

SYSTEMATIC REVIEW

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Risk prediction models for early neurological deterioration after intravenous thrombolysis in acute ischemic stroke patients: a systematic review and meta-analysis

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Abstract

Background An increasing number of risk prediction models have been developed to predict early neurological deterioration (END) in patients with acute ischemic stroke after intravenous thrombolysis. However, the methodological quality and clinical applicability of these models remain unclear.

Objective To systematically review studies on risk prediction models for END in patients with acute ischemic stroke treated with intravenous thrombolysis (IVT).

Design Systematic review and meta-analysis of observational studies.

Methods Seven databases (CNKI, Wanfang Database, VIP database, PubMed, Web of Science, the Cochrane Library, and Embase) were systematically searched from inception to December 20, 2025. Information extracted from the included studies comprised study design, data sources, outcome definitions, sample size, predictors, model development methods, and model performance. The Prediction Model Risk of Bias Assessment Tool (PROBAST) was used to assess evaluate the risk of bias and applicability of the included studies.

Results Eighteen studies were ultimately included, comprising 18 prediction models. All studies utilized logistic regression to predict END. The incidence of END after IVT among patients with acute ischemic stroke patients ranged from 7.7% to 31.3%. The baseline National Institutes of Health Stroke Scale (NIHSS) score was the most frequently identified predictor. All studies were rated as having a high risk of bias based on the PROBAST assessment, primarily due to inconsistent outcome definitions, inappropriate data sources, and inadequate reporting within the analysis domain. The pooled area under the curve (AUC) for the five validated models was 0.87 (95% CI: 0.84–0.91), suggesting moderate predictive performance.

Conclusion Although the included prediction models showed moderate discriminative performance for END in patients with acute ischemic stroke following intravenous thrombolysis, all studies were assessed as having a high risk of bias based on the PROBAST checklist. These findings emphasize the need for nurse-led risk monitoring, standardized neurological assessments, and early preventive nursing interventions for high-risk patients.

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Clinical trial registration The protocol for this study is registered with PROSPERO (registration number: CRD42025628890).

Keywords Stroke, AIS, Acute ischemic stroke, Early neurological deterioration, END, Thrombolysis, Risk prediction models

Introduction

Stroke is a critical global health concern and remains the second leading cause of death as well as the third most common cause of combined death and disability worldwide, with the majority of the stroke burden borne by China [1]. Ischemic stroke constitutes the largest proportion of incident strokes. Among treatments for acute ischemic stroke (AIS), IVT plays a significant role due to its function in systemic reperfusion [2], which is considered a key step in improving functional outcomes within a few hours after symptom onset. Appropriate patient selection and timely treatment have been shown to be crucial factors for better functional outcomes, quality of life, and neurological recovery [3]. Unfortunately, fewer than 5% of AIS patients in China receive IVT, primarily due to missing the optimal treatment window [4]. Furthermore, IVT does not always result in favorable outcomes; approximately 10% of patients undergoing thrombolysis may experience early neurological deterioration (END) [5].

END in patients with AIS following IVT is a common and serious complication, typically characterized by a decline in neurological function occurring within hours or days after treatment. The occurrence of END significantly increases the risk of severe disability and mortality [6]. As an operational concept, the definition of END varies depending on the clinical scale, cutoff values, and timing of assessment, with no formal consensus established to date. For instance, Saleem defined END as an increase of ≥ 2 points on the National Institutes of Health Stroke Scale (NIHSS) score after stroke [7], whereas Simonsen described END as an increase of 4 or more points on the NIHSS within the first 24 h post-stroke [8]. Regardless of the definition applied, END is consistently associated with poorer functional outcomes and greater dependency. Early identification and prediction of END in AIS patients after IVT can enable healthcare providers to implement timely interventions and reduce the risk of further neurological decline. Nurses play a pivotal role in early neurological assessment, continuous monitoring, prompt escalation, and the implementation of preventive measures following intravenous thrombolysis. Therefore, it is essential to identify predictive factors for END in AIS patients after IVT.

