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CT-based nomogram predicts esophageal gastric variceal bleeding in noncirrhotic portal hypertension caused by hepatic schistosomiasis

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Abstract

Background To construct a nomogram combining CT varices vein evaluation and clinical laboratory tests for predicting the risk of esophageal gastric variceal bleeding (EGVB) in patients with noncirrhotic portal hypertension (NCPH).

Methods A total of 315 NCPH patients with non-EGVB and EGVB were retrospectively enrolled and randomly divided into training and testing cohorts. Thirteen collateral vessels were identified and evaluated after CT portal vein system reconstruction. Multivariate binary logistic regression analysis was used to choose CT images and clinical predictors of EGVB. The varices score of each patient was calculated. A nomogram was built by combining the varices score with the selected clinical predictors of EGVB. The receiver operating characteristic (ROC) curve was used to evaluate the predictive performance of the nomogram.

Results Platelet count and prothrombin time were selected as clinical predictors; the esophageal vein, gastroepiploic vein and omental vein were selected as CT image predictors for predicting EGVB. A reduced platelet count, prolonged prothrombin time, severe esophageal and gastroepiploic vein tortuosity and less omental vein tortuosity were predictors of EGVB in NCPH patients. The specificity, sensitivity, negative predictive value, positive predictive value and AUC of the ROC of the nomogram were 0.82, 0.81, 0.89, 0.70, and 0.88 (95% CI: 0.84–0.93) in the training cohort and 0.87, 0.86, 0.88, 0.84, and 0.91 (95% CI: 0.84–0.97) in the testing cohort, respectively.

Conclusions The nomogram combining CT images and clinical predictors could be useful to individualize and predict the risk of EGVB in NCPH patients.

Clinical relevance statement Results showed that the nomogram combining CT-evaluated collateral vessels (varices score) and clinical laboratory tests could be used to realize personalized prediction of first-time EGVB in NCPH patients.

Keywords Esophageal gastric variceal bleeding, Collateral vessels, Nomogram, Noncirrhotic portal hypertension

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Background

Chronic hepatic schistosomiasis is characterized by progressive liver fibrosis and noncirrhotic portal hypertension (NCPH), which gradually leads to esophageal gastric variceal bleeding (EGVB) [1, 2]. NCPH patients with EGVB have a high mortality rate. Patients who undergo a first episode of EGVB are likely to experience more than one episode of bleeding, and one-third of them die from uncontrolled bleeding [3]. Thus, it is important to predict the risk of first-time bleeding in NCPH patients.

A key feature in predicting EGVB is the visualization of collateral vessels that decompress portal hypertension by returning blood to the systemic circulation [4, 5]. Endoscopy is currently the gold standard for diagnosing esophageal varices, which could be used for predicting EGVB [6]. The signs of endoscopy include observing varices and esophageal red wall marks directly [7]. However, endoscopy is invasive, painful and has a potential risk of triggering variceal bleeding. Furthermore, endoscopy cannot display shunting vessels other than esophageal and gastric varices.

Ultrasound could be used to assess the esophageal varices, diameter and hemodynamics of the enlarged portal and spleen veins [8]. In recent years, non-invasive methods for liver stiffness assessment, such as elastography, have emerged as valuable tools for evaluating liver fibrosis and portal hypertension. Transient elastography, in particular, has shown promise in assessing liver elasticity in patients with advanced schistosomiasis. Studies have demonstrated the utility of transient elastography in grading liver fibrosis, which could indirectly reflect the severity of portal hypertension in NCPH patients [9]. Additionally, research by Veiga et al. evaluated both hepatic and spleen stiffness in patients with hepatosplenic schistosomiasis, showing a correlation between increased stiffness and portal hypertension, which may influence the risk of bleeding [10]. However, limited diagnostic performance in predicting EGVB was achieved because of the limitation of scanning resolution and dependency on patients' condition and operators' technology [11]. CT has high spatial resolution, which can be used to evaluate each varices vein of the portal vein system [12]. Previous studies tried noninvasive methods to predict EGVB in cirrhotic patients. The results showed that the paraumbilical vein and the model for end-stage liver disease (MELD) score can be used to predict EGVB in cirrhotic patients [13, 14]. However, the MELD score does not consider liver cirrhosis or liver fibrosis. Furthermore, in NCPH patients, the collateral vessels are different from those in cirrhosis or other liver diseases [15]. The paraumbilical vein was less frequently observed in NCPH patients.

We assumed that CT and clinical laboratory markers in predicting EGVB in cirrhotic patients could also be used in NCPH. However, the relative markers need further investigation. To achieve this goal, a nomogram was built by combining CT-evaluated collateral vessels (varices score) and clinical laboratory tests to realize personalized prediction of first-time EGVB in NCPH patients.

Methods

Patient selection

This retrospective study was reviewed and approved by the Institutional Review Board of Jinshan Hospital, Fudan University (JIEC 2023-S82). Written informed consent was obtained from all patients. The methods carried out in this study were in accordance with the relevant guidelines and regulations.

Study design

This study was a retrospective case-control study designed to identify predictors of EGVB in patients with NCPH. Patients diagnosed with NCPH were included in the study and classified into two groups: the EGVB group, consisting of patients who experienced a first episode of EGVB, and the Non-EGVB group, consisting of NCPH patients who did not experience EGVB within a month before or after CT scanning.

Data collection

From March 2020 to March 2023, consecutive patients were reviewed by searching inpatients' electronic medical records. Inclusion criteria for this study encompassed all patients with a diagnosis of NCPH due to hepatic schistosomiasis, confirmed through imaging findings (liver calcification or typical strong echoes on CT or ultrasound) and medical history. The following criteria were used to define the groups: EGVB: Patients with NCPH who presented with a first episode of EGVB. EGVB was diagnosed by clinical symptoms and confirmed via endoscopy. The patients received contrast-enhanced CT within 30 days before EGVB. Non-EGVB: Patients with NCPH who did not experience EGVB within the one month before or after CT scanning, and no history of previous EGVB. These patients were selected from the control database and matched to cases based on sex and age to minimize selection bias. The exclusion criteria were as follows: (1) NCPH patients with viral hepatitis or alcoholic cirrhosis; (2) Patients with ulcer bleeding; (3) Patients who had previously undergone surgical interventions for portal hypertension prior to CT scanning; (4) CT images with significant artifacts, which could interfere with accurate evaluation; (5) Patients who experienced rebleeding episodes of EGVB; (6) Patients with other liver diseases known to affect portal hypertension, including: fatty liver disease, cholestatic liver diseases, autoimmune liver diseases, and hereditary liver diseases; (7) Patients with portal vein thrombosis (assessed using

contrast-enhanced CT images). The NCPH patients were randomly assigned into a training cohort and testing cohort.

