
A	39 (8.9%)	269 (30.8%)	
B	54 (12.3%)	372 (42.6%)	
C	307 (69.8%)	206 (23.6%)	
D	40 (9.1%)	27 (3.1%)	
Tumor size			<0.001
≤5 cm	79 (18.0%)	508 (58.1%)	
>5 cm	361 (82.0%)	366 (41.9%)	
Satellite opacities	135 (30.7%)	181 (20.7%)	<0.001
WBC ($\times10^9$/L)	5.35 (3.92-7.15)	5.16 (3.52-7.15)	0.101
N ($\times10^9$/L)	3.67 (2.52-5.29)	3.19 (1.95-4.97)	<0.001
L ($\times10^9$/L)	0.90 (0.66-1.30)	1.05 (0.73-1.47)	<0.001
M ($\times10^9$/L)	0.46 (0.31-0.67)	0.45 (0.30-0.63)	0.228
HB (g/L)	122 (104-135)	119 (99-135)	0.184
HCT	36.7 (31.6-40.8)	35.7 (30.3-40.9)	0.143
MCV (fL)	93.9 (89.4-98.3)	95.0 (90.3-100.0)	0.019
PLT ($\times10^9$/L)	120 (81-179)	111 (67-178)	0.041
MPV (fL)	11.0 (9.7-11.9)	11.0 (9.9-11.9)	0.634
TB (μmol/L)	28.0 (18.6-50.2)	21.9 (14.5-39.7)	<0.001
TBA (μmol/L)	21.9 (9.3-47.7)	19.5 (7.0-48.0)	0.087
ALB (g/L)	32.8 (28.9-37.1)	33.2 (28.8-38.3)	0.245
ALT (U/L)	50.3 (32.2-78.0)	39.6 (25.8-65.7)	<0.001
AST (U/L)	92.1 (57.0-150.9)	55.4 (36.2-97.5)	<0.001
ALP (U/L)	167.8 (119.0-264.2)	126.7 (90.0-192.3)	<0.001
GGT (U/L)	203.1 (107.5-341.1)	102.1 (52.7-224.5)	<0.001
BUN (mmol/L)	5.24 (4.03-6.96)	5.17 (4.06-6.55)	0.255
CR (μmol/L)	66.0 (56.0-78.6)	68.0 (57.7-81.6)	0.081
PT (s)	13.3 (12.1-14.7)	12.9 (11.7-14.9)	0.048
INR	1.16 (1.05-1.28)	1.13 (1.02-1.31)	0.040
FIB (g/L)	2.61 (1.88-3.34)	2.22 (1.58-3.19)	<0.001
DDi (mg/L)	2.35 (1.16-4.75)	1.11 (0.43-2.92)	<0.001

NLR	4.03 (2.61-6.07)	2.92 (1.90-4.93)	<0.001
PLR	131.67 (92.42-182.80)	102.33 (67.04-165.77)	<0.001

WBC, white blood cell count; N, neutrophil count; L, lymphocyte count; M, monocyte; HB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; PLT, platelet count; MPV, mean platelet volume; TB, total bilirubin; TBA, total bile acid; ALB, albumin; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; PT, prothrombin time; INR, international normalized ratio; DDi, D-dimer; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Table 3. Independent predictors for development of nomogram

Variable	OR	95% CI	P
Sex			
Female	ref		
Male	1.991	1.314-3.017	0.001
BCLC stage			
A	ref		
B	0.899	0.531-1.523	0.693
C	8.043	4.334-14.926	<0.001
D	7.977	3.532-18.017	<0.001
Tumor size			
≤5 cm	ref		
>5 cm	1.792	1.116-2.876	0.016
DDi	1.126	1.083-1.171	<0.001

DDi, D-dimer.

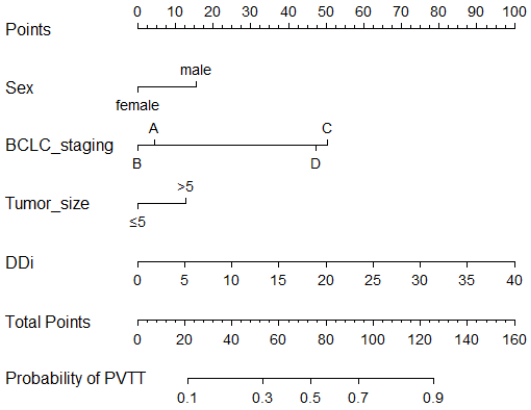

Figure 1. Nomogram for predicting the probability of tumor thrombus.

ing set and 0.822 (95% CI 0.782-0.862) in the validation set (**Figure 3A** and **3B**). The nomogram achieved sensitivity values of 86.6% and 90.7% and specificity values of 68.2% and 71.8% in the training set (**Figure 3A**) and validation set (**Figure 3B**), respectively.