Several complex mechanisms contribute to the development of END, including failure of collateral circulation, clot progression, recurrent stroke, increased intracranial pressure, seizures, and hemorrhagic transformation

[9]. Previous studies have identified diabetes, hypertension, hyperuricemia, hypertriglyceridemia, and elevated homocysteine levels as known predictors of END [6, 10, 11]. Currently, END risk prediction models for AIS patients include the WORSEN score and the CNS-LAND score. The WORSEN score, proposed by Miyamoto et al. [12], and the CNS-LAND score, proposed by Jin et al. [13], were developed earlier to assess the risk of END in AIS patients. As new knowledge has emerged, numerous models predicting the risk of END in AIS patients after IVT have been developed. However, the methodological rigor and reporting quality of these models have not been systematically reviewed.

This study aims to systematically review the existing END risk prediction models developed and published for AIS patients following IVT. The findings will provide a theoretical foundation for clinical practice and future research.

Methods

This study protocol was registered on PROSPERO (registration number: CRD42025628890).

Search strategy

We aimed to identify all studies by searching the China National Knowledge Infrastructure (CNKI), Wanfang Database, China Science and Technology Journal Database (VIP), PubMed, Web of Science, The Cochrane Library, and Embase from their inception to December 20, 2025. Relevant keywords and search terms included “stroke,” “AIS,” “acute ischemic stroke,” “early neurological deterioration,” “END,” “thrombolysis,” and “risk prediction models.” Further details on the search terms used are provided in the supplementary materials. Additionally, the reference lists of relevant articles were reviewed.

The PICOTS framework, as recommended by the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) checklist, was applied to guide the conduct of this systematic review. The key components of the review are presented as follows:

P (Population): AIS patients after IVT.

I (Intervention model): Risk prediction models for END in AIS patients following IVT have been developed.

C (Comparator): No competing models.

O (Outcome): The outcome was the end.

T (Timing): The outcome was predicted at a specific time using clinical scoring scale results and laboratory indicators.

S (Setting): The intended use of the risk prediction model is to individualize the prediction of END in patients with acute stroke.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) studies involving patients with AIS who underwent IVT alone; (2) observational study design; (3) reporting a prediction model; and (4) END as the outcome. Studies were excluded if they: (1) did not develop a prediction model; (2) were not published in English or Chinese; or (3) had no accessible full text. (4) were clinical guidelines, case reports, consensus documents, clinical trials and reviews, conferences and congress abstracts.

Study selection and screening

Two reviewers independently conducted the study selection process. Duplicate records were first removed, followed by screening of titles and abstracts to identify potentially eligible studies. The full texts of these studies were then assessed according to the predefined inclusion and exclusion criteria. Any discrepancies in study selection were resolved through discussion with the third reviewer until consensus was achieved.

Data extraction

Data extracted from the included studies were grouped into two categories: (1) Study characteristics, including author, publication year, study design, participants, data sources, and sample size. (2) Model characteristics, including the variable selection method, model development approach, validation type, model performance indicators, final predictors, and model presentation format. Particular attention was given to predictors relevant to nursing assessment and bedside monitoring, such as neurological scores, vital signs, and laboratory indicators. Data extraction was performed by one reviewer and cross-checked by a second reviewer to ensure accuracy and consistency.

Quality assessment

The methodological quality and potential risk of bias of the included studies were assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [14] and the available version of the Prediction Model Risk of Bias Assessment Tool (PROBAST) [15]. GRADE evaluates the quality of evidence based on six domains: study design, risk of bias, inconsistency, indirectness, imprecision, and other factors such as publication bias. PROBAST assesses risk of

bias across four domains: participants, predictors, outcomes, and analysis.

Data synthesis and statistical analysis

A meta-analysis was conducted on the area under the curve (AUC) values reported by the included prediction models using Stata 17.0 (StataCorp, College Station, USA). Heterogeneity was quantified using the I^2 statistic, and publication bias was assessed with Egger's test [16].

Results

Study selection

Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flowchart, illustrating the comprehensive search process and results. The initial search yielded a total of 2,359 indexed records. After removing 620 duplicate records identified across all databases, 1,739 titles and abstracts were screened for eligibility. Following this screening, 74 articles were selected for further evaluation. During the subsequent assessment, 21 studies were excluded because they did not establish prediction models or focused solely on risk factors. Additionally, 11 studies were excluded due to inconsistencies with the review population: five studies involved populations that did not receive thrombolysis, two studies included fewer than two predictors, three studies reported outcomes limited to subgroups, and ten studies were reviews or conference proceedings. Ultimately, 18 studies encompassing 18 models were included in this study.

