Research Square

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Development and Validation of a Risk Prediction Model for Poor Prognosis in Acute Ischemic Stroke Based on VILIP-1

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Research Article

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Abstract

Background

To develop and internally validate a nomogram for predicting poor 90-day prognosis in patients with acute ischemic stroke (AIS) using serum visinin-like protein 1 (VILIP-1) combined with clinical indicators.

Methods

A total of 120 patients with AIS admitted between January 2025 and June 2025 were enrolled. Patients were classified into a poor prognosis group (mRS ≥ 3, n = 52) and a favorable prognosis group (mRS < 3, n = 68) based on 90-day modified Rankin Scale (mRS) scores. Univariate and multivariate logistic regression were used to screen independent prognostic factors. A nomogram model was constructed with R software, and its performance was assessed using the area under the receiver operating characteristic curve (AUC), calibration curve, and Hosmer–Lemeshow test. Internal validation was performed using the bootstrap method.

Results

Multivariate logistic regression identified VILIP-1 level (P < 0.001) and posterior circulation lesion (P = 0.001) as independent predictors of poor prognosis. The final nomogram included VILIP-1, lesion location, and age. In the training set, the AUC was 0.835 (95% CI 0.751–0.919), with a sensitivity of 67.34% and specificity of 88.57%. In the validation set, the AUC was 0.814 (95% CI 0.663–0.966), with a sensitivity of 73.68% and specificity of 82.35%. The model showed good discrimination and calibration.

Conclusion

The nomogram based on serum VILIP-1, lesion location, and age provides reliable risk stratification for poor 90-day prognosis in AIS and can support early clinical decision-making.

Introduction

Acute ischemic stroke (AIS) is the leading cause of adult mortality and disability in China, accounting for more than 80% of the total incidence of stroke. The severity and recovery of neurological deficits directly affect patients' quality of life and long-term survival [1–3]. The Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2023 clearly state that early and accurate identification of high-risk populations for poor prognosis and implementation of individualized intervention are key measures to reduce the disability rate and improve the clinical outcomes of AIS patients [4].

Visinin-like protein 1 (VILIP-1) is a calcium-binding protein specifically expressed in central nervous system neurons and plays an important role in some neurodegenerative and brain injury diseases [5]. After AIS occurs, cerebral ischemia and hypoxia lead to neuronal cell damage, and intracellular VILIP-1 can be rapidly released into the peripheral blood circulation, resulting in elevated VILIP-1. Its serum expression level is positively correlated with cerebral infarction area and neuronal injury degree, making it a specific marker reflecting acute cerebral neuronal injury [6, 7]. In recent years, many studies have shown that VILIP-1 can be used as a potential indicator for evaluating the prognosis of neurological diseases such as ischemic stroke and hemorrhagic stroke [8, 9]. However, few studies have constructed a risk prediction model for poor prognosis in AIS patients based on VILIP-1 combined with clinical risk factors. Therefore, this study intends to construct a prediction model for poor prognosis in acute ischemic stroke using serum VILIP-1 combined with clinical data, and the results are reported as follows.

Materials and Methods

Study Subjects

A total of 120 patients with acute ischemic stroke admitted to the neurology department of our hospital from January 2025 to June 2025 were selected as research subjects. All patients and their family members voluntarily participated and signed informed consent forms. The study was approved by the hospital ethics committee (approval number: XYDWFYLSK-2025-158).

Inclusion criteria

Meeting the diagnostic criteria of AIS in the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2023 [3] and diagnosed with acute ischemic cerebral infarction by head CT or MRI; Time from onset to admission ≤ 48 h; Age ≥ 18 years; Complete clinical data, laboratory test results and 90-day follow-up data; Obtained consent from patients or their family members and able to actively cooperate.

Exclusion criteria

Hemorrhagic stroke, transient ischemic attack; complications with other central nervous system diseases, such as intracranial infection, brain tumor, and craniocerebral trauma; complications with severe liver and kidney insufficiency, malignant tumor, and autoimmune disease; complicated with mental illness.

Data Collection

General data, clinical indicators, laboratory test results and related serological indicators of all patients were collected. General data included sex, age, smoking history (smoking continuously for ≥ 1 year), history of alcohol consumption (previous or current drinking behavior clearly stated by the patient or

family members, including regular drinking, intermittent drinking and occasional heavy drinking), hypertension history (previously diagnosed or blood pressure ≥ 140/90 mmHg after admission and confirmed by a specialist), and diabetes history (previously diagnosed or fasting blood glucose ≥ 7.0 mmol/L, 2-hour post-prandial blood glucose ≥ 11.1 mmol/L). Clinical indicators included lesion location (determined by head MRI/CT, divided into anterior circulation infarction and posterior circulation infarction) and length of hospital stay (actual days from admission to discharge). Laboratory indicators included white blood cell count, D-dimer, homocysteine (Hcy), blood glucose, etc. All laboratory data were obtained from tests on the day of admission.