DCA demonstrated a superior risk threshold probability compared to the baseline, highlighting the nomogram's clinical utility and its robust performance for guiding treatment decisions (**Figure 4**).

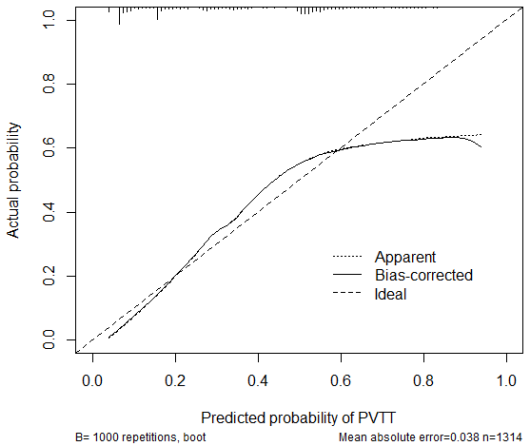

Figure 2. Calibration curves of the nomogram in the training set.

Discussion

Hepatocellular carcinoma (HCC) is the most common form of liver cancer, with a high fatality rate, posing a significant global health challenge [15]. PVTT is a common complication of HCC, and its treatment remains a major clinical challenge, with poor long-term survival outcomes. Therefore, early assessment and diagnosis of PVTT risk in HCC are critical.

A nomogram translates each regression coefficient in a predictive model into a scoring system based on its contribution to risk and prognosis [16], making it a widely used tool for various cancers [17-19]. PVTT in HCC increases the risk of varices and variceal bleeding [20]. Compared to HCC without PVTT, treatment options for HCC with PVTT are limited, and survival rates are worse. Predicting PVTT risk is vital for early intervention and improved patient outcome. While most studies focus on the prognosis of HCC with PVTT, our research aimed to predict PVTT risk itself.

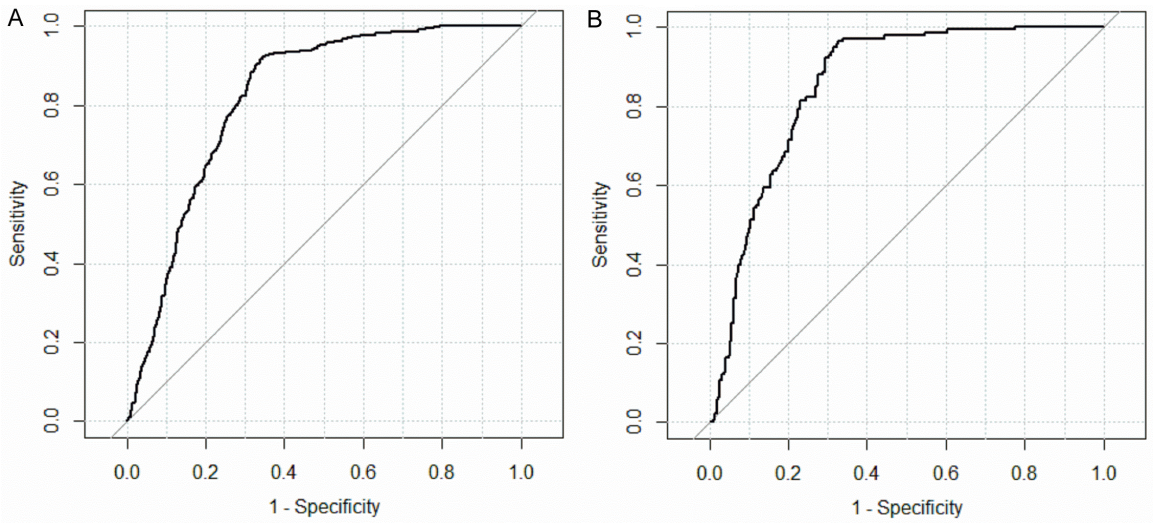

Figure 3. ROC curves for tumor embolus prediction model. ROC curves for tumor embolus prediction model in the training set (A). ROC curves for tumor embolus prediction model in the validation set (B).