Study characteristics

Table 1 presents the design and participant characteristics of the 18 included studies. These studies were published between 2021 and 2024, with 17 conducted in China (eight published in Chinese) and one conducted in France. Among the included studies, two were prospective—one of which was a multicenter study—while the remaining studies were retrospective, including three multicenter studies. All studies focused on patients with acute ischemic stroke who received intravenous thrombolysis. Two studies specifically defined stroke subtypes: one targeted elderly patients with mild strokes, and another focused on patients with acute minor stroke and large vessel occlusion. Additionally, we summarized the various definitions of END used across the studies. The most common definition of END was an increase of more than 4 points in the NIHSS score within 24 h of thrombolysis compared to the admission score. Sample sizes ranged from 120 to 9,141 participants.

Table 2 presents the model information from the included studies. Logistic regression analysis was used to develop prediction models in 13 studies, while lasso regression was employed in 4 studies. Machine learning

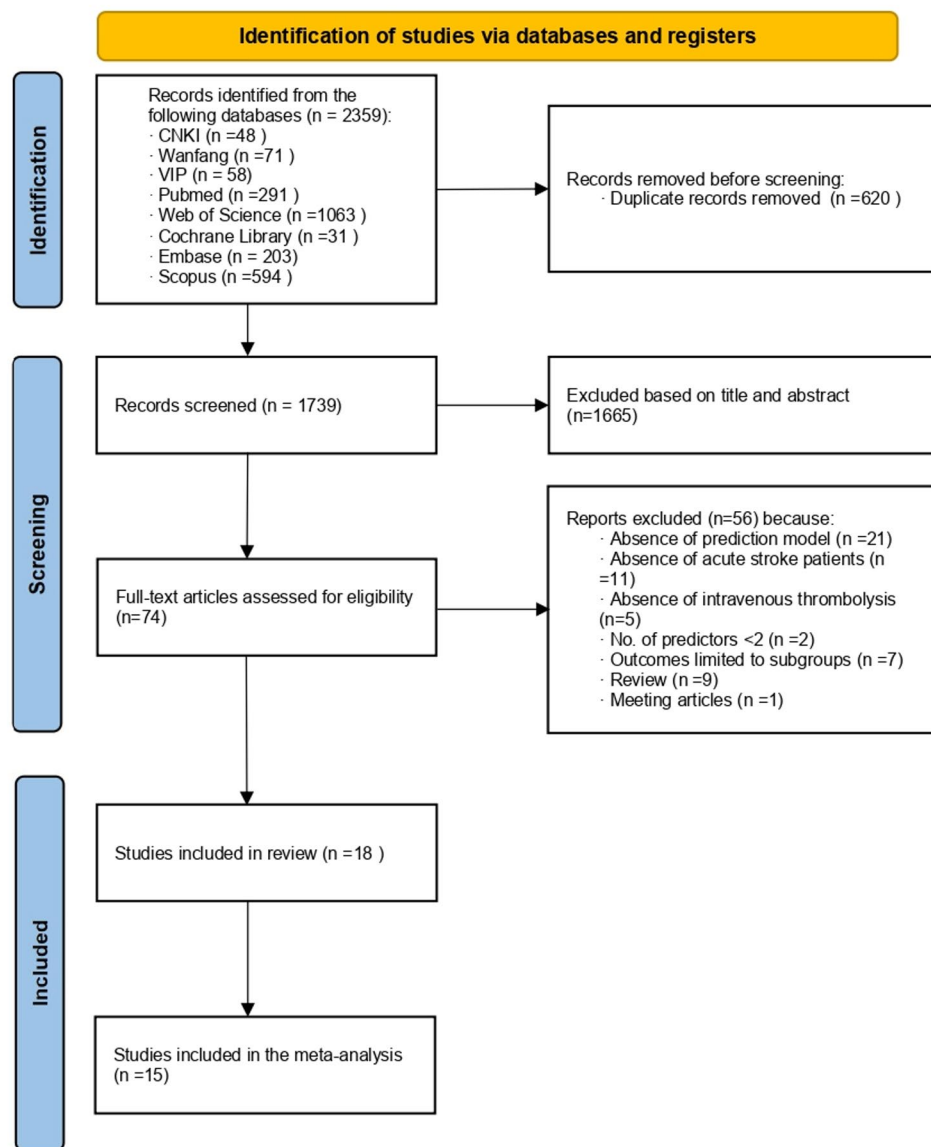


Fig. 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart of literature search and selection

methods such as K-Nearest Neighbors (KNN), Support Vector Machine (SVM), and Random Forest (RF) were also utilized. The NIHSS score, blood glucose level, white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), and systolic blood pressure (SBP) were the five most common predictors used across the models, appearing in nine, seven, six, six, and five models, respectively. Table 3 presents all factors associated with END identified in the included studies, along with their corresponding measures of association (e.g., odds ratio,).

