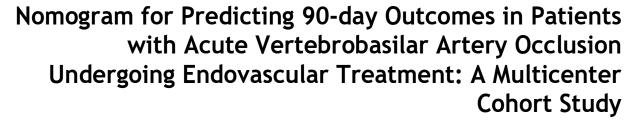
ORIGINAL RESEARCH



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#### ABSTRACT

**BACKGROUND AND PURPOSE:** In this study, we aimed to develop and validate a novel nomogram model for predicting 90-day non-favorable clinical outcomes in patients with acute vertebrobasilar artery occlusion after endovascular treatment by integrating clinical and MRI features.

MATERIALS AND METHODS: This multicenter retrospective study analyzed data from 181 patients with vertebrobasilar artery occlusion eligible for endovascular treatment from two Chinese stroke centers. We developed a predictive model for non-favorable clinical outcomes (modified Rankin Scale score >3) using the data of 125 patients from Stroke Center A (2019-2023). The model was constructed using univariate and multivariate logistic regression analyses of clinical and MRI characteristics, with continuous variables dichotomized based on receiver operating characteristic curve analysis. Internal validation employed smooth bootstrapping, while external validation utilized 56 cases from Stroke Center B (2019-2023), ensuring model reliability and generalizability across diverse clinical settings.

**RESULTS:** Age, NIHSS baseline score, recanalization, novel posterior circulation scores, and MRA-based posterior circulation collateral scores were independent predictors of 90-day prognosis, which were used to create a nomogram model. Internal validation demonstrated excellent discriminative performance of the model (mean area under the curve, 0.92 [95% CI: 0.91-0.93]), while external validation further confirmed its robust generalizability (area under the curve, 0.88). The patients were effectively stratified into the low-risk and high-risk groups using the nomogram model.

**CONCLUSIONS:** The posterior circulation collateral score was an independent predictor of prognosis. Our novel nomogram model, based on clinical and MRI characteristics, effectively predicts 90-day non-favorable clinical outcomes in patients with vertebrobasilar artery occlusion following endovascular treatment.

ABBREVIATIONS: AUC = area under the curve; ETO = estimated time of onset; EVT = endovascular treatment; FCO = favorable clinical outcome; mTICI = modified TICI; Novel-PCS = novel posterior circulation score; pc-ASPECTS = posterior circulation Acute Stroke Prognosis Early CT score; PC-CS = posterior circulation collateral score; ROC = receiver operating characteristic; VBAO = vertebrobasilar artery occlusion

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## SUMMARY SECTION

**PREVIOUS LITERATURE:** MRI can evaluate early ischemic changes in patients with VBAO; however, the overall application of MRI in the management of patients with VBAO is limited by the lack of a validated predictive model.

**KEY FINDINGS:** Age, NIHSS baseline score, recanalization, novel posterior circulation scores, and MRA-based posterior circulation collateral score were independent predictors of 90-day prognosis in patients with VBAO who underwent endovascular treatment. A nomogram developed based on these factors demonstrated excellent discriminative performance and robust generalizability for predicting 90-day outcomes in these patients.

**KNOWLEDGE ADVANCEMENT:** We have developed and validated a novel nomogram model, based on clinical and MRI characteristics, that effectively predicts 90-day clinical outcomes in patients with basilar artery occlusion following endovascular treatment.

### INTRODUCTION

Stroke is among the leading causes of disability and death worldwide<sup>1</sup>. Posterior circulatory stroke caused by vertebrobasilar artery occlusion (VBAO) is associated with neurological deficits<sup>2</sup>. In recent years, endovascular treatment (EVT) has been recommended for the treatment of patients with acute VBAO and widely adopted clinically<sup>3</sup>. Two recent large studies have further confirmed the clinical value of EVT in this patient population; nonetheless, the prognosis for disability and mortality remains high<sup>4,5</sup>.

Baseline assessment based on neuroimaging plays a key role in the indication selection and prognosis of EVT in patients with post-circulation stroke<sup>4-8</sup>. However, two recent prospective randomized cohort studies did not reach a consensus on the best examination method for preoperative neuroradiological evaluation<sup>4,5</sup>, which may be one of the factors influencing the patient selection criteria for EVT.

MRI has a unique advantage in evaluating early ischemic changes in patients with VBAO<sup>9,10</sup>. The novel post-circulation score (Novel-PCS) based on DWI, as proposed earlier, provides a new perspective for the prognostic assessment of patients with VBAO<sup>10</sup>. However, the value of MRA in evaluating posterior circulation collateral status is unclear<sup>11</sup>. Additionally, a comprehensive predictive model integrating clinical and MRI data has not been reported, potentially limiting the overall application of MRI in the management of patients with VBAO.

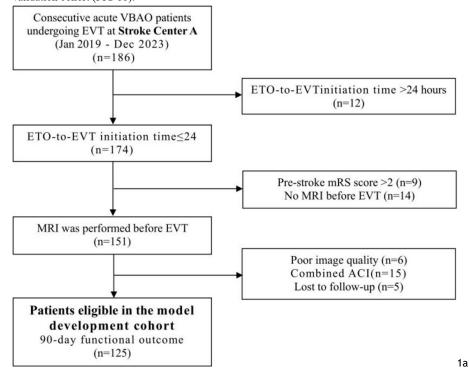
Accordingly, we aimed to develop and validate a nomogram model for predicting functional outcomes 90 days after EVT in patients with VBAO by integrating demographic, clinical, and MRI data. We also aimed to evaluate the predictive value of the model in an independent external validation cohort to ensure its robustness and generalization in clinical practice.