Clinical laboratory data acquisition and selection

All patients' clinical laboratory data were collected, including sex, age, alanine aminotransferase (ALT), aspartate aminotransferase (AST), platelet count, total bilirubin (TB), prothrombin time (PT), high-density lipoprotein (HDL), low-density lipoprotein (LDL), C-reactive protein (CRP), international normalized ratio (INR), albumin and creatinine. For the EGVB group, we recorded laboratory test results from the closest date within 30 days before the EGVB event. For the non-EGVB group, we recorded laboratory test results from the closest date within 30 days before or after the CT scan. Multivariate logistic regression analysis was used to select clinical laboratory predictors for predicting EGVB.

CT acquisition and varices score calculation

CT was performed on a 64-row-detector scanner (SOMATOM; Siemens, Erlangen, Germany). The protocol and scanning parameters were as follows: slice thickness=1.0 mm with interval=0.6 mm; detector collimation=64×0.625 mm; pitch=1.08; scan time=5–7 s; matrix=512×512; tube voltage=120 kVp and tube current=250 mA. The scanning range extended from above the diaphragm to the inferior pole of the right kidney. The contrast medium (Bayer Healthcare, Berlin, Germany) was administered intravenously at a dose of 2 mL/kg.

All CT images with 1.0-mm-thick sections were processed on a workstation using the picture archiving communicating system. Three-dimensional reconstruction was used to construct the portal vein system. Collateral vessels were observed in axial, sagittal and coronal views. Both pre- and postcontrast CT scanning were viewed to identify a certain varices vein. Two readers (Radiologists 1 and 2 with 10 and 5 years experience in abdominal radiology) evaluated the presence, anatomy and varices score of the collateral vessels using a three-point scale: stage 1=no varices (score=0); stage 2=small and mild tortuous (score=1); and stage 3=obvious tortuous (score=2). Thirteen collateral vessels were identified and evaluated, namely, the coronary vein (left gastric vein), short gastric vein, perisplenic vein, gastroepiploic vein, splenorenal vein, paraesophageal vein, paraesophageal vein, gastrorenal vein, mesenteric vein, paravertebral vein, omental vein, paraumbilical vein and abdominal wall vein.

Interclass correlation coefficients (ICC) were used to evaluate the interobserver consistency of each varices vein. The collateral vessels with an ICC<0.70 were considered to have low consistency and were not included in further analysis. Two algorithms were used to calculate the varices score. Algorithm 1: The varices score was calculated by a linear combination of the scores of the collateral vessels with ICC>=0.70. Algorithm 2: Considering the facilitation of clinical application, the varices score was also calculated by simply summing the scores of the collateral vessels with ICC>=0.70.

Clinical laboratory predictors, varices score and MELD score in predicting EGVB

The predictive ability of clinical laboratory predictors, varices score (algorithms 1 and 2) and MELD score in predicting EGVB was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC) in both the training and testing cohorts. The MELD score was calculated as follows: MELD=9.57×ln (creatinine)+3.78×ln (bilirubin)+11.20+ln(INR)+6.43.

Nomogram building, calibration, discrimination and validation

A nomogram was built for predicting EGVB in NCPH by combining the varices score and clinical laboratory predictors using multivariate binary logistic regression analysis with the lowest Akaike information criterion score.

Calibration curves were used to assess the goodness of fit of the nomogram in the training cohort. The AUC with 95% confidence interval (CI) was used to evaluate the predictive performance of the nomogram, accompanied by the sensitivity, specificity, and positive and negative predictive values in both the training and testing cohorts.

Clinical usefulness

The clinical usefulness of the nomogram and the MELD score were evaluated by a clinical decision curve with net benefit at different threshold probabilities in both the training and testing cohorts.

Statistical analysis

R (Version 4.3.0; http://www.r-project.org/) was used for the statistical analysis. Continuous variables were tested for normality using both the Shapiro-Wilk test and by visually inspecting histograms and Q-Q plots. Student's t test (data conforming to a normal distribution) or the Mann−Whitney U test (data not conforming to a normal distribution) was used to analyze continuous variables. Categorical variables were analyzed by Pearson's chi square test or Fisher's exact test. The "irr" package was used for interobserver agreement analysis; the "glmnet" package was used for multivariate binary logistic regression analysis; the "rms" package was used for nomogram building and calibration curve plotting; and the "pROC" package was used for AUC calculation. $P<0.05$ indicated a statistically significant difference.

Results

Patient characteristics

The 315 NCPH patients (aged 75±8.1, range 44–95) included 196 non-EGVB and 119 EGVB patients. There were 89 females (aged 75±7.2, range 60–94) and 107 males (aged 74±8.1, range 59–95) in the non-EGVB cohort. There were 50 females (aged 77±7.9, range 59–94) and 69 males (aged 75±9.5, range 44–91) in the EGVB cohort. The workflow of this study is shown in Fig. 1.

Clinical characteristics and clinical predictor selection

The clinical characteristics of the NCPH patients in the training and testing cohorts are summarized in Table 1. No significant differences in grander, age, AST, ALT, triglyceride, cholesterol, HDL, LDL, or CRP were found between non-EGVB and EGVB patients in either the training or testing cohort. Marginal statistical differences were found in TB in the training cohort. Decreased platelet count, prolonged PT, decreased albumin, increased creatinine, higher INR and higher MELD score were found in EGVB patients compared with non-EGVB patients in both the training and testing cohorts.