Model validation

Among the included studies, 12 performed internal validation, two conducted both internal and external

validation, while four did not undergo any validation after development.

Results of quality assessment

According to GRADE, all studies included in this review were evaluated as having high certainty. Table 4 illustrates the risk of bias and applicability among the selected studies. In the participant domain, most studies were considered to have a high risk of bias due to inappropriate data sources. In the predictor domain, every study had a low risk of bias. In the outcome domain, six studies were found to have a high risk of bias because they did not report the consistency of outcome definition and ascertainment [17–23]. Additionally, all studies were evaluated as having a high risk of bias overall. Among them,

Table 1 Overview of basic data of the included studies

Author(year)	Country	Study design	Participants	The definition of END	Data source	END cases/sample size (%)
Bian, Li (2021)	China	Respective study	patients with AIS who received IVT	Within 24 h of thrombolysis, the patient's NIHSS score increased by more than 4 points compared with the score at the time of admission or the patient died	one hospital	21/120(17.5%)
Deng, Yong (2024)	China	Respective study	patients with AIS who received IVT	Within 24 h of thrombolysis, the patient's NIHSS score increased by more than 4 points compared with the score at the time of admission or the patient died	one hospital	52/182(28.6%)
Hu, Yanfang (2021)	China	Respective study	patients ≥ 60 years old with minor ischemic stroke who received IVT	Within 24 h of thrombolysis, the patient's NIHSS score increased by more than 4 points compared with the score at the time of admission	Neurology department of a hospital	26/165(15.8%)
Li, Bin (2022)	China	Respective study	patients with AIS who received IVT	(1) The NIHSS score increased by more than 2 points compared with the score at the time of admission; (2) The level of consciousness score or exercise ability score increased by more than 1 point compared with the time of admission; (3) The appearance of new neurological deficits.	Neurology department of a hospital	66/258(25.6%)
Lv, Zhe (2023)	China	Respective study	patients with AIS who received IVT	NIHSS score increase ≥ 2 NIHSS points within 72 h compared with the score at the time of admission	one hospital	99/704(14.1%)
Xu, Shouquan (2023)	China	Respective study	patients with AIS who received IVT	Within 24 h of thrombolysis, the patient's NIHSS score increased by more than 4 points compared with the score at the time of admission or the patient died	Neurology department of a hospital	66/342(19.3%)
Yuan, Chang-hong (2021)	China	Respective study	patients with AIS who received IVT	Within 24 h of thrombolysis, the patient's NIHSS score increased by more than 4 points compared with the score at the time of admission or the patient died	Neurology department of a hospital	31/153(20.3%)
Zhang, mei (2022)	China	Respective study	patients with AIS who received IVT	Patient's NIHSS score increased by more than 2 points compared with the score within 7 days of symptom onset	one hospital	80/263(30.4%)
Gao, Yuan (2023)	China	Prospective study	patients with AIS who received IVT	An increase of more than 2 points in total NIHSS score within 24 h after thrombolysis	Multi-center study	305/1956(15.6%)
Jin, Huijuan (2023)	China	Respective study	patients with AIS who received IVT	NIHSS score increase > 4 points or death within 24 h of stroke onset	Multi-center study	93/1213(7.7%)
Li, Ning (2024)	China	Respective cohort study	patients with AIS who received IVT	An increase of 2 or more points in the NIHSS score, assessed between the initial evaluation and a subsequent assessment conducted 24–36 h later	Two hospitals	-
Luo, Bang (2024)	China	Respective study	patients with AIS who received IVT	NIHSS total score increased by ≥ 4 or the NIHSS individual score increased by ≥ 2 compared to baseline	Stroke center of a hospital	33/217(15.2%)
Seners, P. (2021)	France	Respective cohort study	patients with minor stroke (NIHSS ≤ 5) and LVO (basilar artery, internal carotid artery, first [M1] or second [M2] segment of middle cerebral artery) who received IVT	An NIHSS score increase of 4 points or more within the first 24 h after IVT	Multi-center study	126/1076(11.7%)
Tian, Tian (2023)	China	Respective study	patients with AIS who received IVT	An increase in NIHSS score 4 within the first 24 h after IVT without parenchymal hemorrhage on follow-up imaging or another identified cause	one hospital	88/399(22.1%)