Serum VILIP-1 detection

5 ml of venous blood was collected from all patients on the day of admission and centrifuged at 3000 r/min for 10 min, and the serum was stored at -80°C for testing. The kit was purchased from Abcam (Shanghai) Trading Co., Ltd., and detected by enzyme-linked immunosorbent assay (ELISA) using a microplate reader, with strict adherence to the kit instructions.

Prognosis Evaluation and Grouping

All patients completed a 90-day prospective follow-up via outpatient reexamination and telephone follow-up, focusing on neurological function recovery. The modified Rankin Scale (mRS) was used to score neurological function 90 days after onset. Patients were divided into two groups according to mRS score: poor prognosis group (mRS ≥ 3), indicating moderate to severe neurological deficit and inability to fully take care of themselves; favorable prognosis group (mRS < 3), indicating basic neurological recovery and ability to take care of themselves or only mild dysfunction. The modified Rankin Scale (mRS) is a validated and widely used scale for assessing functional outcome after stroke [29].

Statistical Methods

SPSS 6.0 and R 4.2.1 software were used for statistical analysis, with $P < 0.05$ considered statistically significant. Measurement data with a normal distribution were expressed as the mean±standard deviation ($x \pm s$), and an independent sample t test was used for between-group comparisons. Nonnormally distributed measurement data are expressed as the median (interquartile range) [M(QR)], and the nonparametric rank sum test was used for between-group comparisons. Enumeration data were expressed as cases (percentages) [n (%)], and the χ^2 test was used for between-group comparisons. Univariate and multivariate logistic regression analyses were performed using SPSS 6.0.

Model construction and validation: Based on variables screened by multivariate logistic regression, a binary logistic regression prediction model was constructed using R language. All subjects were randomly divided into a training set and a validation set at a ratio of 7:3 by simple random sampling. The prediction model for poor prognosis was established in the training set and displayed as a nomogram. The discrimination of the model was evaluated by ROC curve, and the calibration was evaluated by

calibration curve and Hosmer–Lemeshow goodness-of-fit test. Internal validation of the model was performed in the validation set using the bootstrap method. $P < 0.05$ was considered statistically significant.

Results

Comparison of Clinical Data Between Patients with Different Prognoses

A total of 120 AIS patients were enrolled, with a median age of 67.00 (61.00, 73.00) years (range 43–84 years), including 68 males and 52 females. There were 52 cases (43.33%) in the poor prognosis group and 68 cases (56.67%) in the favorable prognosis group. Significant differences were found between the two groups in VILIP-1 level, lesion location, age, length of hospital stay, white blood cell count and D-dimer ($P < 0.05$). The poor prognosis group had significantly higher VILIP-1, white blood cell counts and D-dimer, as well as older age, a higher proportion of posterior circulation lesions and a longer hospital stay (Table 1).

Table 1
Comparison of Clinical Data Between Two Prognosis Groups

Clinical Characteristics	Poor Prognosis Group (n = 52)	Favorable Prognosis Group (n = 68)	t/χ²/Z	p
Gender			0.297	0.586
Male	28 (53.85%)	40 (58.82%)		
Female	24 (46.15%)	28 (41.18%)		
Age (years)	69.00 ± 7.65	64.68 ± 9.33	2.716	0.008
Smoking History			1.167	0.280
Yes	16 (30.77%)	15 (22.06%)		
No	36 (69.23%)	53 (77.94%)		
Drinking History			0.012	0.913
Yes	15 (28.85%)	19 (27.94%)		
No	37 (71.15%)	49 (72.06%)		
Hypertension			1.863	0.172
Yes	31 (59.62%)	32 (47.06%)		
No	21 (40.38%)	36 (52.94%)		
Diabetes Mellitus			0.204	0.652
Yes	22 (42.31%)	26 (38.24%)		
No	30 (57.69%)	42 (61.76%)		
Lesion Location			13.230	< 0.001
Posterior circulation	35 (67.31%)	23 (33.82%)		
Anterior circulation	17 (32.69%)	45 (66.18%)		
Length of Hospital Stay	15.00 (9.00, 21.75)	8.00 (5.00, 10.00)	-4.753	< 0.001
White Blood Cell Count	10.19 (8.27, 12.15)	6.86 (5.57, 9.28)	-4.179	< 0.001
D-dimer	370.00 (112.50, 806.75)	169.50 (84.75, 564.50)	-2.058	0.040
Homocysteine (Hcy)	17.00 (13.25, 19.75)	16.00 (13.00, 19.00)	-0.754	0.451

Clinical Characteristics	Poor Prognosis Group (n = 52)	Favorable Prognosis Group (n = 68)	$t/\chi^2/Z$	p
Admission Blood Glucose	6.795 (4.147, 9.422)	6.415 (4.717, 8.870)	-0.511	0.609
VILIP-1	1.45 (0.085, 2.163)	0.74 (0.435, 1.117)	-5.032	< 0.001

Univariate Logistic Regression Analysis of Poor Prognosis in AIS Patients

The length of hospital stay was not included in the logistic regression analysis because it reflects disease severity and cannot be predicted prospectively at admission and may interfere with the true predictive value of other key variables. Taking poor 90-day prognosis in AIS patients as the dependent variable and the other 12 clinical data as independent variables (variable assignment shown in Table 2), univariate logistic regression analysis was performed. The results showed that VILIP-1 level, lesion location, age and white blood cell count were significantly correlated with poor prognosis in AIS patients ($P < 0.05$). Although D-dimer showed a between-group difference, it was not statistically significant in univariate logistic regression (Table 3).