## MATERIALS AND METHODS Study population

This retrospective multicenter study enrolled patients with acute VBAO who underwent EVT at two comprehensive stroke centers (Stroke Center A and Stroke Center B, Xi'an, China) between January 2019 and December 2023. The diagnosis of VBAO was established through DSA. All included patients had undergone pre-EVT MRI examination, including DWI and MRA sequences. The MRA findings were retrospectively evaluated for the presence and extent of occlusions, including the vertebral artery (V4) segment (V4 segment occlusion resulting in absence of flow in the basilar artery), basilar artery, and any extension into the posterior cerebral artery.

The inclusion criteria were 1) age >18 years; 2) pre-stroke mRS score  $\leq 2$ ; 3) a time window from the estimated time of onset of the occlusion (ETO)<sup>12</sup> to the start of EVT (inguinal puncture) within 24 hours; and 4) availability of complete 90-day follow-up data. The exclusion criteria were 1) an ETO-to-EVT initiation time exceeding 24 hours; 2) pre-existing functional disability, characterized by a pre-stroke mRS score  $\geq 3$ ; 3) suboptimal MRI image quality, deemed non-evaluable by consensus of two neuroradiologists; and 4) loss to follow-up.

We enrolled 181 patients. The entire cohort of 125 patients from Stroke Center A was used to construct the prediction model, constituting the model development cohort (FIG 1a). The remaining 56 patients from Stroke Center B formed an independent external validation cohort (FIG 1b).



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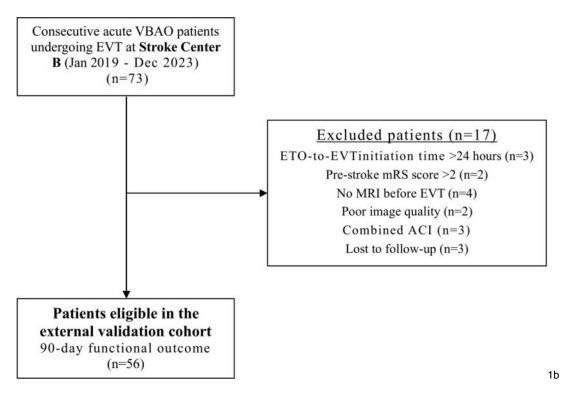


FIG 1. Patient selection flow diagrams. (a) Model development cohort. (b) Independent external validation cohort. Abbreviations: VBAO, vertebrobasilar artery occlusion; EVT, endovascular treatment; ETO, estimated time of onset of the occlusion; ACI, anterior circulation infarcts

The study protocol was approved by the Institutional Review Boards of the participating hospitals. As this was a retrospective study, the requirement for obtaining informed consent was waived by the appropriate review board.

#### Clinical data collection and definitions

We retrospectively analyzed the clinical diagnosis and treatment records of each patient, collecting data such as age, sex, presence of hypertension, presence of diabetes, smoking status, alcohol use, presence of atrial fibrillation, occlusion site, and time from ETO to inguinal puncture. Baseline neurological status was assessed using the NIHSS. Stroke etiology was classified according to the Trial of Org 10172 in the Acute Stroke Treatment classification system, which categorizes stroke into large-artery atherosclerosis, cardioembolism, and other unknown causes. All patients underwent immediate NCCT after EVT to detect intracranial hemorrhage. Symptomatic intracranial hemorrhage is defined as any hemorrhage leading to neurological impairment, accompanied by an increase of at least four points in the NIHSS score within 7 days of onset<sup>13</sup>.

## Image acquisition and assessment

In this study, image acquisition was performed using a Siemens Avanto-1.5T superconducting MRI system (Siemens Healthcare, Erlangen, Germany). For DWI, the scan parameters were set as follows: repetition time (TR), 3250 ms; echo time (TE), 77 ms; b-values, 0 and 1000 S/mm²; FOV, 230×230 mm2; matrix size, 192×192; slice thickness, 5 mm; slice spacing, 1.5 mm; and a total of 19 or 20 slices. The MRA scan parameters were as follows: TR, 22 ms; TE, 7 ms; FOV, 240×240 mm2; matrix size, 320×320; slice thickness 0.6 mm, slice spacing 0 mm, totaling 146 slices. All scans covered the intracranial segment of the vertebral arteries, extending from the foramen magnum to the superior margin of the corpus callosum, and original images were acquired in the axial position using the three-dimensional time-of-flight technique.

NCCT images were acquired using a SOMATOM Definition Flash scanner (Siemens Healthcare). The scanning parameters were as follows: voltage, 120 kV; current, 170 mA; and slice thickness, 5 mm. The coverage extended from the base of the skull to the vertex, with the axial scans continuously aligned parallel to the orbitomeatal line.

Two distinct imaging scoring tools based on DWI sequences were employed in this study: the posterior circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS) and the Novel Posterior Circulation Score (Novel-PCS). The pc-ASPECTS is a 10-point scoring system developed by Puetz et al. <sup>14</sup> based on CTA source images. This scoring system was later adapted for DWI by Tei et al. <sup>15</sup>. Subsequently, Bai et al. <sup>10</sup> developed the Novel-PCS, a 27-point scoring system based on DWI sequences. In addition, the baseline posterior circulation collateral status of the patients was assessed using the posterior circulation collateral score (PC-CS) based on MRA <sup>16</sup>. This scoring system, proposed by Van der Hoven et al. <sup>17</sup>, is a crucial indicator for predicting the prognosis of posterior circulation strokes. Two experienced neuroradiologists (HSS with 7 years of experience and NC with 3 years of experience), blinded to the treatment outcomes, independently reviewed the MRA and DWI images and the corresponding apparent diffusion coefficient maps for patients from both stroke centers. To ensure consistency across centers, the same two neuroradiologists evaluated all images from both sites. The inter-rater agreement for the three scoring systems (pc-ASPECTS, Novel-PCS, and PC-CS) was evaluated using Cohen's kappa coefficient to assess the reliability between raters. Cases with initial discrepancies were re-evaluated until a consensus was reached.