Table 1 (continued)

Author(year)	Country	Study design	Participants	The definition of END	Data source	END cases/sample size (%)
Wang, Mei (2023)	China	Respective study	patients with AIS who received IVT	If any of the following conditions was met: (1) Death within 24 h after intravenous thrombolysis, or when compared to before thrombolysis, the NIHSS score increased by more than 4 points; (2) Imaging showing an increased area of stroke; (3) Appearance of new stroke foci.	Neurology department of a hospital	90/321(28.0%)
Wen, Rui (2024)	China	Respective study	patients with AIS who received IVT	A neurological deterioration with a ≥ 4 points increase on the NIHSS score compared with baseline within 24 h after the treatment	Multi-center study	1766/9141(19.3%)
Yang, Huan (2023)	China	Respective study	patients with AIS who received IVT	An NIHSS score rise of ≥ 2 points within 72 h of hospitalization.	stroke center of a hospital	99/704(14.1%)
Zhu, Bifeng (2024)	China	Prospective study	patients with AIS who received IVT	An increase of ≥ 4 points in the NIHSS score, recorded between admission and 24 h	Neurology department of a hospital	66/211(31.3%)

Abbreviations: AIS acute ischemic stroke, NIHSS National Institutes of Health Stroke Scale, IVT intravenous thrombolysis, LVO large vessel occlusion

14 studies [13, 18–20, 23–32] had insufficient sample sizes, failing to meet the recommended guideline of more than 20 events per variable (EPV). Eleven studies [18–21, 24–28, 30, 33] did not report appropriate methods for addressing missing data. Two studies did not fully evaluate the predictive performance of their models [13, 18]. Five studies did not adequately address model overfitting or underfitting in model performance [19, 26, 27, 33, 34]. Four studies did not provide information on internal or external model validation of participant data [20, 24, 28, 32], and none of the studies accounted for complexities in the data. Regarding the applicability assessment of the 18 included studies, two were classified as having a high risk. In the participant domain, the inclusion criteria in these two studies were limited to specific subgroups of acute ischemic stroke [26, 33]. However, all models demonstrated good applicability in the other two domains (predictor and outcome domains).

Meta-analysis of validation models included in the review

Only 15 studies were eligible for synthesis due to insufficient reporting of model details. Among these, three studies employed multiple methods for model development using the same sample. The pooled AUC was calculated using a random-effects model, yielding a value of 0.87 (95% Confidence Interval: 0.84–0.91) (Fig. 2). However, there was a high degree of heterogeneity among the included studies ($I^2 = 90.3\%$, $P < 0.001$).

Discussion

It is crucial to effectively assess the potential risk factors of END, as this can help medical staff understand the causal mechanisms and thereby prevent END. In this study, we identified 18 studies involving 18 models for predicting END, most of which are based on data from Chinese patients. According to the PROBAST checklist,

all studies were evaluated as having a high risk of bias. The pooled area under the curve (AUC) value of the 15 validated models included in the meta-analysis was 0.87 (95% confidence interval: 0.84–0.91). However, the heterogeneity among these models was high, which may be related to differences in the definitions of END, included predictors, and methodologies.