Table 2
Variable Assignment

Variable	Assignment
Gender	Male = 0, Female = 1
Smoking History	No = 0, Yes = 1
Drinking History	No = 0, Yes = 1
Hypertension	No = 0, Yes = 1
Diabetes Mellitus	No = 0, Yes = 1
Lesion Location	Anterior circulation = 0, Posterior circulation = 1

Table 3
Univariate Logistic Regression Analysis of Poor Prognosis in AIS Patients

Independent Variable	B	S.E.	Wald χ^2	p	OR (95%CI)
Gender	0.203	0.372	0.297	0.586	1.224 (0.591, 2.537)
Age (years)	0.060	0.023	6.677	0.010	1.061 (1.014, 1.110)
Smoking History	0.451	0.419	1.159	0.282	1.570 (0.690, 3.572)
Drinking History	0.045	0.408	0.012	0.913	1.046 (0.470, 2.328)
Hypertension	0.507	0.373	1.852	0.174	1.661 (0.800, 3.448)
Diabetes Mellitus	0.010	0.379	0.001	0.980	1.010 (0.480, 2.121)
Lesion Location	1.549	0.397	15.228	< 0.001	4.705(2.161, 10.240)
White Blood Cell Count	0.142	0.054	6.825	0.009	1.153 (1.036, 1.283)
D-dimer	0.000	0.000	3.704	0.054	1.000 (1.000, 1.001)
Homocysteine (Hcy)	0.007	0.014	0.278	0.598	1.007 (0.980, 1.036)
Admission Blood Glucose	0.007	0.041	0.032	0.859	0.993 (0.929, 1.092)
VILIP-1	1.559	0.345	20.403	< 0.001	4.753 (2.417, 9.349)

Multivariate Logistic Regression Analysis of Poor Prognosis in AIS Patients

According to univariate logistic regression results, VILIP-1, lesion location, age and white blood cell count (all $P < 0.05$) were included in multivariate logistic regression analysis. The results showed that VILIP-1 level and posterior circulation lesion were independent risk factors for poor 90-day prognosis in AIS patients. Age and white blood cell count were not significantly associated with poor prognosis after adjusting for confounders ($P > 0.05$). Each 1-unit increase in VILIP-1 was associated with a 2.703-fold (OR = 3.703,95%, CI:1.773–7.734, $P < 0.001$) higher risk of poor prognosis (Table 4).

Table 4
Multivariate Logistic Regression Analysis of Poor Prognosis in AIS Patients

Independent Variable	B	S.E.	Wald χ^2	p	OR (95%CI)
Age (years)	0.043	0.028	2.413	0.318	1.044 (0.989, 1.103)
Lesion Location	1.439	0.452	10.140	0.001	4.218 (1.739, 10.229)
White Blood Cell Count	0.056	0.066	0.719	0.396	1.058 (0.929, 1.205)
VILIP-1	1.309	0.376	12.133	< 0.001	3.703 (1.773, 7.734)

Construction of the Prediction Model for Poor AIS Prognosis

Based on the two independent risk factors (VILIP-1 and lesion location) screened by multivariate logistic regression, age was added to the model considering previous studies and clinical practice. The binary logistic regression prediction model was constructed with VILIP-1, lesion location and age as independent variables and poor 90-day prognosis (yes = 1, no = 0) as the dependent variable. Variable assignment: VILIP-1 (measured value, ng/mL), age (measured value, years), lesion location (anterior circulation = 0, posterior circulation = 1). No significant differences were found in any baseline variables between the training set and validation set ($P > 0.05$), indicating good balance and comparability (Table 5, Fig. 1).

Table 5
Baseline Equilibrium Comparison Between the Training Set and Validation Set

Variable	Validation Set (n = 36)	Training Set (n = 84)	p
Age	67.7 ± 7.87	66.1 ± 9.27	0.327
Gender			0.213
Male	12 (33.3%)	40 (47.6%)	
Female	24 (66.7%)	44 (52.4%)	
Smoking History			0.927
No	26 (72.2%)	63 (75.0%)	
Yes	10 (27.8%)	21 (25.0%)	
Drinking History			0.894
No	25 (69.4%)	61 (72.6%)	
Yes	11 (30.6%)	23 (27.4%)	
Hypertension			0.338
No	20 (55.6%)	37 (44.0%)	
Yes	16 (44.4%)	47 (56.0%)	
Diabetes Mellitus			0.902
No	23 (63.9%)	51 (60.7%)	
Yes	13 (36.1%)	33 (39.3%)	
Lesion Location			0.403
Posterior circulation	20 (55.6%)	38 (45.2%)	
Anterior circulation	16 (44.4%)	46 (54.8%)	
White Blood Cell Count	9.17 ± 3.64	8.93 ± 4.00	0.753
Blood Glucose	7.77 ± 3.72	7.68 ± 4.77	0.913
D-dimer	958 ± 2002	612 ± 896	0.326
Homocysteine	17.3 ± 4.56	19.2 ± 15.5	0.307
VILIP-1	1.24 ± 0.82	1.08 ± 0.66	0.331