## EVT and functional outcome assessment

In this study, the two participating stroke centers each perform over 60 EVT procedures annually for cerebrovascular diseases. EVT was

primarily conducted using stent retrievers and/or aspiration techniques. Tirofiban was administered to patients showing residual stenosis on DSA during the procedure. Rescue treatments, including stenting or balloon-assisted angioplasty, were implemented according to center-specific protocols. All patients received standardized optimal medical care at each center. Postprocedural reperfusion was assessed using DSA and quantified using the modified TICI (mTICI) scale, with scores of 2b/3 defined as successful recanalization.

To evaluate post-stroke functional impairment and dependency, this study used an mRS score of 0–3 at 90 days, defined as a favorable clinical outcome (FCO), which was considered the primary clinical outcome of this research.

### Development of the nomogram model

Based on the results of the univariate analysis, variables with a P-value of <0.05 were included in the multivariate logistic regression analysis to develop the predictive model. Before proceeding with the multivariate regression analysis, all variables were subjected to collinearity testing, and variables with a variance inflation factor greater than 5 were excluded.

Particular attention was paid to the two baseline DWI scores, the pc-ASPECTS, and the Novel-PCS. These scores are designed to assess the severity of cerebral infarction at baseline and overlap to some extent in describing the infarct location. In the model development cohort, pc-ASPECTS was included in the first multivariate analysis (Model 1) and Novel-PCS was included in the second multivariate analysis (Model 2) to avoid interpretation difficulties caused by conceptual overlap. The performances of Models 1 and 2 were compared, and the better performing model was visualized as a nomogram to improve its clinical applicability. The performance of the predictive model was evaluated using pseudo-R-squared, the Akaike information criterion, the Bayesian information criterion, and the area under the curve (AUC). Delong's test was used to compare the AUCs between Models 1 and 2.

Internal validation of the nomogram model was performed in the model development cohort using smooth bootstrapping (1000 resamples) to correct for optimism and overfitting in the predictive performance. The diagnostic performance of the nomogram model was further evaluated in the external validation cohort.

The Brier score was used to assess the calibration and overall predictive accuracy of the model, with scores closer to 0 indicating higher predictive accuracy. The optimism score was employed to evaluate the degree of model overfitting, where positive values suggest potential overfitting, while values close to zero or slightly negative indicate good generalizability. The optimism-corrected Brier score was calculated using 1000 bootstrap resamples to provide a more accurate assessment of model performance, reducing bias from overly optimistic estimates.

#### Statistical analyses

The normality and homogeneity of variance assumptions for continuous data were assessed using the Shapiro–Wilk and Levene's tests, respectively. Continuous variables are presented as the mean  $\pm$  standard deviation or median (interquartile range) for non-parametric data, while categorical variables are reported as frequencies (percentages). Intergroup comparisons were performed using Student's t-test or the non-parametric Mann–Whitney U test for continuous variables. For categorical variables, the chi-square ( $\chi$ 2) test was employed. Age, NIHSS, pc-ASPECTS, Novel-PCS, and PC-CS were converted into binary variables using truncated values. Statistical analyses were performed using SPSS version 22 (IBM, Armonk, NY, USA) and Python version 3.12. MedCalc software (MedCalc, Ostend, Belgium) was used for receiver operating characteristic (ROC) curve analysis. Statistical significance was set at P <0.05.

#### RESULTS

#### Baseline characteristics of the participants

This study evaluated the 90-day functional outcomes of 181 patients with acute VBAO who underwent EVT, including 125 in the model development cohort and 56 in the external validation cohort (FIG 1). Based on 90-day post-treatment mRS scores, patients were divided into two groups: the FCO group (mRS score 0–3) and the non-FCO group (mRS score 4–6). Inter-rater consistency was measured using Cohen's kappa coefficient, resulting in kappa values of 0.87, 0.79, and 0.79 for pc-ASPECTS, Novel-PCS, and MRA-based PC-CS, respectively. The baseline characteristics of the model development and validation cohorts were comparable (Online Supplemental Data).

Table 1 shows the clinical and imaging characteristics of the patients in the model development cohort. The patients in the FCO group had a significantly lower average age (63.6±11.5 years) compared with those in the non-FCO group (69.8±13.0 years) (P=0.001), indicating a better prognosis in younger patients. A lower baseline NIHSS score (7 vs. 19; P<0.001), higher pc-ASPECTS (8 vs. 7; P<0.001), lower Novel-PCS (3 vs. 5; P<0.001), and higher PC-CS (7 vs. 5; P<0.001) were indicative of a better prognosis. The rate of successful recanalization was significantly higher in the FCO group than in the non-FCO group (85.1% vs. 47.1%, P<0.001), while the incidence of symptomatic intracranial hemorrhage was significantly lower (4.1% vs. 23.5%, P=0.01), indicating that successful recanalization and a lower risk of symptomatic intracranial hemorrhage were associated with better functional outcomes.

ROC analysis identified the following cutoff values for key clinical and imaging indicators affecting prognosis: age >66 years, baseline NIHSS score >12, DWI pc-ASPECTS  $\leq$ 7, Novel-PCS >3, and PC-CS  $\leq$ 5 (Online Supplemental Data).

## Logistic regression analysis

To screen for independent predictors of 90-day non-FCOs in patients with VBAO after EVT, we performed univariate and multivariate analyses in the model development cohort. Univariate analyses revealed that age >66 years (OR, 4.54; 95% confidence interval [CI], 2.07 to 9.93; P<0.001), NIHSS score >12 (OR, 9.58; 95% CI, 4.19 to 21.91; P<0.001), pc-ASPECTS  $\leq$ 7 (OR, 8.13; 95% CI, 3.12 to 20.03; P<0.001), Novel-PCS >3 (OR, 6.80, 95% CI, 2.68 to 13.41; P<0.001), PC-CS  $\leq$ 5 (OR, 5.52; 95% CI, 2.54 to 12.02; P<0.001), failed recanalization (OR, 5.71; 95% CI, 2.53 to 12.89; P<0.001), and symptomatic intracranial hemorrhage (OR, 7.28; 95% CI, 1.94 to 27.37; P=0.003) were correlated with 90-day clinical outcomes (Online Supplemental Data).