The process of model development offers valuable insights. Firstly, machine learning algorithms were widely incorporated into the model development in the included studies. As a powerful analytical approach, machine learning delivers superior predictive accuracy and robust model performance, demonstrating significant potential for prognostic refinement and optimized clinical decision-making. Second, several high-quality studies adopted rigorous methodological designs. Wen et al. [34] enrolled a large sample from the Shenyang Stroke Emergency Map database, adopted the multiple imputation by chained equations (MICE) approach to handle missing data, and conducted external validation to ensure broad applicability. This methodological step is frequently overlooked in other predictive studies. Besides, Gao et al. [21] conducted a prospective, multicenter, large-scale registry study with thorough assessments of model calibration and discrimination. Notably, they adopted SHapley Additive exPlanations (SHAP) analysis to improve the interpretability of black-box machine learning models and visualized SHAP values via a web-based application. Seners et al. further strengthened methodological robustness by recruiting two large multicenter cohorts and adopting standardized END definitions consistent with the European Cooperative Acute Stroke Study criteria [33]. Overall, most established END models achieved moderate to good performance; however, the overall risk of bias remained high across the included studies. Substantial heterogeneity was also observed, mainly attributable to

Table 2 Overview of the information of the included prediction models

Author(year)	Variable selection	Model development method	Calibration Method	Validation method	Final Predictors	Model performance	Model presentation
Bian, Li (2021)	Cat-egorical variables	Binary logistic regression model	Hosmer-Lemeshow	-	Age $\geq$ 60 years old; HMCAS positive; concomitant AF; high baseline NIHSS score; high blood glucose; WBC count; D-dimmer level	A:0.905(0.832–0.977)	Script
Deng, Yong (2024)	Cat-egorical variables	Binary logistic regression model	Calibration curve	Internal validation	High baseline NIHSS score; Admission- high HbA1c; severe stenosis of responsible vessels; Admission- high NLR and low PNI	A:0.928(0.880–0.961)	Formula of risk score obtained by regression coefficient of each other & nomogram model
Hu, Yanfang (2021)	Cat-egorical variables	logistic regression analysis	-	Internal validation	hyperglycemia; high WBC count; CAS; high platelet count	A:0.857(0.826–0.888)	nomogram model
Li, Bin (2022)	Con-tinuous variables	logistic regression analysis	Hosmer-Lemeshow	External validation	blood glucose; BMI; WBC count; lipoprotein; creatinine level; proportion of responsible great occlusion; NIHSS score at admission	A:0.93(0.88–0.97); B:0.92	Formula of risk score obtained by regression coefficient of each other
Lv, Zhe (2023)	Con-tinuous variables	LR; KNN; SVM; RF	-	Internal validation	Admission- high NIHSS score; high SBP; high lymphocyte percentage; high PLR	LR:0.789(0.675–0.902); KNN:0.797(0.685–0.910); SVM:0.851(0.751–0.952); RF:0.809(0.699–0.919)	Script
Xu, Shouquan (2023)	Con-tinuous variables	BP neural networks; RF; Decision Tree	-	Internal validation	HMCAS positive; Before IVT-fasting plasma glucose; D dimmer; WBC count; MHR; DNT; SBP; The type of TOAST; smoking history	BP neural networks: 0.957(0.918–0.995); RF: 0.969(0.913–1.000); Decision Tree: 0.848(0.737–0.59)	Decision tree
Yuan, Chang-hong (2021)	Con-tinuous variables	Multivari-able logistic regression analysis	Hosmer-Lemeshow	-	HMCAS positive; Before IVT-glucose level; WBC count; SBP; D-dimmer	A:0.872(0.802–0.943)	Script
Zhang, mei (2022)	Con-tinuous variables	Multivari-able logistic regression analysis	Calibration curve	-	High fasting plasma glucose; High SBP; NIHSS baseline score; ONT	A:0.90(0.87–0.94)	nomogram model
Gao, Yuan (2023)	Con-tinuous variables	Multivari-able logistic regression analysis	Hosmer-Lemeshow	Internal validation	Hemoglobin; WBC count; LMR; thrombin time; OTT; prothrombin time	A:0.754	Script
Jin, Huijuan (2023)	Con-tinuous variables	Multivari-able logistic regression analysis	Hosmer-Lemeshow	Internal validation & External validation	CK-MB; NIHSS score; SBP; LDH; ALT; Neutrophil ratio; D-dimmer	A:0.862; B:0.851	Script
Li, Ning (2024)	Cat-egorical variables	Lasso regres-sion analysis	Calibration Plot	Internal validation	Previous stroke history; BMI; age; OTT; lymphocyte count; blood glucose level	A:0.867(0.818–0.916); B:0.880(0.799–0.961)	nomogram model
Luo, Bang (2024)	Con-tinuous variables	Multivari-able logistic regression analysis	Calibration curve	Internal validation	Smoking history; NIHSS score; homocysteine level; NLR	A:0.826(0.719–0.932); B:0.887(0.763–1.000)	nomogram model

