

Featured Article

Construction and evaluation of a short-term prognostic model for acute ischemic stroke in emergency settings

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Abstract: Objective: To develop a prediction model for 14-day poor prognosis in acute ischemic stroke (AIS) patients in emergency settings and evaluate its predictive accuracy. **Methods:** We conducted a prospective cohort study, enrolling AIS patients admitted to our hospital between October 2018 and December 2020, within 72 h of symptom onset. Univariate and multivariate logistic regression analyses were performed to identify factors associated with poor prognosis. Receiver operating characteristic (ROC) curves were used to determine cutoff values for continuous variables, which were subsequently discretized based on clinical relevance. A clinical scoring model for short-term prognosis was constructed using the β coefficients of selected variables. AIS patients admitted between January and December 2021 served as the internal validation cohort to assess the model's performance. **Results:** A total of 321 patients were included, with 223 in the training cohort and 98 in the validation cohort. Multivariate logistic regression identified age, high-sensitivity C-reactive protein(hs-CRP), prealbumin (PA), infarct volume, Frailty Screening Questionnaire (FSQ), and National Institutes of Health Stroke Scale (NIHSS) scores as independent predictors of poor short-term prognosis. The prognostic scoring system, with a total score of 15, included the following components: age ≥ 74 years (1 point), PA ≤ 373 mg/L (2 points), large-artery atherosclerosis (1 point), cardioembolic stroke (2 points), infarct volume ≥ 2.18 cm³ (2 points), FSQ score ≥ 3 (1 point), and NIHSS score ≥ 4 (6 points). The area under the ROC curve (AUC) for predicting poor prognosis was 0.927 (95%CI: 0.894~0.960), with an optimal cutoff score of ≥ 5 points, yielding a sensitivity of 0.770 and specificity of 0.976. The model's performance in the validation cohort was consistent, with an AUC of 0.892 (95%CI: 0.827~0.957). **Conclusion:** The short-term prognostic scoring system for AIS demonstrated strong diagnostic accuracy and offers valuable guidance for clinicians in early prognosis assessment in emergency settings.

Keywords: acute ischemic stroke; prediction model; frailty screening questionnaire

1. Introduction

Acute cerebrovascular disease is a leading cause of disability and mortality worldwide, particularly in China. It is marked by high incidence, recurrence, and disability rates, placing a substantial economic and psychological burden on families, society, and healthcare systems [1]. Over the past 30 years, the stroke-related disease burden in China has steadily increased, now ranking first globally. Among these cases, acute ischemic stroke(AIS) is the most prevalent, accounting for 77.8% of all strokes, with an incidence rate of 11.15 per thousand and a mortality rate of 1.15 per thousand [2]. Despite advancements in stroke treatment, effective clinical interventions for AIS remain limited, underscoring the need for further research to improve patient outcomes.

Current national and international guidelines recommend early recanalization, particularly intravenous thrombolysis in the ultra-early phase, as the primary treatment for AIS [3]. This strategy is well-regarded for its ability to restore blood flow and minimize brain tissue damage. However, despite its proven efficacy, a relatively small proportion of patients receive timely treatment. In China, only 21.5% of AIS patients reach the emergency department within 3 h, 12.6% are eligible for intravenous thrombolysis, and only 2.4% ultimately receive the treatment, with 1.6% receiving intravenous alteplase [4]. This disparity highlights the significant gap in AIS treatment outcomes between China and developed countries like the United States. Furthermore, even among those who receive timely thrombolysis, many patients fail to achieve the desired clinical outcomes. A significant proportion continue to experience functional impairments, and some even face worsening conditions [5]. This suggests that reliance on time-to-treatment alone is insufficient to predict prognosis accurately. Frailty, a common geriatric syndrome, has gained attention for its role in exacerbating clinical outcomes in stroke patients. Frail patients lack the physiological reserves to manage acute conditions, increasing their risk of complications, extended hospital stays, and mortality [6].