The results of the multifactorial logistic regression analyses for the model development cohort are shown in Online Supplemental Data. In the first multifactorial regression analysis (Model 1), age >66 years, NIHSS score >12, failed recanalization, pc-ASPECTS  $\leq$ 7, and pc-CS  $\leq$ 5 were determined to be independent risk factors for 90-day non-FCOs. In the second multifactorial regression analysis (Model 2), we replaced pc-ASPECTS with Novel-PCS; the results showed that Novel-PCS was also an independent predictor. Among the models,

Model 2, which included Novel-PCS, had a higher pseudo-R2 value of 0.66, coupled with a lower Akaike information criterion score of 91.57 and a Bayesian information criterion score of 108.54 (Online Supplemental Data). The results of ROC curve analysis showed that Model 2 (AUC=0.91) was superior to Model 1 (AUC=0.89) (Online Supplemental Data).

**Table 1:** Comparison of clinical and imaging characteristics of the patients in the model development cohort with acute VBAO who underwent EVT.

Variable	FCO group (mRS score 0-3; n=74)	Non-FCO group (mRS score 4-6; n=51)	P value
Age (years)	63.6±11.5	69.8±13.0	0.001
Sex, male, n (%)	51 (68.9)	30 (58.8)	0.25
ETO-to-groin puncture, h	6.1 (3.3-11.5)	6.3 (2.7-15.4)	0.10
Risk factors, n (%)			
Smoking	26 (35.1)	18 (33.3)	0.99
Alcohol use	15 (20.3)	17 (32.3)	0.10
Hypertension	58 (78.4)	40 (78.4)	0.99
Diabetes	24 (32.4)	22 (43.1)	0.22
Atrial fibrillation	11 (14.9)	13 (25.5)	0.14
Stroke cause, n (%)			0.31
Large-artery atherosclerosis	43 (58.1)	24 (47.1)	
Cardioembolic	17 (23.0)	18 (35.3)	
Undetermined cause or others	14 (18.9)	9 (17.6)	
Occlusion site, n (%)			
Vertebral artery (V4)	29 (39.2)	25 (49.0)	0.21
Proximal BA	13 (17.6)	15 (29.4)	0.11
Middle BA	30 (40.5)	23 (45.1)	0.76
Distal BA	23 (31.1)	22 (43.1)	0.10
Admission NIHSS score	7 (5-14)	19 (12-35)	< 0.001
PC-CS	7 (5-8)	5 (4-6)	< 0.001
pc-ASPECTS	8 (8-9)	7 (6-8)	< 0.001
Novel-PCS	3 (2-4)	5 (4-7)	< 0.001
Intravenous thrombolysis, n (%)	21 (29.2)	17 (34.7)	0.57
Recanalization (mTICI 2b, 3), n (%)	63 (85.1)	24 (47.1)	< 0.001
Rescue treatment (stenting or balloon-assisted angioplasty), n (%)	31 (41.9)	18 (35.3)	0.48
Symptomatic intracranial hemorrhage, n (%)	3 (4.1)	12 (23.5)	0.01

Abbreviations: PC-CS, posterior circulation collateral scores; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT score; Novel-PCS, novel posterior circulation score; mTICI, modified TICI; BA, basilar artery; ETO, estimated time of onset *Development and validation of the nomogram model* 

Based on the results of multivariate logistic regression analysis in Model 2, a predictive nomogram model (Table 2 and FIG 2) was constructed using five independent risk factors (age >66 years, NIHSS score >12, failed recanalization, Novel-PCS >3, and PC-CS  $\leq$ 5). The nomogram score was constructed based on the standardized regression coefficients ( $\beta$  values) of each predictor. The maximum regression coefficient in the model was set as a reference value and assigned 100 points, and the scores of the remaining predictors were

Table 2: Nomogram model for predicting 90-day non-FCOs after EVT in patients with acute VBAO.

Variables	Nomogram mode	Nomogram model	
	ß coefficient	OR (95% CI)	
Age >66 years	1.079	2.94 (1.14-7.60)	0.03
Failed recanalization (mTICI 0-2a)	1.337	3.81 (1.35-10.75)	0.01
NIHSS score >12	1.282	3.61 (1.38-9.40)	0.008
PC-CS≤5	1.076	2.94 (1.13-7.62)	0.03
Novel-PCS >3	1.368	3.93 (1.50-10.26)	0.005

Abbreviations: mTICI, modified TICI; Novel-PCS, novel Posterior Circulation score; PC-CS, Posterior Circulation Collateral score; OR, odds ratio.

calculated by the following formula: Score of a single predictor = (regression coefficient of the variable/maximum regression coefficient in the model)  $\times$  100.

# Nomogram for Predicting 90-day non-FCOs

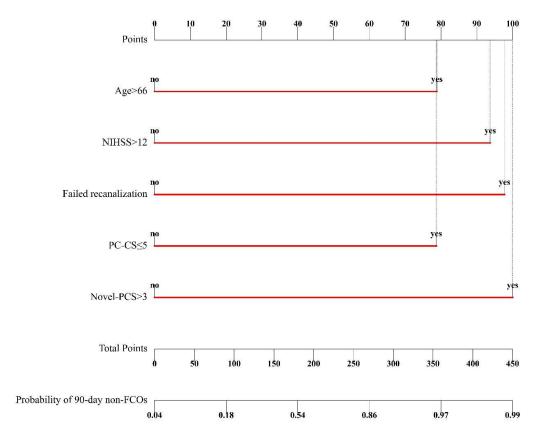


FIG 2. Ninety-day non-FCOs nomogram for patients with acute VBAO undergoing EVT. Abbreviations: Novel-PCS, novel posterior circulation score; PC-CS, posterior circulation collateral score.