Model efficacy and internal validation

In the training set, the model had an AUC of 0.835 (95% CI: 0.751–0.919), Youden index of 0.559, optimal cutoff value of 0.338, sensitivity of 67.34%, and specificity of 88.57%, showing good discrimination (Fig. 2). The Hosmer–Lemeshow test (χ^2=5.085, df = 8, P = 0.748) and calibration curve confirmed high consistency between the predicted and actual prognoses, with an ideal goodness of fit (Fig. 3).

Internal validation was performed in the validation set using the bootstrap method with 1000 resamplings. The model achieved an AUC of 0.814 (95% CI: 0.663–0.966), Youden index of 0.56, optimal cutoff value of 0.396, sensitivity of 73.68%, and specificity of 82.35% (Fig. 4). The Hosmer–Lemeshow test (χ^2=7.161, df = 8, P = 0.519) indicated good fit.

The DeLong test showed no significant difference in AUC between the training and validation sets (D = 0.235, P = 0.815), suggesting comparable predictive ability (Fig. 5).

Discussion

After AIS onset, blood–brain barrier disruption, endothelial dysfunction and neuroinflammation aggravate cytotoxic and vasogenic edema, affecting neurological recovery and prognosis [10]. Many AIS prognosis prediction models have been developed, but few integrate biomarkers. This study analyzed the clinical data of 120 AIS patients and confirmed that VILIP-1 and posterior circulation lesions are independent risk factors for poor 90-day prognosis, consistent with previous studies [11–13].

As the core biomarker, VILIP-1 showed independent prognostic value. It is a neuron-specific calcium-binding protein with low peripheral blood levels under physiological conditions. After AIS, neuronal necrosis leads to the rapid release of VILIP-1 into the blood, with levels positively correlated with injury severity [6, 14]. In this study, VILIP-1 had an OR of 3.703, indicating that it is a strong predictor of poor prognosis, consistent with Olde Heuvel F et al. [15–16]. VILIP-1 has also been used to evaluate acute cerebral infarction treatment efficacy [17–18], supporting its role in objective prognosis assessment.

Lesion location is a classic prognostic indicator related to the functional importance of brain perfusion regions [19]. Posterior circulation supplies the brainstem, cerebellum, occipital lobe and thalamus, so posterior circulation infarction leads to worse outcomes than anterior circulation infarction, consistent with clinical practice [20–22]. The length of hospital stay reflects disease severity and complications; poor prognosis patients often have complications (e.g., dysphagia, pneumonia) that prolong stay and worsen neuronal damage [23–25], making it a simple prognostic indicator.

Age was significantly associated with poor prognosis of AIS patients in univariate analysis and univariate Logistic regression, but lost statistical significance in multivariate Logistic regression analysis, but not in the multivariate analysis, possibly due to the single-center small sample size and concentrated age range. However, age is a well-established prognostic factor [26–28], so it was included to improve clinical applicability.

The model integrating VILIP-1, lesion location and age showed excellent discrimination (AUC = 0.835) and good calibration. It combines a specific biomarker, clinical phenotype and demographic indicator, overcoming the limitations of single biomarkers and subjective clinical indicators and providing a quantitative reference for clinical decision-making.

Limitations

This study is a single-center, prospective small-sample study with certain limitations. Multicenter large-sample studies with external validation are needed to improve generalizability.

Abbreviations

AIS Acute Ischemic Stroke

VILIP-1 Visinin-like protein 1

ROC Receiver operating characteristic

ELISA Enzyme-Linked Immunosorbent Assay

Hcy Homocysteine

CSF Cerebrospinal Fluid

NSE Neuron-Specific Enolase

NLR Neutrophil-to-Lymphocyte Ratio

GFAP Glial Fibrillary Acidic Protein

UCH-L1 Ubiquitin C-Terminal Hydrolase L1

ITLN-1 Intelectin 1

PCSK9 Proprotein Convertase Subtilisin/Kexin Type 9

sCD163 Soluble CD163

Declarations

Author contributions

LPW: Conceptualization, Data curation, Methodology, Writing – original draft

YXQ: Data curation, Validation

YZ: Software

YS: Visualization, Resources

GF: Investigation, Writing – review and editing

HXC: Data curation, Visualization, Writing – review and editing

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Data availability

All data generated or analyzed during this study are included in this published article.

Clinical trial number

not applicable

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of the Fifth Affiliated Hospital of Xinjiang Medical University (approval number: XYDWFYLSK-2025-158). Written informed consent was obtained from all individual participants or their legal guardians prior to enrollment.