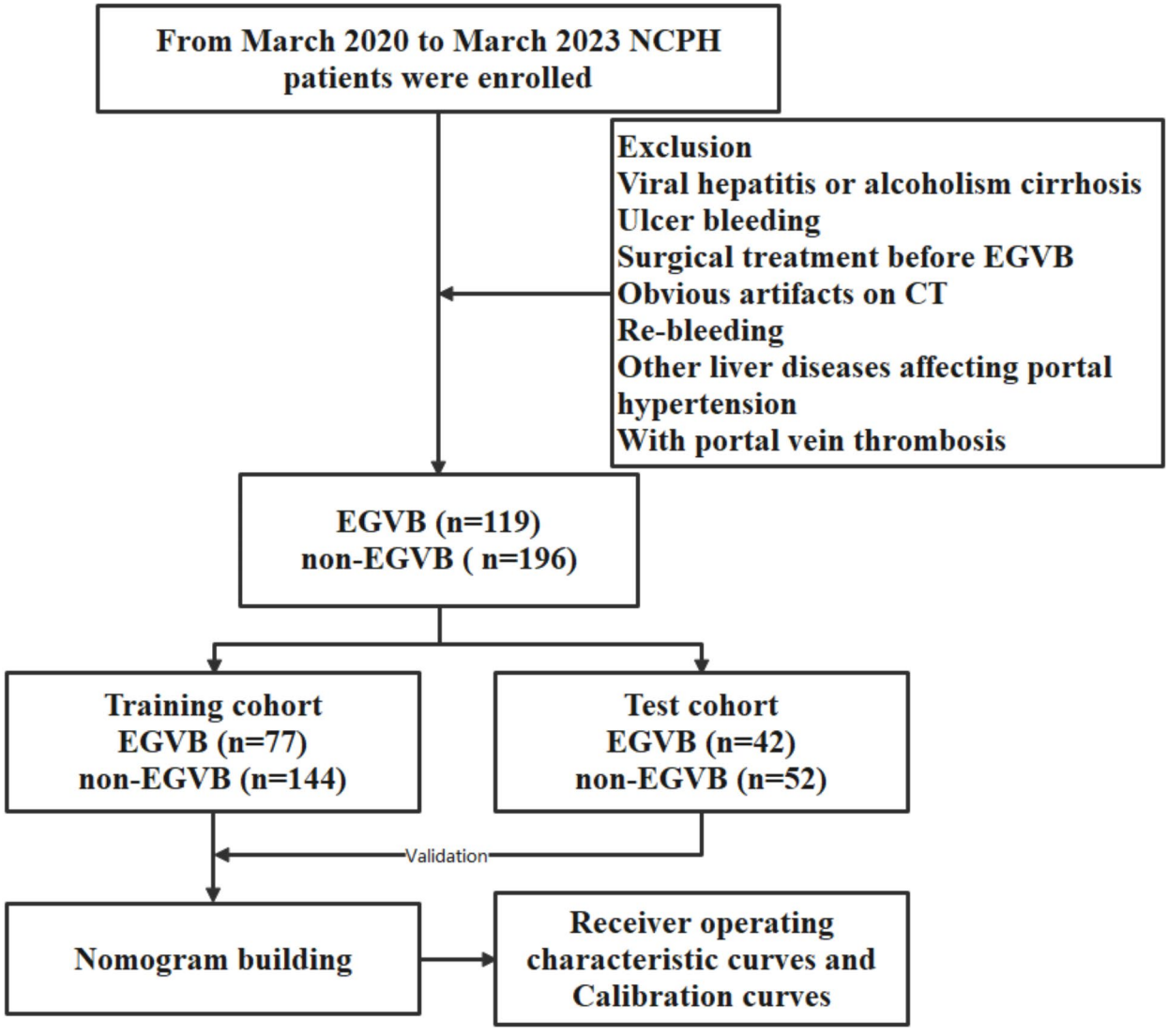

Fig. 1 The workflow of this study
NCPH, noncirrhotic portal hypertension; EGVB, upper gastrointestinal bleeding

Table 1 Clinical characteristics of NCPH patients

	Training cohort			Testing cohort		
	Non-EGVB (*N* = 144)	EGVB (*N* = 77)	*P*	Non-EGVB (*N* = 52)	EGVB (*N* = 42)	*P*
Gender						0.905
Female	66 (45.8%)	30 (39.0%)	0.401	23 (44.2%)	20 (47.6%)	
Male	78 (54.2%)	47 (61.0%)		29 (55.8%)	22 (52.4%)	
Age	74.3 (7.9)	75.4 (9.4)	0.369	74.3 (7.0)	76.6 (7.7)	0.148
ALT (U/L)	22.0 (21.1)	27.9 (32.1)	0.153	19.0 (7.9)	22.4 (13.9)	0.166
AST (U/L)	26.7 (16.0)	31.2 (21.6)	0.105	25.6 (9.4)	28.9 (13.9)	0.194
Platelet	192 (67.0)	155 (53.0)	< 0.001	197 (63.2)	158 (55.2)	0.002
Triglyceride (mmol/L)	1.3 (1.0)	1.3 (1.09)	0.846	1.4 (1.1)	1.3 (1.5)	0.731
Cholesterol (mmol/L)	3.7 (0.9)	3.6 (0.9)	0.434	3.7 (1.2)	3.7 (1.3)	0.888
HDL (mmol/L)	1.0 (0.3)	1.1 (0.4)	0.536	1.0 (0.3)	0.9 (0.3)	0.167
LDL (mmol/L)	2.3 (0.6)	2.2 (0.5)	0.131	2.6 (1.0)	2.3 (0.8)	0.178
CRP (mg/L)	9.9 (16.0)	11.6 (14.7)	0.445	9.9 (13.6)	11.2 (11.3)	0.647
TB (μmol/L)	4.6 (4.3)	5.7 (4.5)	0.075	4.7 (4.5)	5.6 (4.5)	0.354
PT (s)	11.3 (1.4)	13.1 (2.3)	< 0.001	11.0 (1.1)	12.9 (1.8)	< 0.001
Albumin (g/L)	35.2 (4.7)	33.1 (6.2)	0.009	37.2 (4.8)	32.1 (5.0)	< 0.001
Creatinine (μmol/L)	71.3 (28.1)	80.2 (33.7)	0.048	69.1 (31.3)	88.0 (36.7)	0.01
INR	1.0 (0.1)	1.14 (0.2)	< 0.001	0.9 (0.1)	1.1 (0.1)	< 0.001
Varices score algorithms 1	0.27 (0.23)	0.57 (0.20)	< 0.001	0.24 (0.21)	0.55 (0.20)	< 0.001
Varices score algorithms 2	0.8 (1.1)	2.1 (0.8)	< 0.001	0.8 (0.9)	2.0 (0.9)	< 0.001
MELD score	51.0 (4.2)	54.3 (5.2)	< 0.001	50.4 (4.2)	55.0 (5.1)	< 0.001
Beta blocker			< 0.001			< 0.001
Negative	118 (81.9%)	43 (55.8%)		48 (92.3%)	24 (57.1%)	
Positive	26 (18.1%)	34 (44.2%)		4 (7.7%)	18 (42.9%)	

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; EGVB, esophageal gastric variceal bleeding; HDL, high-density lipoprotein; INR, international normalized ratio; LDL, low-density lipoprotein; MELD, model for end-stage liver disease; PT, prothrombin time; TB, total bilirubin

Table 2 The predictive performance of varices score, clinical model, nomogram model and MELD score