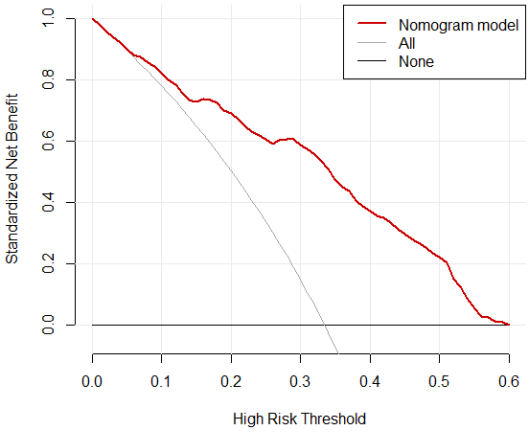

Figure 4. Decision curve analysis for the nomogram.

We identified male sex, BCLC stage, tumor size, and DDi levels as independent risk factors for PVTT in HCC. Based on these factors, a nomogram was developed, demonstrating high sensitivity and specificity. DCA confirmed its superior risk threshold probability.

Male sex has been reported as an independent risk factor for PVTT [6], possibly due to hormonal differences and the higher incidence of HCC in males [21]. Our findings align with this observation. However, another study reported a higher prevalence of males in the PVTT group without a statistically significant association [22]. Whether male sex is an independent risk factor for PVTT warrants further investigation.

The BCLC system, the most widely used staging method for HCC, classifies patients into five stages with distinct prognoses and treatment strategies [23]. HCC with PVTT is categorized as advanced (BCLC Stage-C) [24]. In our study, BCLC stage C and stage D were significantly associated with PVTT risk, consistent with previous findings.

Tumor size is closely related to HCC prognosis, with larger tumors linked to worse outcomes. A high tumor load (number and size of lesions) is associated with PVTT [24]. Tumor size also reflects tumor aggressiveness, indicating a higher likelihood of cancer thrombus formation [25]. In this study, we set 5 cm as the cutoff, finding that tumor size >5 cm was an independent risk factor for PVTT.

DDi, a soluble fibrin degradation product formed during thrombus dissolution, is a biomarker of fibrin formation and degradation [26]. While DDi is associated with venous thromboembolism [27, 28], its relationship with PVTT has been less studied. Our study demonstrated that elevated DDi levels are associated with PVTT in HCC patients.

Nomograms for HCC with PVTT have primarily focused on prognosis [29, 30] and long-term survival prediction [31, 32]. Recently, a risk score for predicting PVTT in HCC patients was developed, based on a large cohort of 2,243 patients. This score incorporated eight risk fac-

tors: three tumor-related factors (tumor diameter, infiltration, alpha-fetoprotein), three liver function indicators (INR, bilirubin, albumin), and two factors related to portal hypertension (portal hypertensive gastropathy, ascites). The risk of PVTT was associated with an OR of 1.30 using a continuous score, and an OR of 11.33 when comparing scores >8 to scores ≤8 [22]. However, the predictive value of this risk score remains uncertain due to the lack of external validation.

In our retrospective study, 1,752 HCC patients were included. We developed a nomogram based on four readily available clinical and laboratory variables (male sex, BCLC staging, tumor size, and DDi) to predict PVTT risk. The nomogram achieved sensitivity values of 86.6% and 90.7%, and specificity of 68.2% and 71.8% in the training and validation sets, respectively. Although our sample size was slightly smaller than the previous study, we performed internal validation by dividing patients into training and validation sets, enhancing the robustness of our findings. Compared to the previous risk score, the key advantages of our nomogram are its simplicity and accuracy.

Despite the satisfactory discrimination and predictive performance of the nomogram, several limitations must be acknowledged. First, as a retrospective study, the development may have been prone to selection bias, potentially limiting the persuasiveness of the findings. Second, we did not distinguish between HBV-related and non-HBV-related HCC, leaving its applicability to these subgroups unclear. Third, the single-center design limits generalizability, and we did not evaluate the nomogram's prognostic utility. Fourth, this study did not include alpha-fetoprotein, a key HCC-specific marker, which may influence PVTT risk.

In conclusion, we developed a nomogram incorporating male sex, BCLC staging, tumor size, and DDi, demonstrating strong predictive ability for PVTT risk. This tool can facilitate comprehensive risk assessment and guide clinicians in optimizing care and treatment allocation.

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Disclosure of conflict of interest

None.

Address correspondence to: Jie Chen, Department of Clinical Laboratory, Hunan Provincial People's Hospital (The First Affiliated Hospital of Hunan Normal University), No. 61, Jiefang West Road, Furong District, Changsha 410002, Hunan, China. E-mail: chenjie0924@126.com

References

[1] Li Z, Zhao M, Qi X, Tang Y and Cheng S. Mechanisms of portal vein tumour thrombus formation and development in patients with hepatocellular carcinoma. J Cell Mol Med 2023; 27: 2103-2111.

[2] Siegel RL, Miller KD and Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020; 70: 7-30.