Consent for publication

Written informed consent for publication of identifying information and clinical data was obtained from all enrolled participants.

Competing interests

The authors declare that they have no competing interests.

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Figures

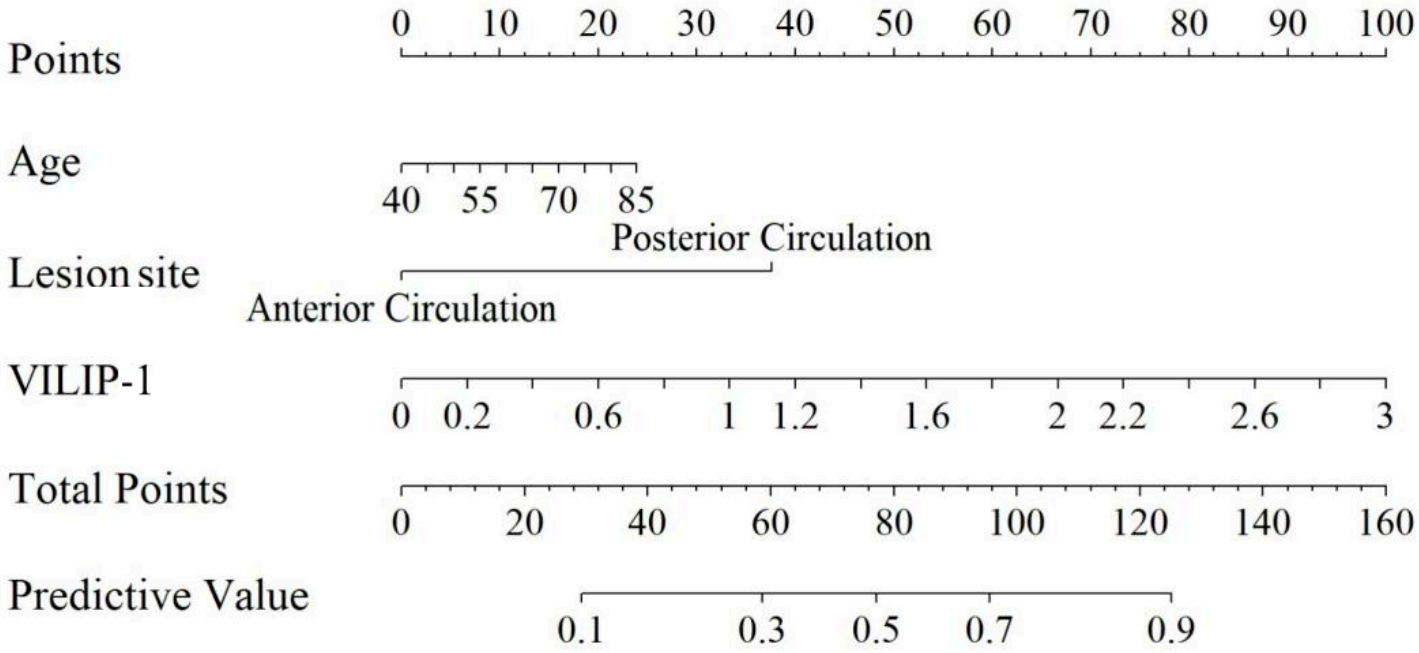


Figure 1

Nomogram for predicting poor 90-day prognosis in patients with acute ischemic stroke

The nomogram was developed based on serum VILIP-1 level, lesion location, and age. Each variable corresponds to a point on the top scale; the total points are calculated and converted to a predicted probability of poor prognosis.