Cohort	Features	SPE	SEN	NPV	PPV	AUC	95%CI	*P**	*P#*
Training cohort	Varices score 1	0.65	0.84	0.89	0.56	0.82	0.77–0.87	0.223	-
	Varices score 2	0.65	0.84	0.89	0.56	0.81	0.76–0.86	-	< 0.001
	Clinical model	0.79	0.64	0.80	0.62	0.76	0.69–0.83	-	< 0.001
	Nomogram	0.92	0.71	0.86	0.82	0.89	0.84–0.94	< 0.001	-
	MELD score	0.67	0.68	0.79	0.52	0.69	0.61–0.77	-	< 0.001
Testing cohort	Varices score 1	0.69	0.90	0.90	0.70	0.83	0.75–0.91	-	-
	Varices score 2	0.71	0.81	0.82	0.69	0.81	0.73–0.89	-	0.002
	Clinical model	0.83	0.71	0.78	0.77	0.83	0.74–0.92	-	0.031
	Nomogram	0.92	0.79	0.84	0.89	0.9	0.84–0.97	0.002	-
	MELD score	0.81	0.69	0.76	0.74	0.76	0.66–0.86	-	0.012

*, compared with varices score 2; #, compared with nomogram; -, not done; Varices scores 1 and 2 were calculated by algorithms 1 and 2, respectively. Clinical model wes built by linear combination of the clinical predictors of platelet, prothrombin time, and creatinine

Multivariate binary logistic regression analysis showed that platelet count redaction and prolonged PT were independent clinical predictors for EGVB. A clinical model was built by combining these clinical predictors for EGVB. The specificity, sensitivity, negative predictive value, positive predictive value and AUC of the ROC curve of the clinical model and MELD score in the training and testing cohorts are shown in Table 2. The results of multivariate binary logistic regression analysis of clinical predictors is shown in supplementary Table 1. The information of bleeding site and the form and location of the varices under endoscopy is provided in Supplementary Table 2.

CT varices vein selection and varices score calculation

The median time between CT scanning and EGVB was 9 days (range 0–30 days). CT portal vein system reconstruction and variceal vein evaluation are shown in Fig. 2. The types and frequency of the collateral vessels are shown in Fig. 3A. The results showed that the coronary vein (ICC=0.75), gastroepiploic vein (ICC=0.72), perisplenic vein (ICC=0.80) and omental vein (ICC=0.71),

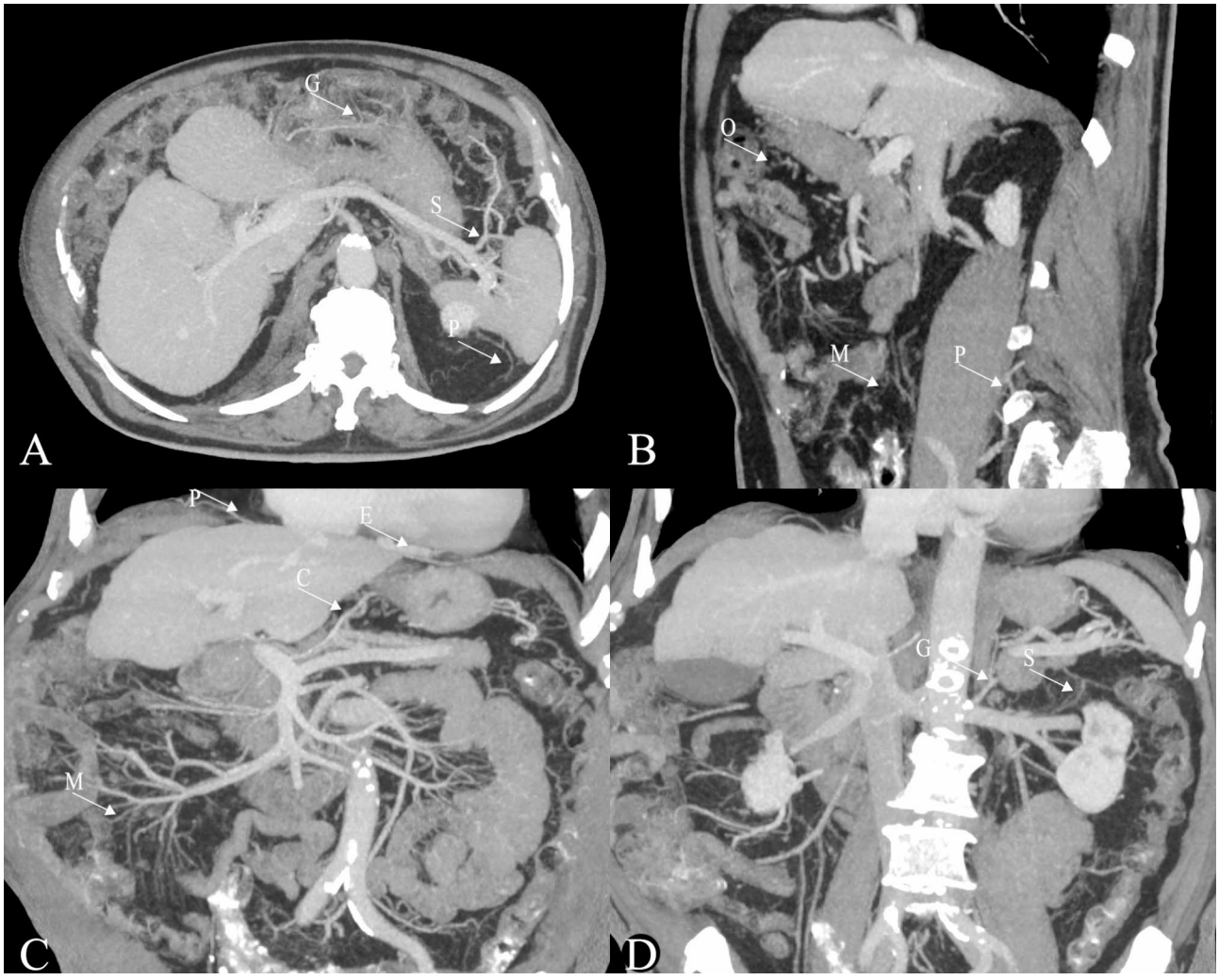

Fig. 2 Postcontrast CT and portal vein system reconstruction of an NCPH patient with EGVB. The short gastric vein (S), gastroepiploic vein (G) and perisplenic vein (P) were tortuous on the axle CT image, and no obvious tortuous paraumbilical vein or abdominal wall vein was observed (**A**). Mild tortuosity of the omental vein (O) paravertebral vein (P) and mesenteric vein (M) is seen on the sagittal CT image (**B**). Tortuosity of the coronary vein (C), esophageal vein (E), paraesophageal vein (P) and mesenteric vein (M) is seen on the coronal CT image (**C**). Tortuosity of the splenorenal vein (S) and gastrorenal vein (G) is seen on the coronal CT image (**D**)

with acceptable agreement between the two readers, could be used for further selection. The varices scores of the 13 collateral vessels in the training and testing cohorts are summarized in Table 3. The ICC results for each collateral vessel is shown in the supplementary Table 3.