Internal and external validation of the nomogram model

The nomogram model exhibited robust discriminative performance in the model development cohort, with an AUC of 0.91. Internal validation via bootstrap resampling (n=1000) yielded a mean AUC of 0.90 (95% CI, 0.88 to 0.91), with an optimism of 0.01. The ROC curve analysis (FIG 3a) demonstrated high concordance between the full dataset and bootstrap average curves, both outperforming random prediction. The narrow 95% CI of bootstrap estimates (gray shaded area) confirmed the model's stability. AUC distribution analysis further corroborated the model's consistency, with most bootstrap samples clustering between 0.88 and 0.91. External validation affirmed the model's generalizability, achieving an AUC of 0.89 (95% CI, 0.85 to 0.93) (FIG 3b).

Calibration assessment utilizing the Brier score revealed an apparent score of 0.12 in the development cohort, with an optimism-corrected Brier score 0.13. Bootstrap analysis produced a mean Brier score of 0.13 (95% CI, 0.12 to 0.14), with an optimism of -0.01. External validation yielded a consistent Brier score of 0.13, underscoring the model's robust calibration performance alongside its discriminative capacity.

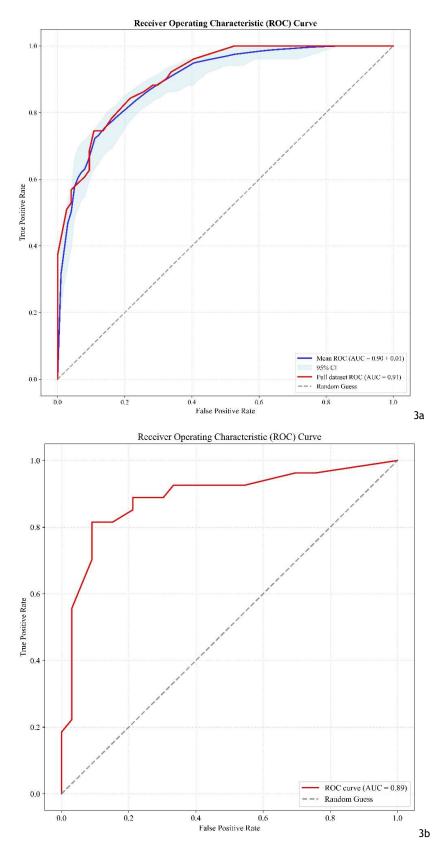


FIG 3. Internal and external validation of the nomogram model. (3a) ROC curve for internal validation of the nomogram model. The red line represents the ROC curve for the full dataset, while the blue line depicts the mean ROC curve derived from 1000 bootstrap replicates. The gray shaded area indicates the 95% confidence interval. (3b) ROC curve for the nomogram model in the external validation cohort. Abbreviation: ROC, receiver operating characteristic.

Decision curve analysis was employed to evaluate the nomogram's clinical utility. In the development cohort, the model demonstrated

superior net benefit at thresholds exceeding 3.5% (FIG 4a). External validation decision curve analysis results (FIG 4b) further substantiated the model's clinical value, exhibiting positive net benefit across a broad range of thresholds, notably between 13.0% and 85.0%.

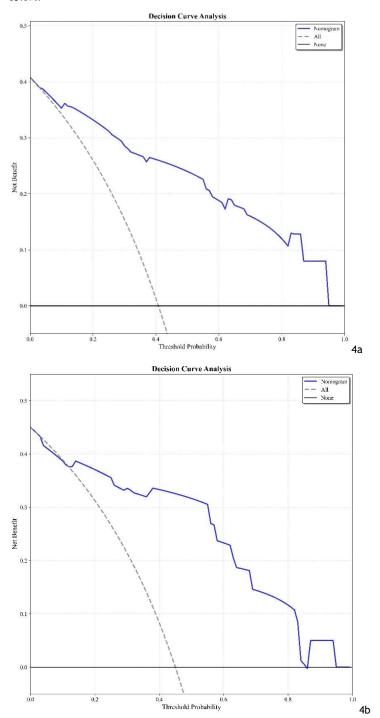


FIG 4. Decision curve analysis for evaluating the nomogram model. "None" indicates that no individuals are predicted to be non-FCOs. "All" indicates that all individuals are predicted to be non-FCOs by default. Non-FCOs, non-favorable clinical outcomes. (a) Decision curve analysis for internal validation of the nomogram model. (b) Decision curve analysis for external validation of the nomogram model.

## Risk stratification based on the nomogram model

The optimal cutoff value for total nomogram points (251.29) was determined using ROC curve analysis based on the Youden index in the model development cohort and applied to the external validation cohort. Patients were stratified into low-risk (≤251.29 points) and high-risk (>251.29 points) groups. Two representative cases (low-risk with FCOs; high-risk with non-FCOs) demonstrated concordance with nomogram-based predictions (Online Supplemental Data).

In the development cohort, the non-FCO rates were 16.5% and 82.6% in the low-risk (n=79) and high-risk (n=46) groups, respectively

(Online Supplemental Data). In the external validation cohort, the corresponding rates were 15.6% and 87.5% for the low-risk (n=32) and high-risk (n=24) groups (Online Supplemental Data). Statistical analysis revealed a significantly higher likelihood of non-FCOs in the high-risk group compared with that in the low-risk group (OR, 24.12; 95% CI, 9.17 to 63.42; P<0.001) in the development cohort; this finding was corroborated in the validation cohort (OR,32.70; 95% CI, 9.49 to 87.67; P<0.001). The risk distribution was similar between the two cohorts, with no significant difference (p=0.54) (Online Supplemental Data). These results demonstrate robust risk stratification capabilities of the nomogram model in both the cohorts.