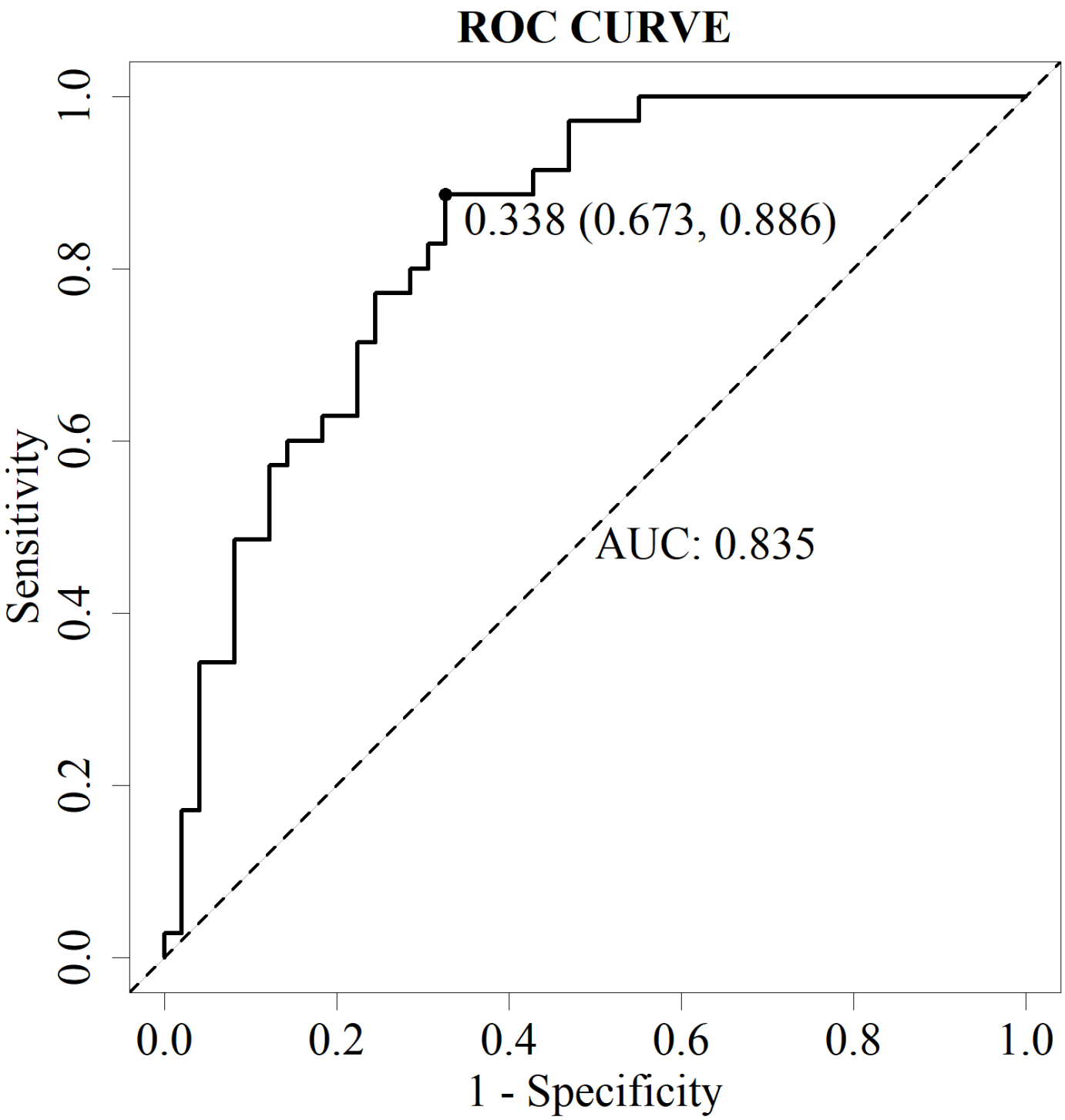


Figure 2

Receiver operating characteristic (ROC) curve of the prediction model in the training set

The area under the ROC curve (AUC) was 0.835 (95% CI: 0.751–0.919), indicating good discriminative ability of the model for poor prognosis in acute ischemic stroke patients.