In this context, the present study was designed as a prospective cohort investigation to evaluate the 14-day prognosis of AIS patients in emergency settings, using the modified Rankin Scale (mRS) as the primary endpoint for functional recovery. To improve the accuracy of prognostic predictions, the Frailty Screening Questionnaire (FSQ) was employed to assess patient frailty, serving as the basis for constructing a novel prognostic scoring system for AIS. Through multivariate analysis and model validation, this study aims to develop a scoring system capable of early identification of high-risk AIS patients, providing personalized medical decision support in clinical practice and optimizing patient outcomes. The core of this study lies in establishing a new prognostic model for AIS. By enabling earlier and more accurate identification of frailty and its impact on prognosis, this model will assist clinicians in making more informed therapeutic decisions, thereby improving both survival rates and long-term outcomes for AIS patients.

2. Materials and methods

2.1. Study population

This study employed a prospective cohort design. Patients with AIS who were admitted to our hospital's emergency department within 72 h of symptom onset between October 2018 and December 2020 were consecutively enrolled as the training cohort. AIS patients admitted between January and December 2021 were selected as the internal validation cohort, with inclusion and exclusion criteria identical to those of the training set. Inclusion criteria were: (1) diagnosis based on the 2018 Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke; (2) presentation to the emergency department within 72 h of onset; (3) confirmation of AIS by head CT or cranial MRI; (4) initiation of treatment within 72 h of symptom onset. Exclusion criteria were: (1) other neurological conditions causing similar symptoms, such as acute cerebral hemorrhage or space-occupying lesions; (2) inability to cooperate with treatment, such as psychiatric disorders; (3) diseases associated with protein loss, such

as nephrotic syndrome or protein-losing enteropathy; (4) severe wasting diseases, including severe infections, malignant tumors, anorexia, or severe malnutrition. A total of 321 patients with acute ischemic stroke (AIS) were included in the study, with 223 patients in the training cohort and 98 in the internal validation cohort. The median age was 71 years (interquartile range: 60–83), and 62% of the patients were male. Of the total cohort, 61.4% had a poor prognosis (mRS > 2). Baseline characteristics between the training and validation cohorts were comparable. The study was approved by the Medical Ethics Committee of the China Rehabilitation Research Center (approval number: 2018-070-1), and all participants provided written informed consent.

2.2. Research methods

Demographic data were collected at admission, and diagnosis and treatment were conducted according to the Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke (2018). Prognosis was evaluated using the 14-day modified Rankin Scale (mRS). The following data were collected: (1) demographic information (sex, age, height, weight, body mass index); (2) comorbidities, including hypertension, diabetes, coronary artery disease, atrial fibrillation, hyperlipidemia, and history of transient ischemic attack (TIA); (3) personal and family history, including smoking, alcohol consumption, family history of stroke, and antiplatelet drug use; (4) first laboratory test results within 24 h of admission, including complete blood count, blood biochemistry, high-sensitivity C-reactive protein (hs-CRP), insulin, 25-hydroxyvitamin D3, N-terminal pro-brain natriuretic peptide (NT-proBNP), and D-dimer; (5) various scales assessed within 24 h of admission, including TOAST classification, National Institutes of Health Stroke Scale (NIHSS), Frailty Screening Questionnaire (FSQ), and mRS; (6) infarct volume, measured by head CT, CTA, MRI, or MRA within 24 h of admission. Infarct volume was modeled as an ellipsoid and calculated as $1/6\pi \times a \text{ (long axis)} \times b \text{ (short axis)} \times c \text{ (number of layers} \times \text{layer thickness)}$, where *a* is the longest diameter of the infarct, *b* is the longest perpendicular diameter, and *c* is the number of infarct layers in the CT/MRI scans multiplied by the slice thickness. After 14 days of standardized treatment, prognosis was assessed by two attending physicians using the mRS, with patients categorized as having a good prognosis (mRS ≤ 2) or poor prognosis (mRS > 2).