#### DISCUSSION

A growing body of evidence supports EVT for acute VBAO stroke<sup>3-5</sup>. However, the overall rates of disability and mortality remain relatively high. In this study, we analyzed the clinical and MRI characteristics of acute VBAO patients who underwent EVT and developed predictive models for 90-day non-FCOs. We found that Model 2 demonstrated superior predictive capability with a higher pseudo-R² value (0.66 vs. 0.60). Furthermore, Model 2 exhibited lower Akaike information criterion (91.57 vs. 107.34) and Bayesian information criterion (108.54 vs. 124.12) values compared to Model 1, indicating better model fitting while maintaining parsimony. Based on these statistical advantages, the independent predictors from Model 2 were ultimately selected to construct a predictive nomogram. The nomogram model includes the PC-CS, Novel-PCS, age, baseline NIHSS score, and recanalization status. The nomogram model demonstrated consistent predictive performance in both internal and external validation cohorts. Furthermore, when patients were stratified into low- and high-risk groups based on nomogram points, there was a statistically significant difference in the rates of poor outcomes between these groups. The nomogram model aids in predicting prognosis for acute VBAO patients undergoing EVT, rather than for patient selection for EVT.

There is a growing number of cohort studies involving patients with acute VBAO stroke undergoing EVT<sup>6,8,9</sup>. These studies have revealed multiple factors that may affect the clinical prognosis of patients, including age, sex, atrial fibrillation, stroke etiology, infarct site, time from onset to femoral artery puncture, baseline NIHSS score, inflammatory markers, multiple imaging scores (e.g., pc-ASPECTS, Brain Stem Score, Novel-PCS, and PC-CS, among others), and other factors. However, these factors were not consistent across EVT cohorts. Nevertheless, age, NIHSS scores, and imaging scores have been shown to have a significant predictive value in most EVT cohort studies<sup>8,10,18</sup>. Predictive models for 90-day prognosis in patients with acute VBAO stroke have also been reported. Li et al.<sup>19</sup> developed a 90-day prognostic model for patients with acute basilar artery occlusion undergoing EVT based on two large-vessel occlusion EVT cohort studies that performed well in predicting a good 90-day prognosis (AUC=0.87). However, the study had two main limitations: first, it was not specified whether the imaging scoring system used was CT- or MRI-based, and this uncertainty may have affected the predictive value of the model; second, the model was not validated in an independent cohort, which may have limited its robustness and generalizability. Zhang et al.<sup>20</sup> proposed DWI-based radiomics features to predict 90-day clinical outcomes in patients with VBAO stroke, which also demonstrated a high predictive ability (AUC=0.87). However, the study used manual segmentation of the images, which took a long time to process (approximately 20 minutes) and required software that is difficult to apply widely in clinical practice, with obvious limitations, especially in the emergency setting. Given the limitations of existing studies, we constructed a 90-day non-FCO prediction model in a cohort of patients with acute VBAO undergoing EVT and validated it in an independent cohort to demonstrate its ability to predict non-FCOs. The model demonstrated superior predictive value (AUC=0.91) compared with the two previous models 19,20. Our findings identified age, baseline NIHSS score, recanalization, and baseline MRI-based scores (Novel-PCS and PC-CS) as risk factors for 90-day non-FCOs.

Older patients with stroke may present with weaker physiological resilience, several comorbidities, and a higher risk of postoperative complications, all of which may worsen patient prognosis. The baseline NIHSS score, which is often used clinically to assess patients' neurological impairment on admission, has been reported in several studies<sup>8,18</sup> and is strongly associated with the 90-day mRS score, which was confirmed by the findings of our current study. However, the mechanisms by which increasing age and stroke severity contribute to the non-FCOs of EVT are unclear, and studies are needed to evaluate the pathophysiology and treatment options for these patients.

One study<sup>21</sup> showed that patients who were recanalized within 6 hours had a better prognosis. Meanwhile, other studies suggested a benefit of performing EVT within 24 hours<sup>3,4</sup> or later<sup>22</sup>. Our study revealed that time metrics were not independent predictors of clinical outcomes, which aligns with several recent investigations. Pop et al.<sup>23</sup> demonstrated that despite early thrombectomy, poor outcomes could still occur, emphasizing successful recanalization as the crucial determinant of prognosis. Similarly, Kwak et al. 11 found no significant correlation between onset-to-recanalization time and clinical outcomes in patients with basilar artery occlusion, suggesting that time may not be the predominant determinant of outcomes in posterior circulation stroke. These findings indicate that the relationship between time metrics and outcomes in posterior circulation stroke may be more complex than in anterior circulation stroke. This difference might be attributed to the unique pathophysiology of the posterior circulation: studies have shown that the brainstem demonstrates greater ischemic tolerance compared to anterior circulation-dependent brain tissue<sup>24</sup>. Collectively, these findings emphasize that successful recanalization and collateral status, rather than time windows, may be more decisive factors in treatment decisions for VBAO patients. Notably, in our cohort, the 12 patients who did not have successful recanalization but showed good outcomes all had good initial collateral circulation scores (PC-CS >7). This observation highlights the critical value of PC-CS in posterior circulation stroke assessment. The system's comprehensive evaluation of both primary (posterior communicating arteries) and secondary (cerebellar arteries) collateral pathways provides crucial prognostic information<sup>17</sup>, particularly valuable for acute decision-making. Cerebral ischemia is associated with defective cerebral perfusion, and this relationship largely depends on the collateral circulation status<sup>25</sup>. A meta-analysis conducted by Liu et al.<sup>26</sup> demonstrated a significant correlation between favorable baseline collateral circulation and functional outcomes 90 days after posterior circulation stroke. This is corroborated by the findings of the present study. The ability of these 12 acute VBAO patients to recover from ischemia mentioned above may be attributed to their relatively rich collateral circulation, which protects brain tissue by providing an alternative blood supply, thereby reducing ischemic damage.