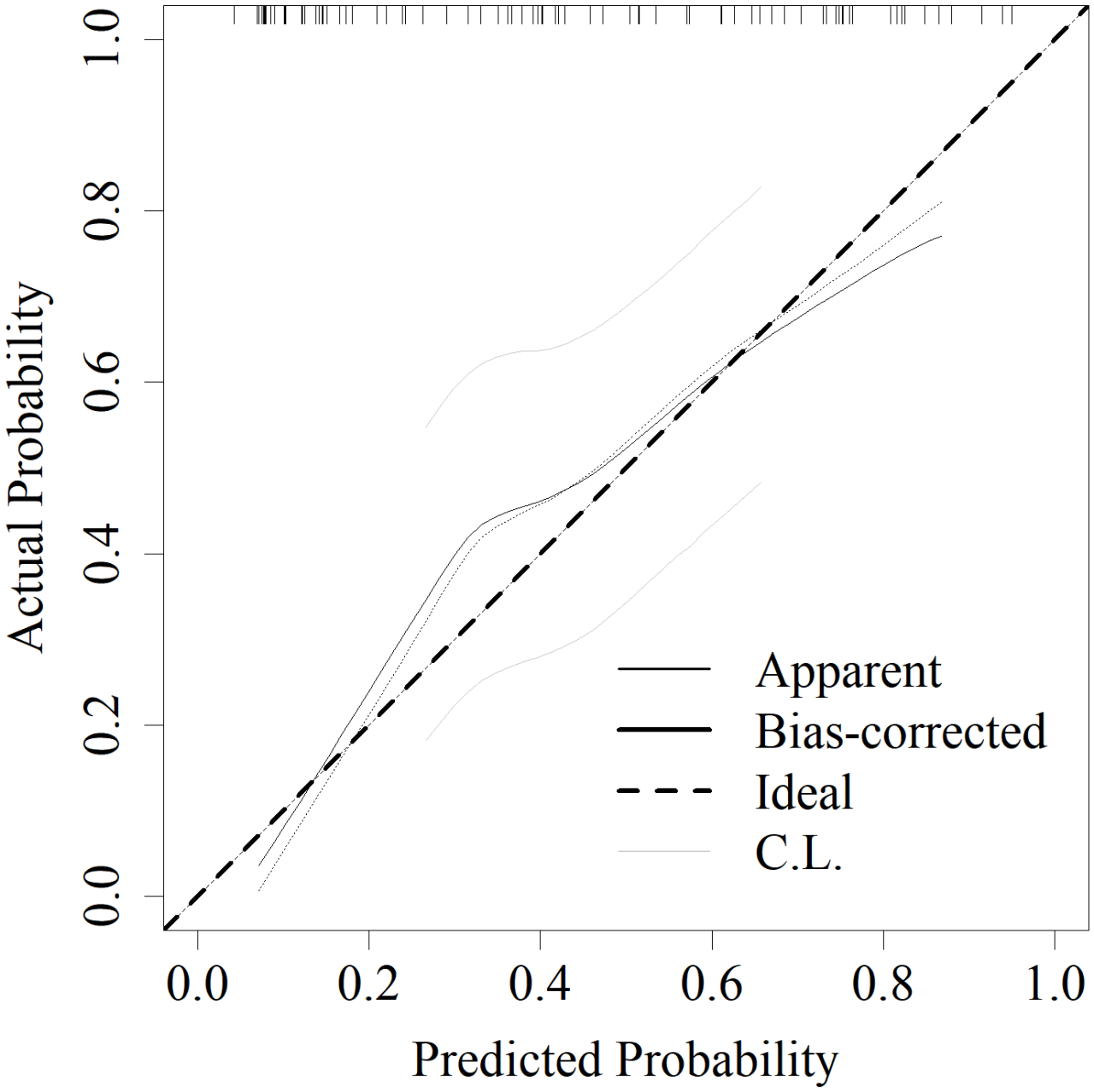


Figure 3

Calibration curve of the prediction model for poor prognosis in acute ischemic stroke

The calibration curve shows high consistency between the predicted probability and actual observed probability of poor prognosis. The Hosmer–Lemeshow test confirmed good fitness of the model.