2.3. Statistical methods

Statistical analyses were performed using SPSS 26.0 and R-studio software. Quantitative data following a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and independent sample *t*-tests were used for group comparisons. Non-normally distributed data were expressed as median (interquartile range) [*M* (Q1, Q3)], with Mann-Whitney U tests used for comparisons. Categorical data were expressed as frequencies (%), with group comparisons made using the χ^2 test. Univariate logistic regression was used to screen factors associated with poor prognosis, and cutoff values for continuous variables were determined using receiver operating characteristic (ROC) curve analysis and clinical judgment for discretization into categorical variables. Multivariate logistic regression was employed to identify

independent risk factors for poor prognosis, using a forward stepwise regression method. Corresponding scores were assigned based on the β regression coefficients of each risk factor, and total risk scores were calculated by summing the individual scores. The predictive performance of the model was evaluated by calculating the area under the ROC curve (AUC), sensitivity, and specificity. Finally, AUC values from the training and validation sets were compared to assess model stability. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Comparison of clinical data between the good and poor prognosis groups in the training set

When comparing the good prognosis group with the poor prognosis group, significant differences were observed in several variables, including age, sex, atrial fibrillation, smoking, hypersensitive C-reactive protein (hs-CRP), white blood cell count, N-terminal pro-brain natriuretic peptide (NT-proBNP), D-dimer, prealbumin (PA), albumin (ALB), NIHSS score, TOAST classification, infarct volume, and FSQ score (all $P < 0.05$). Details are shown in **Table 1**.

Table 1. Compare the clinical data between the good or poor prognosis group inpatients with AIS.

Index	good prognosis group ($n = 321$)	poor prognosis group ($n = 223$)	t/χ^2	P
Age	65(57,76)	79(64,85)	-4.734	<0.001
Male	60(72.3)	78(55.7)	6.070	0.013
BMI (Kg/m ²)	24.2(23.0,27.2)	24.2(21.5,27.0)	-1.488	0.140
Complication				
hypertension	60	108	0.661	0.416
Diabetes	29	61	1.632	0.205
Coronary heart disease	16	43	3.505	0.04
Atrial fibrillation	5	37	14.193	<0.001
Hyperlipidemia	30	45	0.375	0.542
History of TIA	26	30	2.715	0.098
Smoking	47	43	14.536	<0.001
Drinking	27	35	1.473	0.22
Family history of stroke	33	41	2.578	0.109
hs-CRP (mg/dL)	0.16(0.08,0.37)	0.54(0.19,2.72)	-5.865	<0.001
HCY (umol/L)	15.3(10.8,21.1)	15.0(11.6,22.1)	-0.816	0.416
GLU	6.9(5.8,9.4)	7.4(6.1,10.1)	-1.135	0.186
WBC ($\times 10^9$)	6.9(5.2,8.4)	7.8(6.3,9.4)	-3.010	0.003
UA (umol/L)	333(280,410)	322(260,404)	-0.543	0.588
NT-proBNP (mg/L)	115(82,218)	631(208,2022)	-7.553	<0.001
TG (mmol/L)	1.15(0.91,1.66)	1.11(0.79,1.64)	-0.600	0.548
HDL (mmol/L)	1.11(0.96,1.34)	3.93(3.28,4.67)	-1.398	0.162
D-Dimer	0.27(0.19,0.45)	0.83(0.39)4.67	-6.496	<0.001
PA (mg/L)	298.4(227.0,347.3)	177.8(121.3,242.7)	-7.664	<0.001

Table 1. (Continued).

Index	good prognosis group (n = 321)	poor prognosis group (n = 223)	t/ χ^2	P
TCH (mmol/L)	4.16 ± 1.04	4.07 ± 1.09	0.080	0.792
LDL-c (mmol/L)	2.53 ± 0.77	2.58 ± 0.88	0.649	0.422
ALB (g/L)	42.2 ± 4.0	37.5 ± 5.3	7.508	0.007
NIHSS	2(1,2)	6(3,11)	-10.601	<0.001
TOAST			38.986	<0.001
LAA	12(14.5)	55(39.3)		
CE	4(4.8)	32(22.9)		
SAO	67(80.7)	53(37.8)		
FSQ ≥ 2 points	22(26.5)	61(43.5)	7.016	0.007
Infarct volume	0.48(0.25,1.44)	5.40(1.03,24.05)	-7.838	<0.001

3.2. Multivariate logistic regression analysis of risk factors for short-term prognosis in AIS patients

Among the variables that showed significant differences in baseline clinical data, age, hs-CRP, PA, infarct volume, and NIHSS score were continuous variables. ROC curve analysis was used to determine optimal cutoff values by maximizing the Youden index, and the variables were subsequently categorized based on clinical relevance.