Novel-PCS<sup>10</sup>, which was used in the current study to assess early ischemic changes, was more comprehensive for early ischemic area assessment, compared with the pc-ASPECTS, and also assessed the extent of ischemic foci. The results of the present study also confirm

that Novel-PCS is associated with 90-day non-FCOs. Model 2, containing Novel-PCS, had better predictive performance compared with Model 1, containing pc-ASPECTS. We incorporated the novel-PCS into our nomogram model, which, despite its lower specificity compared to pc-ASPECTS, offers higher sensitivity in identifying high-risk patients for poor 90-day outcomes. Our aim is to provide clinicians with an effective preliminary screening tool for more comprehensive identification of potentially high-risk patients. In acute cerebrovascular disease management, minimizing the risk of missed diagnoses is more critical than avoiding overdiagnosis. Clinicians can further evaluate patients identified as high-risk by the novel-PCS, integrating other indicators and professional judgment to optimize treatment decisions.

Certain variables may influence the functional prognosis of patients with VBAO following EVT. A previous study demonstrated that atrial fibrillation is a predictor of favorable clinical outcomes at 1 year<sup>6</sup>. However, our study focused on the clinical prognosis at 90 days following EVT and did not identify a difference between the two groups in terms of outcomes. The results of an earlier study indicated that distal basilar artery occlusion was associated with poor prognosis<sup>27</sup>. Conversely, another recent study showed that distal basilar artery occlusion was associated with a favorable prognosis<sup>11</sup>. These results are diametrically contradictory. Our findings indicated that patients with distal basilar artery occlusion were more prevalent in the non-FCO group than in the FCO group, albeit the between-group difference was not statistically significant. Additionally, inflammatory markers<sup>28</sup>, the EVT modality<sup>29</sup>, GCS scores<sup>30</sup> (as a complement to NIHSS for consciousness assessment), and SWI sequences<sup>31</sup> (as supplementary information to DWI) have been reported to influence prognosis. However, these factors were not included in our current analysis and warrant further investigation in patients with acute ischemic stroke.

We conducted a detailed comparison of baseline characteristics between the development cohort and external validation cohort (Online Supplemental Material). Although there was no statistically significant difference in stroke etiology between the two cohorts (P=0.30), they showed different distribution patterns: the development cohort had a higher proportion of cardioembolic stroke (28.0% vs. 17.9%), while the external validation cohort had a higher proportion of large-artery atherosclerosis (69.6% vs. 53.6%). This distribution difference might be attributed to the presence of a municipal cardiovascular research laboratory in the hospital of the development cohort, which likely received more cardioembolic stroke patients. Notably, the difference in etiology distribution did not affect model performance, as the predictive model demonstrated stable performance in both cohorts with different characteristics, validating the rationality of the predictors and the external applicability of the model.

Overall, the presently proposed nomogram model can support outcome prognostication, improving communication between care providers and patients, and their families, facilitating shared decision-making and informing interventions. In resource-limited settings, the model can help prioritize patients who are most likely to benefit from intensive care and rehabilitation services. Furthermore, future clinical trials in VBAO could use this model to ensure balanced randomization or to identify high-risk subgroups for targeted interventions.

This study has several limitations. Firstly, the retrospective design may have introduced some selection bias, despite our efforts to mitigate this through external validation. However, this validation was conducted in a single country, and further testing across diverse international cohorts would be beneficial for enhancing the model's generalizability. Secondly, as EVT techniques and post-stroke care continue to evolve, periodic recalibration of the model may be necessary to maintain its predictive accuracy. Additionally, CT remains the primary method for screening VBAO patients, and variations in MRI usage across different stroke centers could affect its applicability. Furthermore, the 5-mm slice thickness of DWI may lead to false-negative results in assessing brainstem strokes, thus impacting diagnostic accuracy.

## CONCLUSIONS

Our study presents a robust, externally validated nomogram for predicting 90-day non-FCOs in patients with VBAO undergoing EVT. By integrating clinical and radiological factors, this model offers a tool for prognostication and clinical decision-making, possibly supporting personalized medicine.

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## Online Supplemental Data

Online Table 1. Comparison of key clinical and imaging characteristics between the model development cohort and the external validation cohort.

Variable	model development cohort (n=125)	external validation cohort (n=56)	P value
Age (years), median (IQR)	66.4±12.6	65.4±9.3	0.42
Sex, male, n (%)	81 (64.8)	24 (75.0)	0.27
ETO-to-groin puncture (hours), median (IQR)	6.7 (3.4-14.0)	8.7 (5.1-16.2)	0.09
Risk factors, n (%)			
Smoking	44 (34.7)	24 (42.9)	0.17
Alcohol use	32 (25.6)	22 (39.3)	0.12
Hypertension	98 (78.4)	38 (67.9)	0.13
Diabetes	46 (36.8)	16 (28.6)	0.21
Atrial fibrillation	24 (19.2)	10 (17.9)	0.95
Stroke cause, n (%)			0.30
Large artery atherosclerosis	67 (53.6)	39 (69.6)	
Cardioembolic	35 (28.0)	10 (17.9)	
Undetermined cause or others	23 (18.4)	7 (12.5)	
Admission NIHSS score, median (IQR)	10 (6-18)	10 (6-13)	0.74
PC-CS, median (IQR)	6 (5-7)	6 (4-7)	0.98
pc-ASPECTS, median (IQR)	8 (7-8)	8 (7-8)	0.10
Novel-PCS, median (IQR)	4 (2-5)	5 (2-6)	0.12
Intravenous thrombolysis, n (%)	38 (30.4)	15 (26.8)	0.53
Recanalization (mTICI 2b, 3), n (%)	88 (70.4)	42 (75.0)	0.87
Rescue treatment (stenting or balloon-assisted angioplasty), n (%)	49 (39.2)	24 (42.9)	0.67
symptomatic Intracranial Hemorrhage, n (%)	15 (12.0)	6 (10.7)	0.68
non-FCOs, n (%)	74 (59.2)	34 (60.7)	0.99

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; PC-CS, posterior circulation collateral scores; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT score; Novel-PCS, Novel posterior circulation score; mTICI, modified TICI; sICH, symptomatic Intracranial Hemorrhage

Online Table 2. Optimal cutoff values for key clinical and imaging indicators influencing prognosis.