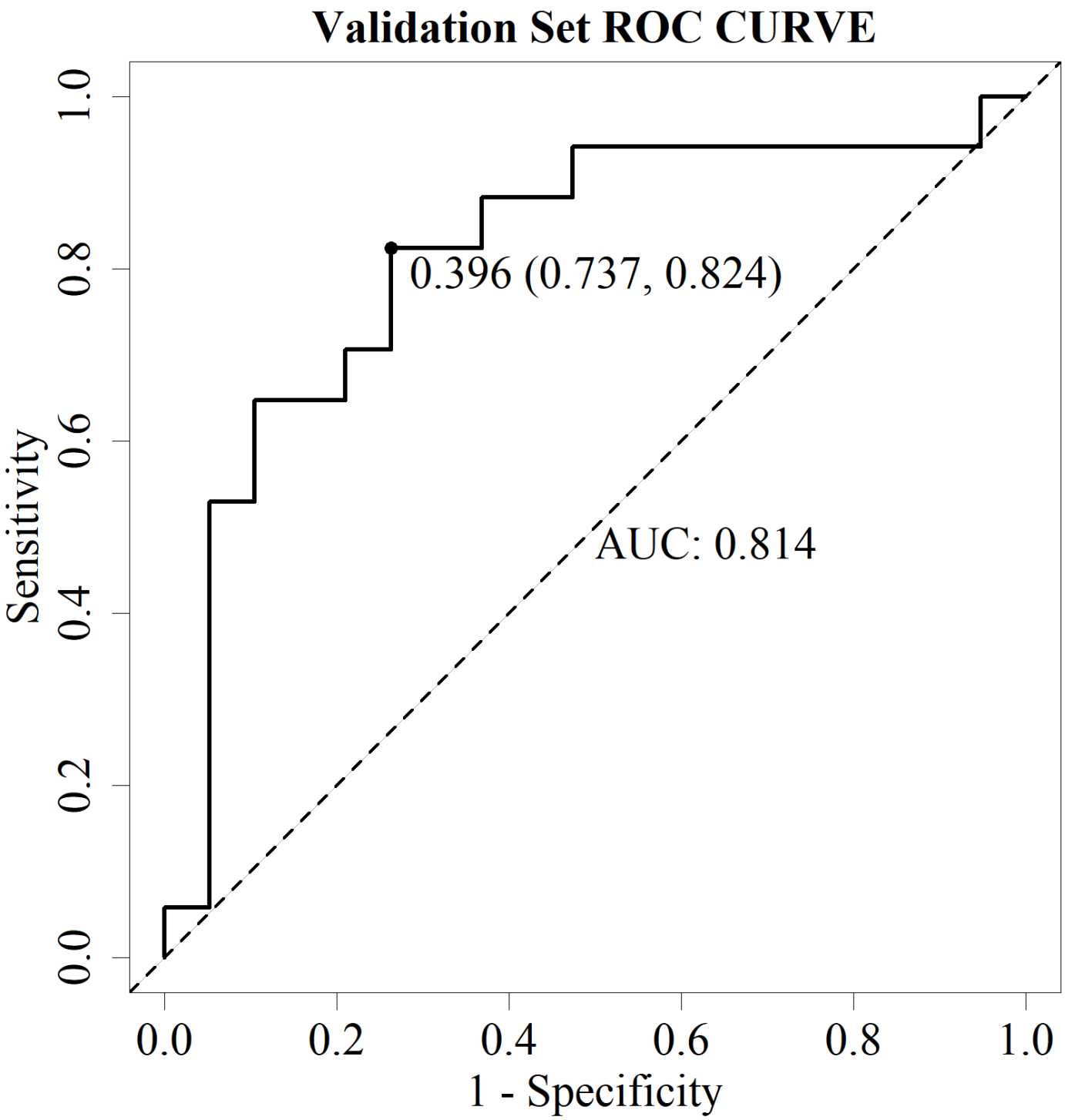


Figure 4

Receiver operating characteristic (ROC) curve of the prediction model in the validation set

After internal validation using the bootstrap method (1000 resamples), the AUC was 0.814 (95% CI: 0.663–0.966), indicating stable and reliable predictive performance.

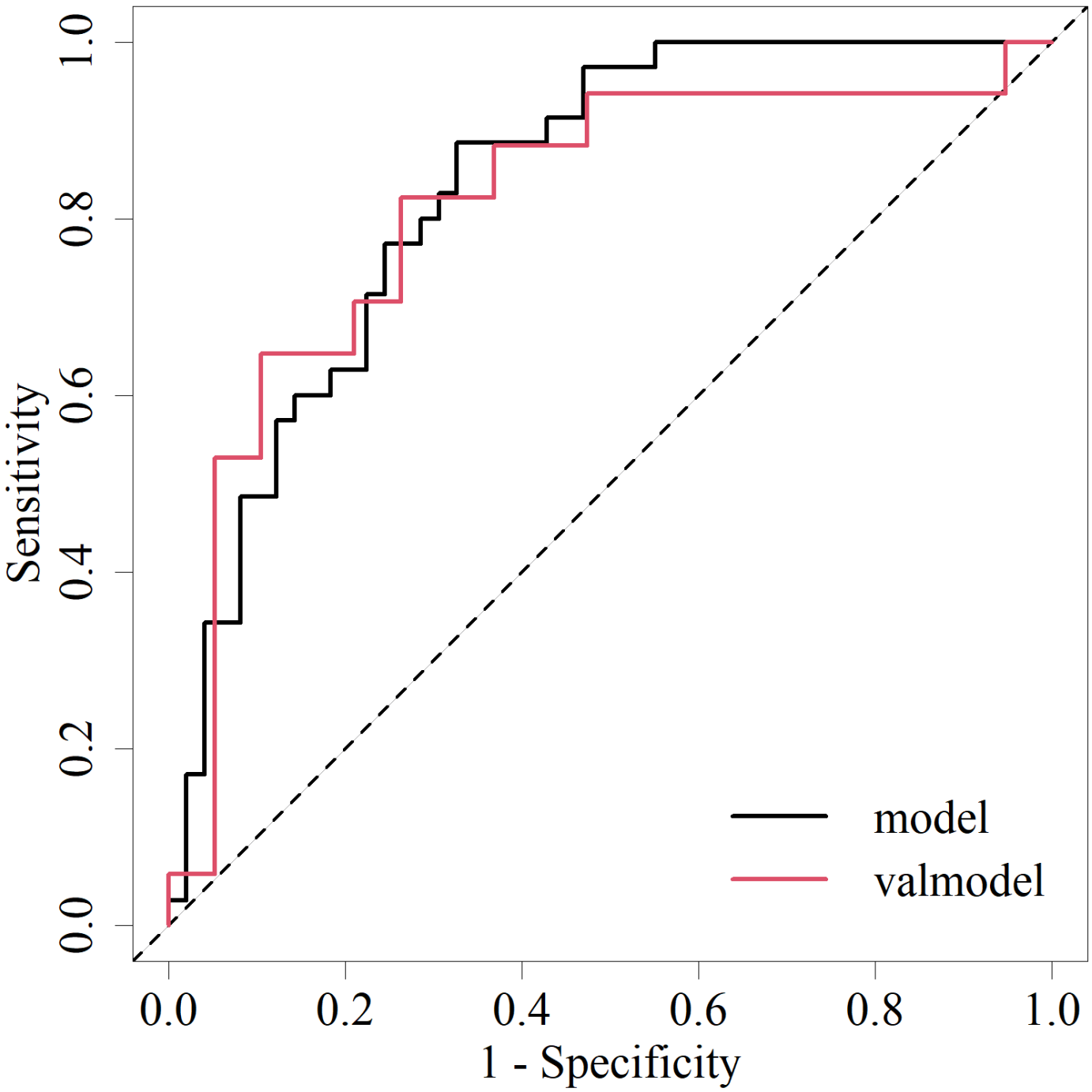


Figure 5

Comparison of ROC curves between the training set and validation set

The DeLong test showed no significant difference in AUC between the two sets (D = 0.235, P = 0.815), demonstrating consistent predictive performance.