Multivariate binary logistic regression analysis showed that the coronary vein, gastroepiploic vein and omental vein (negative predictor) were collateral vessels as predictors for EGVB. The results of multivariate binary logistic regression analysis of CT predictors is shown in supplementary Table 4.

The varices score for each NCPH patient was first calculated by a linear combination of the scores of the collateral vessels (algorithm 1) as follows: Varices score=0.26×score of coronary vein+0.22×score of gastroepiploic vein −0.09×score of omental vein. Then, the varices score was calculated by simply summing the scores of the collateral vessels (algorithm 2) as follows: Varices score=score of coronary vein+score of gastroepiploic vein - score of omental vein. The DeLong test showed no difference between the two algorithms (AUC of algorithm 1=0.82, AUC of algorithm 2=0.81, P=0.223). The specificity, sensitivity, negative predictive value, positive predictive value and AUC of the ROC curve of the varices score in the training and testing cohorts are shown in Table 2. Figure 3B shows the correlation of CT and clinical data in NCPH patients.

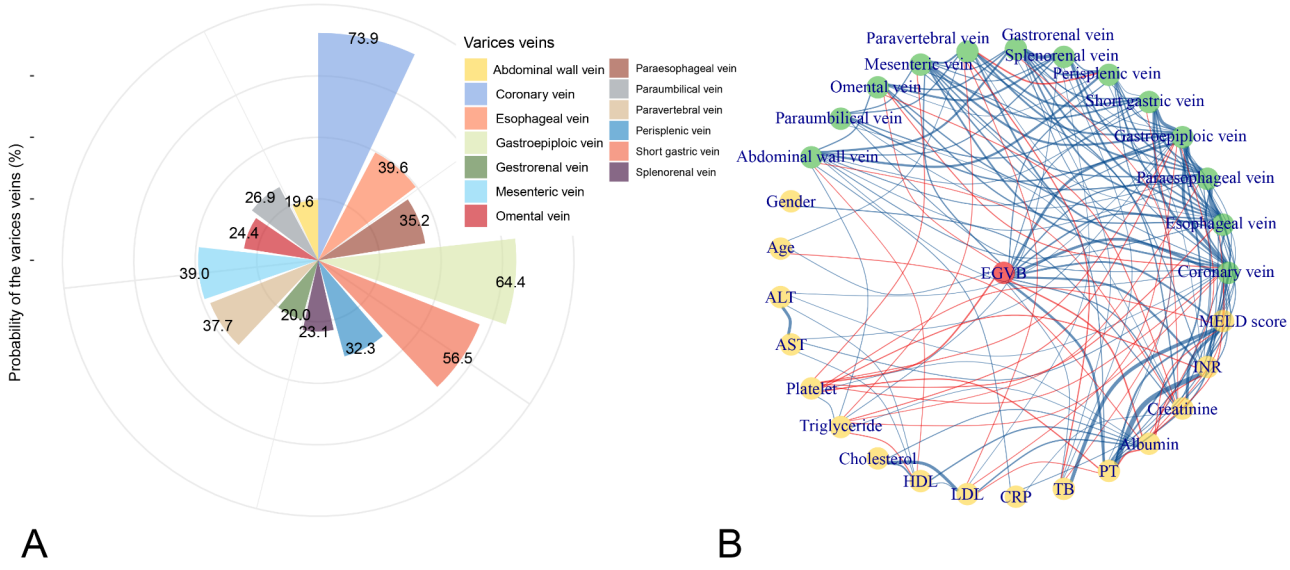

Fig. 3 Nightingale rose diagram shows the types and frequency of the collateral vessels in NCPH patients (**A**). The co-occurrence matrix shows the correlations of the EGVB patients (red), clinical features (yellow) and collateral vessels (green). The blue/red curves indicate positive/negative correlations ($P < 0.05$) (**B**)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; HDL, high-density lipoprotein; INR, international normalized ratio; LDL, low-density lipoprotein; MELD, model for end-stage liver disease; PT, prothrombin time; TB, total bilirubin

Nomogram building, calibration, discrimination and validation

A clinical model was built by linear combination of the clinical predictors. The nomogram combining the varices score and clinical predictors with the lowest Akaike information criterion score was chosen as the best model for predicting EGVB (data from the training cohort, Fig. 4). The calibration curves showed good discrimination performances of the nomogram (Fig. 4B and C). The specificity, sensitivity, negative predictive value, positive predictive value and AUC of the ROC of the nomogram were 0.82, 0.81, 0.89, 0.70, and 0.88 (95% CI: 0.84–0.93) in the training cohort and 0.87, 0.86, 0.88, 0.84, and 0.91 (95% CI: 0.84–0.97) in the testing cohort, respectively.

Clinical usefulness

The nomogram model added net benefit for clinical decisions compared with the consider-all or consider-none scheme in both the training and testing cohorts. A better net benefit of the nomogram than the MELD score is seen in most of the threshold probability areas (Fig. 5).

Discussion

This retrospective study explored the predictive factors of EGVB and found CT-based collateral vessels as predictors, including the coronary vein and gastroepiploic vein as positive predictors and the omental vein as a negative predictor and clinical predictor, including decreased platelet count and prolonged PT in NCPH patients. The results provide a new evaluation model for clinical practice to solve the current problems of EGVB prediction, which could be expected to further guide clinical intervention.

Schistosoma affects humans via contaminated water, and the larva migrates through the bloodstream to the liver and the egg deposits in the small veins of the liver [1, 2]. As a consequence, the host immune response leads to periportal fibrosis and NCPH and finally leads to EGVB [16]. When portal hypertension develops, the coronary vein is the main blood supply for gastroepiploic and esophageal varices [17, 18]. Endoscopy is regarded as the gold standard to identify EGVB, but endoscopy cannot observe the collateral vessels beyond the mucosal surface or evaluate the degree of collateral vessels [7]. CT reconstruction of the portal vein system is noninvasive, easy to perform and highly reproducible. It is an effective inspection method to display the collateral vessels and the small vascular branches of the portal vein system, which can quantitatively evaluate the risk of EGVB.