Variable	Cutoff Value	Sensitivity	Specificity	P value	
Age	>66	72.5	67.6	0.001	
NIHSS score	>12	73.5	80.6	<0.001	
	_				
pc-ASPECTS	≤7	58.1	79.9	<0.001	
Novel-PCS	>3	82.6	69.7	<0.001	
PC-CS	≤5	68.7	71.2	<0.001	

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT score; Novel-PCS, Novel Posterior Circulation score; PC-CS, posterior circulation collateral scores

Online Table 3. Univariate analysis of factors associated with 90-day non-FCOs

Variable	OR	95% CI	P value
Age >66 years	4.54	2.07-9.93	<0.001
Sex, male	0.59	0.31-1.36	0.25
ETO-to-groin puncture(hours)	1.00	0.96-1.06	0.73
Risk factors			
Smoking	1.16	0.48-2.13	0.99
Alcohol use	1.97	0.87-4.43	0.10
Hypertension	1.00	0.42-2.39	0.99
Diabetes	1.58	0.76-3.30	0.22
Atrial fibrillation	1.96	0.80-4.81	0.14
NIHSS score >12	9.58	4.19-21.91	<0.001
pc-ASPECTS ≤7	8.13	3.12-20.03	<0.001
Novel-PCS >3	6.80	2.68-13.41	<0.001
PC-CS ≤5	5.52	2.54-12.02	<0.001
Failed recanalization (mTICI 0~2a)	5.71	2.53-12.89	<0.001
sICH	7.28	1.94-27.37	0.003

Abbreviations: ETO, estimated time of onset of the occlusion; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT score; Novel-PCS, Novel posterior circulation score; PC-CS, Posterior Circulation Collateral score; mTICI, modified TICI; sICH, symptomatic Intracranial Hemorrhage

Online Table 4. Multivariable models for predicting 90-day prognosis after EVT in patients with acute VBAO

Variables	Model 1	— P value	Model 2	— P value	
variables	OR (95% CI)	— P value	OR (95% CI)	— P value	
Age ≤66 years	7.66 (2.32-25.27)	0.001	11.24 (2.95-42.79)	< 0.001	
Failed recanalization (mTICI 0-2a)	4.59 (1.45-14.60)	0.01	5.11 (1.54-16.99)	0.008	
NIHSS score >12	4.68 (1.50-14.54)	0.008	4.26 (1.34-13.50)	0.01	
pc-ASPECTS≤7	4.39 (1.33-14.51)	0.02	Not included		
PC-CS≤5	4.72 (1.48-14.99)	0.009	5.53 (1.63-18.78)	0.002	
Novel-PCS >3	Not included		9.38 (2.28-38.59)	0.002	
sICHa	3.70 (0.78-17.62)	0.10	1.99 (0.39-10.09)	0.40	

Abbreviations: mTICI, modified Thrombolysis in Cerebral Infarction; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT score; Novel-PCS, Novel Posterior Circulation score; PC-CS, Posterior Circulation Collateral score; sICH, symptomatic Intracranial Hemorrhage; EVT, endovascular treatment; a Not identified as an independent predictor and therefore not included in the final model

Online Table 5. Comparison of multivariable models for predicting 90-day prognosis after EVT in patients with acute VBAO

	Model 1	Model 2
Pseudo R-squared value	0.60	0.66
Akaike Information Criterion	107.34	91.57
Bayesian Information Criterion	124.12	108.54

Abbreviations: EVT, endovascular treatment; VBAO, vertebrobasilar artery occlusion

Online Table 6. Incidence of non-FCOs stratified by risk groups in development cohort

Development cohort	FCOs, n (%)	non-FCOs, n (%)	P value
Low-risk group(n=79)	66(83.5)	13(16.5)	<0.001
High-risk group(n=46)	8(17.4)	38(82.6)	<0.001

Abbreviations: FCOs, favorable clinical outcomes

Online Table 7. Incidence of non-FCOs stratified by risk groups in external validation cohort

External validation cohort	FCOs, n (%)	non-FCOs, n (%)	P value
Low-risk group (n=32)	27(84.40)	5(15.63)	<0.001
High-risk group (n=24)	3(12.50)	21(87.50)	<b>~0.001</b>

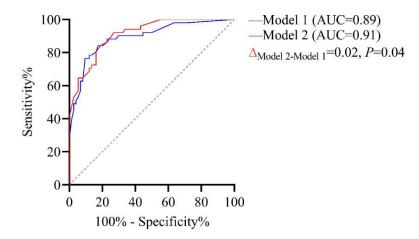
Abbreviations: FCOs, favorable clinical outcomes

Online Table 8. Risk stratification of development and external validation cohorts based on the Nomogram model

	low-risk group	high-risk group	P value
Development cohort	79	46	0.54
External validation cohort	32	24	0.54

Abbreviations: FCOs, favorable clinical outcomes

Online FIG 1. Comparison of ROC curves for multivariable models predicting 90-day prognosis after EVT in patients with acute VBAO



Abbreviations: ROC, receiver operating characteristic; EVT, endovascular treatment; VBAO, vertebrobasilar artery occlusion.