With mRS > 2 as the dependent variable, the categorized variables were included in a multivariate logistic regression model, and forward stepwise regression was employed to identify independent risk factors for poor prognosis (see **Table 2**).

Table 2. Multivariate logistic regression analysis of poor prognosis in emergency AIS patients (n = 223).

Variable	β	S.E	χ^2	P	HR	95%CI
Age ≥ 74	0.849	0.371	5.230	0.022	2.336	1.129~4.835
PA ≤ 373 mg/L	1.324	0.564	5.507	0.019	3.759	1.244~11.360
TOAST						
LAA	0.907	0.454	4.001	0.045	2.477	1.018~6.025
CE	1.831	0.628	8.516	0.004	6.243	1.825~21.360
Infarct volume ≥ 2.18 cm ³	1.749	0.415	17.763	<0.001	5.746	2.548~12.958
FSQ ≥ 3 point	1.189	0.384	9.579	0.002	3.283	1.547~6.971
NIHSS ≥ 4 point	5.508	1.025	28.886	<0.001	246.629	33.092~838.074
Constant	-1.639	0.313	27.427	<0.001	0.194	—

Based on the results, a prediction model for the short-term prognosis of AIS patients was constructed. The predicted value (PRE) was calculated from the combined variable model derived from the logistic regression equation: $PRE = 1/(1+e^{-Y})$, where $Y = -1.639 + 0.849 \times \text{age} + 1.324 \times \text{PA} + 0.907 \times \text{large-artery atherosclerosis} + 1.831 \times \text{cardioembolism} + 1.749 \times \text{infarct volume} + 1.189 \times \text{FSQ} + 5.508 \times \text{NIHSS}$. The ROC curve for the model yielded an AUC of 0.929 (95% CI: 0.897–0.962). The optimal cutoff value for PRE was 0.902, with a sensitivity of 0.784 and a specificity of 0.976. Model validation demonstrated good discriminative ability (see **Figure 1**). The Hosmer-Lemeshow goodness-of-fit test indicated no statistically

significant difference between the current model and the ideal model ($P = 0.980$), reflecting a good fit.

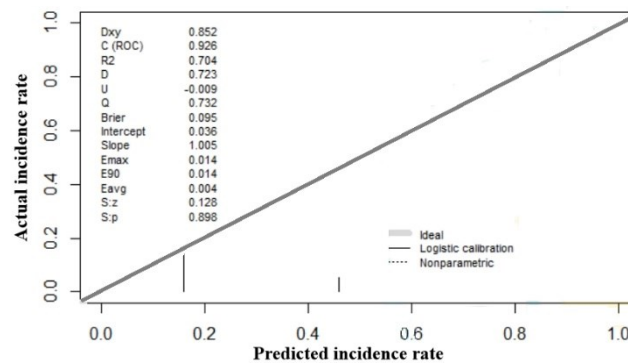


Figure 1. Calibration curve of predictive models to validate the occurrence of adverse outcomes in AIS patients.

3.3. Scoring system and optimal cutoff value

The β coefficients from the logistic regression analysis were used to assign scores. The ratio of each variable's β coefficient to the smallest β coefficient was calculated to determine the score for each variable. A clinical scoring system for predicting the short-term prognosis of AIS patients in emergency settings was developed: age ≥ 74 years (1 point), PA ≤ 373 mg/L (2 points), large-artery atherosclerosis (1 point), cardioembolism (2 points), infarct volume ≥ 2.18 cm³ (2 points), FSQ score ≥ 3 (1 point), and NIHSS score ≥ 4 (6 points), with a total score of 15 points (see **Table 3**). The predictive value of the scoring system for poor AIS prognosis was evaluated using the ROC curve. The AUC was 0.927 (95% CI: 0.894–0.960), $P < 0.001$. The optimal cutoff value, determined by the maximum Youden index, was ≥ 5 points, with a sensitivity of 0.770 and a specificity of 0.976. The AUC of the NIHSS score alone for predicting poor AIS prognosis was 0.911 (95% CI: 0.873–0.949) (see **Figure 2**).