Both hepatitis cirrhosis and schistosomiasis cirrhosis are intrahepatic portal hypertension, which is characterized by varices of the coronary vein (also known as the left gastric vein) and esophageal vein [19, 20]. The frequency of coronary vein varices is higher, with an incidence of approximately 80% [21]. Studies have suggested that when the diameter of the gastroepiploic vein exceeds 5 mm, it is often regarded as an indication of bleeding risk [22, 23]. Another study showed that the small/absent paraumbilical vein could help to predict EGVB in cirrhotic patients [13]. However, in NCPH patients,

Table 3 Varices scores of the thirteen collateral vessels in NCPH patients

Collateral vessels	Score	Training cohort			Testing cohort		
		Non-EGVB (*N* = 144)	EGVB (*N* = 77)	*P*	Non-EGVB (*N* = 52)	EGVB (*N* = 42)	*P*
Coronary vein	0	56 (38.9%)	2 (2.6%)	< 0.001	23 (44.2%)	1 (2.4%)	< 0.001
	1	85 (59.0%)	56 (72.7%)		28 (53.8%)	32 (76.2%)	
	2	3 (2.1%)	19 (24.7%)		1 (1.9%)	9 (21.4%)	
Esophageal vein	0	98 (68.1%)	31 (40.3%)	< 0.001	43 (82.7%)	18 (42.9%)	< 0.001
	1	35 (24.3%)	36 (46.8%)		6 (11.5%)	20 (47.6%)	
	2	11 (7.6%)	10 (13.0%)		3 (5.8%)	4 (9.5%)	
Paraesophageal vein	0	98 (68.1%)	37 (48.1%)	0.014	46 (88.5%)	23 (54.8%)	< 0.001
	1	36 (25.0%)	30 (39.0%)		6 (11.5%)	15 (35.7%)	
	2	10 (6.9%)	10 (13.0%)		0 (0%)	4 (9.5%)	
Gastroepiploic vein	0	69 (47.9%)	7 (9.1%)	< 0.001	32 (61.5%)	4 (9.5%)	< 0.001
	1	71 (49.3%)	55 (71.4%)		20 (38.5%)	31 (73.8%)	
	2	4 (2.8%)	15 (19.5%)		0 (0%)	7 (16.7%)	
Short gastric vein	0	68 (47.2%)	31 (40.3%)	0.102	28 (53.8%)	10 (23.8%)	0.007
	1	72 (50.0%)	39 (50.6%)		23 (44.2%)	28 (66.7%)	
	2	4 (2.8%)	7 (9.1%)		1 (1.9%)	4 (9.5%)	
Perisplenic vein	0	103 (71.5%)	45 (58.4%)	0.069	45 (86.5%)	20 (47.6%)	< 0.001
	1	41 (28.5%)	32 (41.6%)		7 (13.5%)	22 (52.4%)	
Splenorenal vein	0	105 (72.9%)	62 (80.5%)	0.455	45 (86.5%)	30 (71.4%)	0.105
	1	34 (23.6%)	13 (16.9%)		7 (13.5%)	10 (23.8%)	
	2	5 (3.5%)	2 (2.6%)		0 (0%)	2 (4.8%)	
Gastrorenal vein	0	117 (81.3%)	59 (76.6%)	0.427	46 (88.5%)	30 (71.4%)	0.113
	1	19 (13.2%)	15 (19.5%)		5 (9.6%)	10 (23.8%)	
	2	8 (5.6%)	3 (3.9%)		1 (1.9%)	2 (4.8%)	
Paravertebral vein	0	93 (64.6%)	44 (57.1%)	0.098	34 (65.4%)	25 (59.5%)	0.263
	1	49 (34.0%)	28 (36.4%)		17 (32.7%)	13 (31.0%)	
	2	2 (1.4%)	5 (6.5%)		1 (1.9%)	4 (9.5%)	
Mesenteric vein	0	99 (68.8%)	32 (41.6%)	< 0.001	38 (73.1%)	23 (54.8%)	0.166
	1	40 (27.8%)	37 (48.1%)		11 (21.2%)	16 (38.1%)	
	2	5 (3.5%)	8 (10.4%)		3 (5.8%)	3 (7.1%)	
Omental vein	0	93 (64.6%)	66 (85.7%)	0.002	45 (86.5%)	34 (81.0%)	0.651
	1	51 (35.4%)	11 (14.3%)		7 (13.5%)	8 (19.0%)	
Paraumbilical vein	0	101 (70.1%)	56 (72.7%)	0.804	40 (76.9%)	33 (78.6%)	1
	1	43 (29.9%)	21 (27.3%)		12 (23.1%)	9 (21.4%)	
Abdominal wall vein	0	115 (79.9%)	58 (75.3%)	0.543	46 (88.5%)	34 (81.0%)	0.468
	1	29 (20.1%)	19 (24.7%)		6 (11.5%)	8 (19.0%)	

The varices scores were derived from reader 1

the primary pathological changes were marked fibrosis, relatively intact hepatic sinusoids and slight hepatocyte injuries that are different from those in hepatitis cirrhosis (sinus subtype) with a high frequency of umbilical and abdominal wall vein varices [15, 21]. This study found a high frequency of coronary and esophageal vein varices in NCPH patients and a low frequency of umbilical and abdominal wall vein varices as a characteristic manifestation of intrahepatic presinusoidal portal hypertension. Few studies have investigated the correlation between the omental vein and EGVB. However, interestingly, we found that the omental vein was a negative predictor of EGVB. The finding that the omental vein is a negative predictor of EGVB suggests a potential protective mechanism. Physiologically, the omental vein is part of the portosystemic collateral system, which decompresses portal hypertension by diverting blood flow away from the high-pressure portal system. When the omental vein is well-developed, it may indicate effective collateral circulation, reducing pressure within the portal system and lowering the risk of variceal rupture and bleeding. This suggests that patients with a more prominent omental vein may experience less severe portal hypertension. Clinically, this finding highlights the importance of evaluating collateral vessels in addition to varices when assessing bleeding risk. A more developed omental vein may act as a compensatory mechanism, diverting blood flow and reducing the pressure in esophageal and gastric