[3] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.

[4] Zhou XH, Li JR, Zheng TH, Chen H, Cai C, Ye SL, Gao B and Xue TC. Portal vein tumor thrombosis in hepatocellular carcinoma: molecular mechanism and therapy. Clin Exp Metastasis 2023; 40: 5-32.

[5] Yuan Y, He W, Yang Z, Qiu J, Huang Z, Shi Y, Lin Z, Zheng Y, Chen M, Lau WY, Li B and Yuan Y. TACE-HAIC combined with targeted therapy and immunotherapy versus TACE alone for hepatocellular carcinoma with portal vein tumour thrombus: a propensity score matching study. Int J Surg 2023; 109: 1222-1230.

[6] Liu B, Liu J, Mei X, Zhang ZQ, Fang J, Zhou LL, Zheng JL, Lin HY, Zhu XL and Li DL. Pretreatment non-invasive biomarkers as predictors to estimate portal vein tumor thrombosis (PVTT) risk and long-term survival in HBV-related hepatocellular carcinoma patients without PVTT. J Hepatocell Carcinoma 2023; 10: 2367-2382.

[7] Zhou W, Fang DL and He Y. Screening potential prognostic biomarkers for portal vein emboli in patients with hepatocellular carcinoma. J Gastrointest Oncol 2021; 12: 1927-1938.

[8] Zhu WH, Chen J, Huang RK, Zhang Y, Huang ZX, Pang XQ, Hu B, Yang Y and Li X. Erythroid-transdifferentiated myeloid cells promote portal vein tumor thrombus in hepatocellular carcinoma. Theranostics 2023; 13: 4316-4332.

[9] Qi LN, Ma L, Wu FX, Chen YY, Xing WT, Jiang ZJ, Zhong JH, Chen ZS, Gong WF, Ye JZ, Li HH, Shang JJ, Xiang BD and Li LQ. S100P as a nov-