Table 3. Coefficients and scores of each predictive index of poor prognosis.

Index	β	Ratio	Point
Age ≥ 74	0.849	1.000	1
PA ≤ 373 mg/L	1.324	1.559	2
TOAST			
LAA	0.907	1.068	1
CE	1.831	2.157	2
Infarct volume ≥ 2.18 cm ³	1.749	2.060	2
FSQ ≥ 3 point	1.189	1.400	1
NIHSS ≥ 4 point	5.358	6.311	6
total score			15

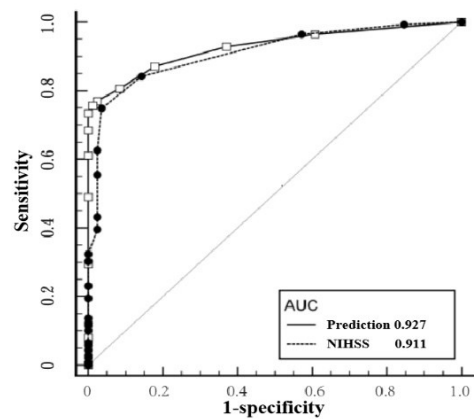


Figure 2. ROC curve predicting the poor prognosis of patients with AIS by the new clinical scoring system and NIHSS scoring system.

3.4. Internal validation of the new scoring model

The newly established scoring system was applied to the internal validation cohort, and the scores for all patients were calculated. The clinical predictive value of the scoring system for poor AIS prognosis was assessed using the ROC curve. The AUC in the validation cohort was 0.892 (95%CI: 0.827–0.957)(see **Figure 3**). A comparison of AUC values between the training and validation cohorts ($Z = 0.519$, $P = 0.604$) revealed no statistically significant difference, indicating good stability of the newly developed model.

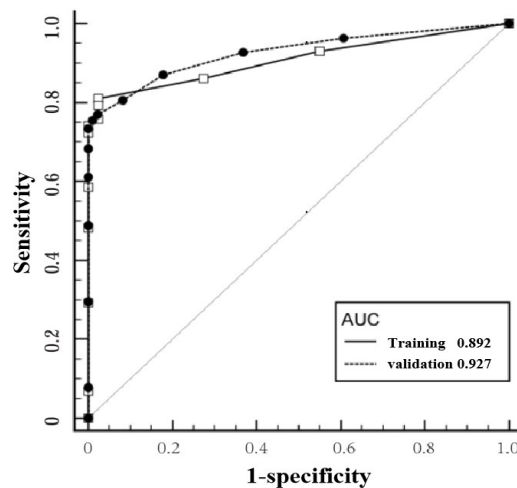


Figure 3. Comparison of the ROC curves between the training and validation sets.

4. Discussion

This study identified independent risk factors associated with poor prognosis in AIS patients and developed a predictive model to guide clinical stratification. The primary objective was to facilitate early identification of high-risk patients, enabling targeted interventions to improve outcomes. Using univariate and multivariate logistic regression analyses, we identified age, prealbumin (PA), large-artery atherosclerosis (LAA), cardioembolism (CE), infarct volume, FSQ score, and NIHSS score as independent predictors, which were incorporated into a clinical scoring system with a total score of 15.

Aging is a global issue, with the population over 60 years expected to exceed 400 million by 2050 [7]. The incidence, disability, mortality, and chronic complications of stroke increase with age, making it a critical non-modifiable factor in AIS prognosis. Gao et al. demonstrated that patients over 60 years old had significantly higher 1-year mortality, poor prognosis, and stroke recurrence risk. Studies consistently show that older age is correlated with worse stroke outcomes, likely due to lower thrombolysis rates, delayed recognition of symptoms, and missed treatment windows [8]. Furthermore, older patients often have multiple comorbidities and reduced organ reserve, increasing the risk of complications such as pneumonia and gastrointestinal bleeding. Effective control of risk factors and improved management of comorbidities are essential to reducing mortality and poor outcomes in this population [9].