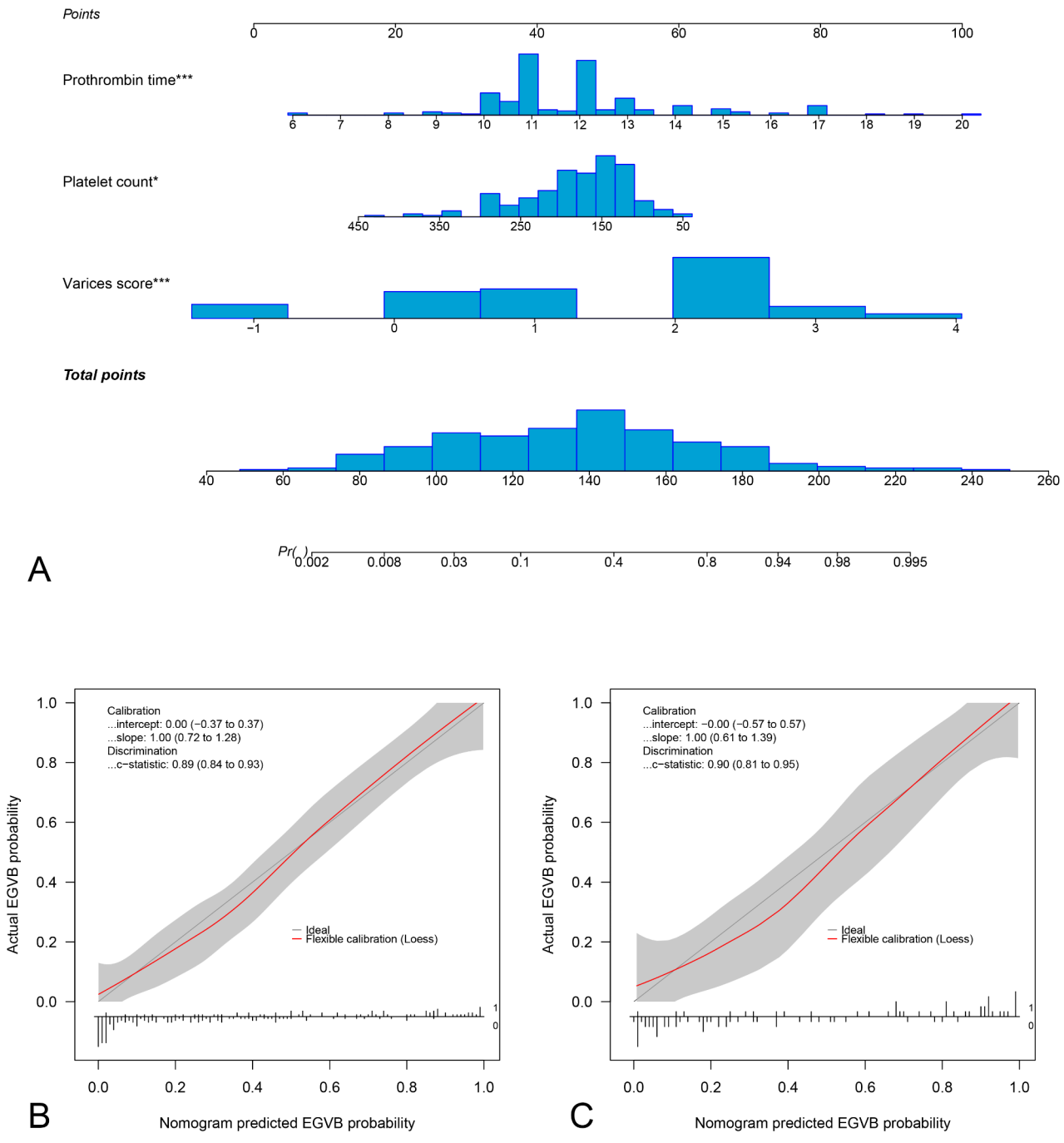

Fig. 4 The nomogram for predicting EGVB in NCPH patients (data from the training cohort using algorithm 2) (**A**). The calibration curves of the nomogram in the training (**B**) and testing cohorts (**C**)
AUC, area under the curve; ROC, receiver operating characteristic

varices, which could inform risk stratification and treatment decisions.

In our study, several collateral vessels, including the paravertebral vein, mesenteric vein, splenorenal vein, and gastrorenal vein, had an interclass correlation coefficient (ICC) of less than 0.7, indicating lower inter-rater agreement. This discrepancy may be attributed to several factors. First, anatomical variability in these vessels can make consistent identification challenging, particularly in cases where the veins are small. Second, variations in image quality, such as suboptimal contrast enhancement, may have contributed to inconsistent evaluations.

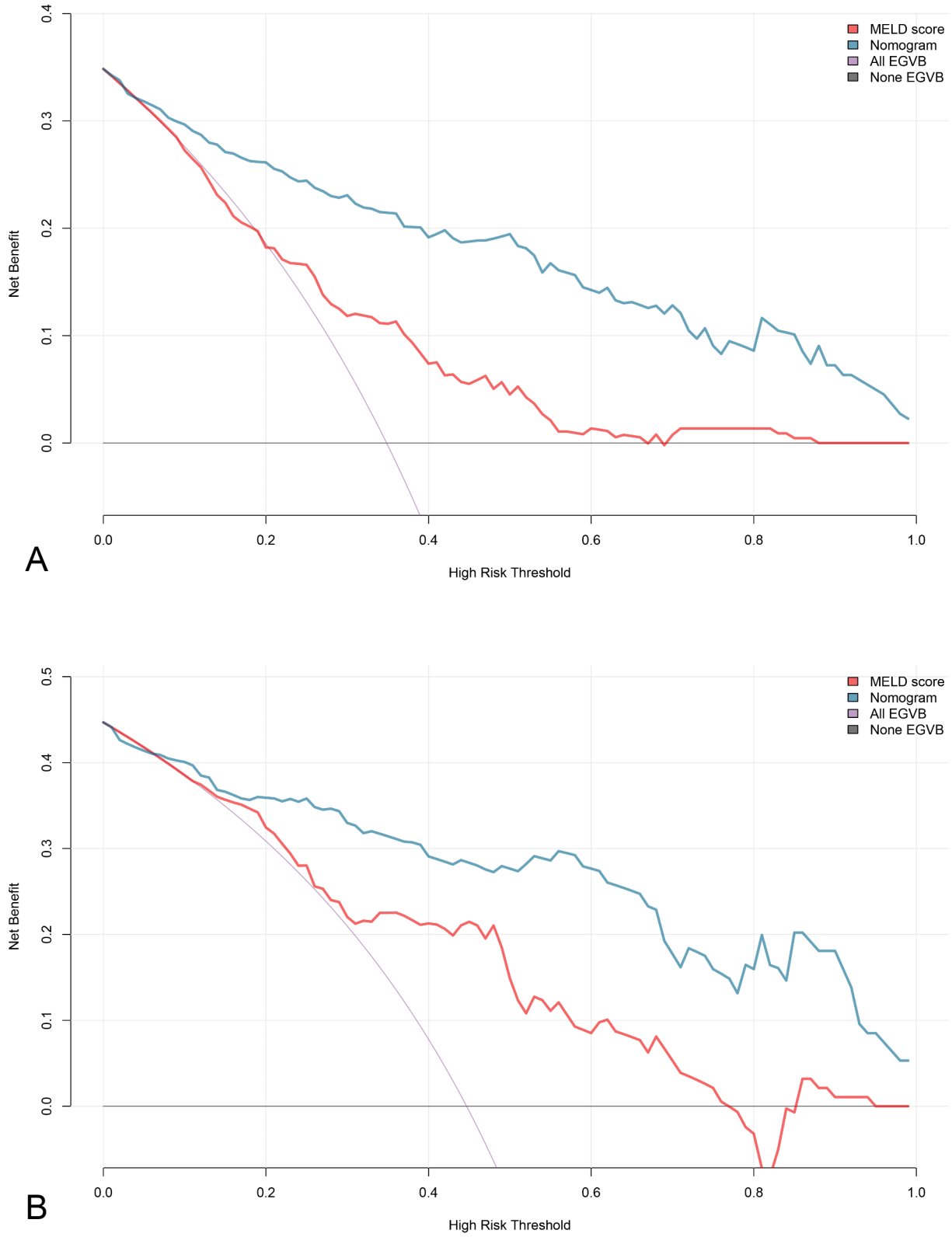

Fig. 5 Clinical decision curves of the nomogram and MELD score for predicting EGVB. Clinical decision curves in the training cohort (**A**) and testing cohorts (**B**)