el biomarker of microvascular invasion and portal vein tumor thrombus in hepatocellular carcinoma. Hepatol Int 2021; 15: 114-126.
[10] Xu F, Zhang L, He W, Song D, Ji X and Shao J. The diagnostic value of serum PIVKA-II alone or in combination with AFP in Chinese Hepatocellular carcinoma patients. Dis Markers 2021; 2021: 8868370.
[11] Guo Y, Tian S, Zhan N, Liu C, Li J, Hu J, Qiu M, Huang B and Dong W. Ascitic microbiota alteration is associated with portal vein tumor thrombosis occurrence and prognosis in hepatocellular carcinoma. mBio 2024; 15: e0024524.
[12] Bureau of Medical Administration, National Health Commission of the People's Republic of China. Standardization for diagnosis and treatment of hepatocellular carcinoma (2022 edition). Zhonghua Gan Zang Bing Za Zhi 2022; 30: 367-388.
[13] Forner A, Reig M and Bruix J. Hepatocellular carcinoma. Lancet 2018; 391: 1301-1314.
[14] Sun J, Guo R, Bi X, Wu M, Tang Z, Lau WY, Zheng S, Wang X, Yu J, Chen X, Fan J, Dong J, Chen Y, Cui Y, Dai C, Fang C, Feng S, Ji Z, Jia W, Jia N, Li G, Li J, Li Q, Li J, Liang T, Liu L, Lu S, Lv Y, Mao Y, Meng Y, Meng Z, Shen F, Shi J, Sun H, Tao K, Teng G, Wan X, Wen T, Wu L, Xia J, Ying M, Zhai J, Zhang L, Zhang X, Zhang Z, Zhao H, Zheng D, Zhi X, Zhou J, Zhou C, Zhou J, Zeng Z, Zhu K, Chen M, Cai J and Cheng S. Guidelines for diagnosis and treatment of hepatocellular carcinoma with portal vein tumor thrombus in China (2021 Edition). Liver Cancer 2022; 11: 315-328.
[15] Nagaraju GP, Dariya B, Kasa P, Peela S and El-Rayes BF. Epigenetics in hepatocellular carcinoma. Semin Cancer Biol 2022; 86: 622-632.
[16] Zhong X, Pan Y, Wu K, Wang L, Dou P, Tan P, Zhang P and Li X. A novel nomogram based on body composition and nutritional indicators to predict the prognosis of patients with muscle-invasive bladder cancer undergoing radical cystectomy. Cancer Med 2023; 12: 21627-21638.
[17] Shi W, Yan H, Liu X, Yu L, Xie Y, Wu Y, Liang Y and Yang Z. Development and validation of a novel prognostic nomogram based on platelet and CD8(+)T cell counts in hepatocellular carcinoma patients with portal vein tumor thrombosis. J Hepatocell Carcinoma 2024; 11: 1049-1063.
[18] Liu C, Zhao W, Xie J, Lin H, Hu X, Li C, Shang Y, Wang Y, Jiang Y, Ding M, Peng M, Xu T, Hu A, Huang Y, Gao Y, Liu X, Liu J and Ma F. Development and validation of a radiomics-based nomogram for predicting a major pathological response to neoadjuvant immunochemotherapy for patients with potentially resectable non-small cell lung cancer. Front Immunol 2023; 14: 1115291.
[19] Wu W, Zheng L, Li F, Chen H, Huang C, Chen Q, Lin Y, Xu X and Dai Y. Survival analysis and nomogram for pulmonary sarcomatoid carcinoma: an SEER analysis and external validation. BMJ Open 2023; 13: e072260.
[20] Lim J, Kim HI, Kim E, Kim J, An J, Chang S, Kim SO, Lee HC, Lee YS and Shim JH. Variceal bleeding is aggravated by portal venous invasion of hepatocellular carcinoma: a matched nested case-control study. BMC Cancer 2021; 21: 11.
[21] Keng VW, Largaespada DA and Villanueva A. Why men are at higher risk for hepatocellular carcinoma? J Hepatol 2012; 57: 453-454.
[22] Tortora R, Farella N, Morisco F, Coppola C, Izzo F, Salomone Megna A, Federico A, Messina V, Nardone G, Piai G, Ragone E, Adinolfi LE, D'Adamo G, Stanzione M, Francica G, Torre P, De Girolamo V, Coppola N, Guarino M, Dallio M, Rocco L and Di Costanzo GG; Progetto Epatocarcinoma Campania Group. Development of a risk score to predict portal vein tumor thrombosis in patients with hepatocellular carcinoma. Eur J Gastroenterol Hepatol 2023; 35: 734-741.
[23] Guiu B, Garin E, Allimant C, Edeline J and Salem R. TARE in hepatocellular carcinoma: from the right to the left of BCLC. Cardiovasc Intervent Radiol 2022; 45: 1599-1607.
[24] Khan AR, Wei X and Xu X. Portal vein tumor thrombosis and hepatocellular carcinoma - the changing tides. J Hepatocell Carcinoma 2021; 8: 1089-1115.
[25] Cao S, Lyu T, Fan Z, Guan H, Song L, Tong X, Wang J and Zou Y. Long-term outcome of percutaneous radiofrequency ablation for periportal hepatocellular carcinoma: tumor recurrence or progression, survival and clinical significance. Cancer Imaging 2022; 22: 2.
[26] Wauthier L, Favresse J, Hardy M, Douxfils J, Le Gal G, Roy PM, van Es N, Ay C, Ten Cate H, Lecompte T, Lippi G and Mullier F. D-dimer testing: a narrative review. Adv Clin Chem 2023; 114: 151-223.
[27] Liang S, Tang W, Ye S, Xiang L, Wu X and Yang H. Incidence and risk factors of preoperative venous thromboembolism and pulmonary embolism in patients with ovarian cancer. Thromb Res 2020; 190: 129-134.
[28] Yuan JL, Xiao WK, Zhang CQ, Sun L, Lin YK and Hong CX. Incidence and characteristic of deep venous thrombosis in hospitalized chronic heart failure patients. Heart Vessels 2024; 39: 597-604.
[29] Cheng S, Yu X, Liu S, Jin Z, Xue H, Wang Z and Xie P. Development of a prognostic nomogram in hepatocellular carcinoma with portal vein tumor thrombus following trans-arterial chemoembolization with drug-eluting beads. Cancer Manag Res 2021; 13: 9367-9377.

[30] Huang YM, Wang TE, Chen MJ, Lin CC, Chang CW, Tai HC, Hsu SM and Chen YJ. Radiomics-based nomogram as predictive model for prognosis of hepatocellular carcinoma with portal vein tumor thrombosis receiving radiotherapy. Front Oncol 2022; 12: 906498.

[31] Cheng S, Hu G, Jin Z, Wang Z and Xue H. CT-based radiomics nomogram for prediction of survival after transarterial chemoembolization with drug-eluting beads in patients with hepatocellular carcinoma and portal vein tumor thrombus. Eur Radiol 2023; 33: 8715-8726.

[32] Li X, Ye Z, Lin S and Pang H. Predictive factors for survival following stereotactic body radiotherapy for hepatocellular carcinoma with portal vein tumour thrombosis and construction of a nomogram. BMC Cancer 2021; 21: 701.