Multiple studies have confirmed that infarct volume and baseline NIHSS scores are strongly associated with AIS mortality and prognosis [10]. Freyschlag et al. [11] found that infarct volume correlates with 6-month mRS scores and is an independent predictor of poor outcomes. Tonetti et al. [12] identified smaller infarct volumes, male sex, and rt-PA thrombolysis as independent predictors of favorable outcomes after endovascular treatment. Ganesh et al. [13] highlighted age, infarct volume, comorbidities, secondary prevention, and stroke unit care quality as key predictors of 90-day mRS scores. Our findings also show that infarct volume and baseline NIHSS scores within 72 h of stroke onset are significant predictors of poor short-term outcomes.

Frailty, with a prevalence of 12% to 24%, increases vulnerability to stress across multiple systems. Its pathophysiology involves neuroendocrine, immune-inflammatory, energy metabolism, and cognitive-psychosocial components, all contributing to poor outcomes. While nearly 70 frailty assessment scales exist, none are considered the gold standard. The self-reported Frailty Screening Questionnaire (FSQ), developed based on the Fried criteria and validated in large prospective cohort studies, was used in this study to assess frailty and its correlation with 14-day mRS scores in AIS patients [14]. Frailty was found to be an independent risk factor for poor prognosis, closely linked to adverse outcomes in multiple conditions. Early frailty screening in AIS patients can optimize diagnosis and treatment, providing clinicians with early prognostic insights [15].

Nutritional status plays a pivotal role in frailty, with both factors being interrelated and mutually reinforcing. Frailty can lead to malnutrition, which in turn impairs immune function and drug efficacy, increasing the risk of multisystem dysfunction and infection, thereby worsening frailty [16]. A cross-sectional study also found a positive correlation between frailty and nutritional indicators such as PA and albumin (ALB). PA, with a short half-life of 2–3 days, is a marker of acute nutritional and inflammatory changes. Low PA levels are associated with increased infection risk and severity in AIS and poorer rehabilitation outcomes. Our study identified decreased serum PA as an independent predictor of poor short-term AIS prognosis, suggesting its utility as a prognostic marker. Timely nutritional risk assessment and early intervention may help mitigate disease progression.

The TOAST classification is a widely accepted method for categorizing AIS etiologies [17]. A large retrospective study revealed that LAA is the most common stroke subtype in Asians, accounting for 33% of cases, followed by CE (16%) and

small-artery occlusion (SAO, 24%) [18]. The TOAST classification is linked to stroke severity and prognosis, with CE associated with the highest recurrence and mortality rates, while SAO generally has a better prognosis. Compared to LAA, CE often results in larger infarcts due to insufficient time for collateral circulation to develop, and hemorrhagic transformation after embolism is more common, leading to worse outcomes. Early TOAST classification can facilitate targeted treatment, improving patient outcomes.

The novelty of this study lies in its quantification of frailty's impact on AIS prognosis and its analysis of treatment effects. The variables used in the model are simple, easily obtainable, and do not require additional testing, making the model suitable for clinical use. However, the study has limitations, including its single-center design, which introduces potential selection bias. Additionally, the number of factors included in the model was limited by the sample size. Future research with larger sample sizes is needed to validate these findings further.

Author contributions: Conception and design, NC and LZ; method, JW and YL; data collection, JW and YL; manuscript writing, NC; manuscript revision, LZ; research supervision, LZ. All authors have read and agreed to the published version of the manuscript.

Data availability: The data associated with this study are available from the corresponding author upon reasonable request (Email: qingdao12352630@163.com).

Ethical approval: This study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of the Second Affiliated Hospital of Xingtai Medical College (No. XT-2022112165).

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflict of interest: The authors declare no conflict of interest.

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