Furthermore, the subjective nature of assessing the degree of tortuosity or dilation, especially in smaller or peripheral veins, could lead to differences in interpretation between radiologists. The experience level and familiarity of the radiologists with these specific vessels may also have played a role.

Decreased platelet count and prolonged prothrombin time were previously reported in cirrhotic patients with EGVB [24, 25]. The results of this study showed that decreased platelet count and prolonged PT could be used to predict EGVB in NCPH patients. Other studies showed that the AST-to-platelet ratio index, albumin-bilirubin score, platelet-albumin-bilirubin score, King's score, albumin-bilirubin score, fibrosis 4 index and MELD score (AUC=0.64) could be used as noninvasive methods for predicting EGVB in cirrhotic patients. The MELD score had the best predictive ability [14]. Both APRI and liver stiffness, measured through elastography, have been shown to predict the risk of EGVB in patients with cirrhosis and could potentially have predictive value in NCPH as well. APRI is a noninvasive marker used to assess liver fibrosis, and higher APRI values are associated with a greater likelihood of bleeding in cirrhosis patients [13]. Additionally, liver stiffness, assessed by transient elastography, has demonstrated utility in predicting portal hypertension and variceal bleeding in cirrhotic patients [10]. While our study focused on CT-based collateral vessels and traditional laboratory predictors, future research should explore the integration of these alternative markers to improve the predictive model for EGVB in NCPH patients. In this study, mild prediction performance was achieved using the MELD score to predict EGVB in NCPH patients (AUC=0.68 in the training cohort and AUC=0.76 in the testing cohort).

The nomogram combines CT imaging and clinical predictors, which is a promising approach to change management and precision medicine [26]. The results suggest that good prediction performance was achieved by the nomogram in predicting EGVB in NCPH patients. The DeLong test suggested that the nomogram added benefit to the varices score and the clinical model. The clinical decision curve analysis showed that the nomogram had a better net benefit than the MELD score in predicting EGVB. In our study, CT imaging was used to evaluate collateral vessels as predictors of EGVB. While CT is less invasive than endoscopy, it is important to recognize that contrast-enhanced CT is not without risks. Complications such as allergic reactions to contrast agents and contrast-induced nephropathy can occur, especially in patients with renal impairment. In contrast, endoscopy, though considered more invasive, carries a different risk profile. Complications associated with endoscopy include bleeding, infection, and, in rare cases, perforation, with an overall complication rate of less than 1% [7]. The choice between contrast-enhanced CT and endoscopy for screening should therefore depend on the patient's overall risk profile and clinical context. For patients at higher risk of contrast-related complications, such as those with kidney dysfunction, endoscopy may be a safer option despite its invasive nature. Conversely, for patients where endoscopy poses a higher procedural risk, CT may be preferred. Thus, while CT offers detailed anatomical information and the ability to assess collateral vessels non-invasively, the potential for contrast-related complications should not be overlooked, and its safety compared to endoscopy should be carefully considered on a case-by-case basis.

While this study focuses on NCPH due to hepatic schistosomiasis, it is important to acknowledge that advanced cases of hepatic schistosomiasis can lead to periportal fibrosis, which may affect the progression of portal hypertension and complicate the distinction between noncirrhotic and fibrotic liver conditions. Although fibrosis in schistosomiasis does not equate to cirrhosis, it may influence the predictive factors for EGVB. Additionally, the generalizability of our findings to other NCPH etiologies, such as idiopathic noncirrhotic portal hypertension (INCPH), Budd-Chiari syndrome, or portal vein thrombosis, must be considered. These conditions share similarities in the development of portal hypertension without cirrhosis, which suggests that our nomogram combining CT-based collateral vessel assessment and clinical laboratory predictors could potentially apply to other forms of NCPH. However, further studies are necessary to evaluate the nomogram's predictive performance in a broader range of NCPH etiologies, given that the underlying pathophysiology and clinical characteristics may differ depending on the cause of portal hypertension.

This study had several limitations. First, selection bias exists because of the retrospective nature of this study. Second, the robustness and reproducibility of the nomogram need to be further validated in prospective studies with larger data sets. Third, a potential selection bias exists, as this study only included patients who underwent CT scans. It is likely that patients with more severe presentations of NCPH were prioritized for CT imaging, given that CT scans are typically ordered in cases where there is clinical suspicion of significant varices or other complications. This may have resulted in an overrepresentation of patients with advanced disease or higher risk factors for bleeding. Furthermore, we did not directly evaluate the morphology and size of esophageal and gastric varices, which are known to be key predictors of EGVB. Instead, we focused on collateral vessels assessed through CT imaging. Lastly, the collateral vessels beyond the canning range were not accessed in this

study. Expanding the scanning range in future studies could provide a more complete evaluation.

Conclusion

Therefore, CT reconstruction of the portal vein system can provide comprehensive anatomical information on variceal veins. The nomogram combining CT and clinical predictors could be useful to predict EGVB in NCPH patients.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the receiver operating characteristic curve
CRP	C-reactive protein
EGVB	Esophageal gastric variceal bleeding
HDL	High-density lipoprotein
ICC	Interclass correlation coefficients
INR	International normalized ratio
LDL	Low-density lipoprotein
MELD	Model for end-stage liver disease
NCPH	Noncirrhotic portal hypertension
PT	Prothrombin time
ROC	Receiver operating characteristic
TB	Platelet count, total bilirubin

Supplementary Information

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Supplementary Material 1

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Author contributions

WC and KYW Data analysis and writing the first draft. WC, WQL, YL and XYL data acquisition and writing the first draft. SJ The study concept, design and implementation, revised and edited the manuscript.

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Data availability

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This prospective study was reviewed and approved by the Institutional Review Board of Jinshan Hospital, Fudan University (JIEC 2023-S82). Written informed consent was obtained from all patients. The methods carried out in this study were in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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