Table 2 (continued)

Author(year)	Variable selection	Model development method	Calibration Method	Validation method	Final Predictors	Model performance	Model presentation
Seners, P. (2021)	Continuous variables	backward stepwise method (logistic regression model)	-	Internal validation & External validation	Occlusion site; thrombus length	A:0.76(0.70–0.82); B:0.78(0.70–0.86)	Script
Tian, Tian (2023)	Continuous variables	backward stepwise method (logistic regression model)	Hosmer-Lemeshow & Brier score	Internal validation	NLR; MPV; BMI; AF	A:0.981(0.961–1.000); B:0.9815(0.9809–0.9821); 0.926(0.868–0.985)	nomogram model
Wang, Mei (2023)	Continuous variables	Lasso regression analysis	Calibration curve	Internal validation	NIHSS score after thrombolysis; Pre-thrombolytic SBP; Albumin; Complication with AF	A:0.796(0.738–0.853); B:0.785(0.727–0.845)	nomogram model
Wen, Rui (2024)	Continuous variables	Lasso regression analysis; SVM; RF; GBDT; MLP	-	Internal validation	ONT; Admission-NIHSS Score; Swallowing Function Score; Antiplatelet Therapy; Age; Urokinase; gender; DBP	Lasso regression: 0.829(0.799–0.86); MLP:0.820(0.799–0.858); RF:0.797(0.764–0.829); GBDT:0.774(0.741–0.808); SVM:0.753(0.711–0.795)	Script
Yang, Huan (2023)	Continuous variables	Lasso regression analysis	Calibration curve	Internal validation	NLR; PNR; PLR	A:0.862(0.806–0.917); B:0.816(0.717–0.915)	nomogram model
Zhu, Bifeng (2024)	Categorical variables	logistic regression analysis	Hosmer-Lemeshow	-	Large artery disease; transient ischemic attack; high blood glucose; high NLR; important perforator diseases; low ASPECTS	A:0.809(0.7429–0.8751); B:0.816(0.6783–0.9527)	nomogram model

Abbreviations: M1 first segment of the middle cerebral artery, M2 second segment of the middle cerebral artery, HMCAS hyperdense middle cerebral artery sign, AF Atrial Fibrillation, NIHSS National Institutes of Health Stroke Scale, HbA1c Glycosylated hemoglobin is tested on fingerstick blood, WBC White blood cell, NLR Neutrophil to lymphocyte ratio, PNI Prognostic Nutritional Index, CAS carotid artery stenosis, BMI Body Mass Index, LR Logistic regression, KNN K-Nearest Neighbor Method, SVM support vector machine, RF random forest, PLR Platelet-to-Lymphocyte ratio, MHR Monocyte to high-density lipoprotein cholesterol ratio, MPV Mean platelet volume, DNT Door to needle time, SBP systolic blood pressure, SVM Support vector machine, RF Random forest, GBDT Gradient-boosted Decision Tree, MLP Multi-layer perceptron, ONT Onset to needle time, LMR Lymphocytes to monocytes ratio, CK-MB Creatine Kinase Myocardial Band, LDH Lactic dehydrogenase, ALT alanine transaminase, OTT Onset to Treatment Time, DBP Diastolic blood pressure, NLR Neutrophil-to-lymphocyte ratio, PNR Platelet-to-Neutrophil ratio, ASPECTS Alberta Stroke Program Early CT Score

inconsistent END definitions, and diverse modeling and validation strategies. Therefore, future model development should prioritize standardized data collection and rigorous data processing, unified outcome definition, and optimized study design for model construction, internal validation and external validation.

This study offers several important clinical implications. First, a high baseline NIHSS score was the most frequently documented factor predicting END, as it typically indicates more severe neurological deficits and is associated with an increased risk of malignant cerebral edema and hemorrhagic transformation [35]. Although the NIHSS provides a standardized measure of stroke severity, it is less sensitive to posterior circulation strokes, which may result in underrecognition of neurological impairments [36]. Therefore, acute stroke emergency management should prioritize comprehensive

neurological examinations rather than relying solely on a single scoring scale, especially in cases of suspected posterior circulation stroke. Since nurses play a central role in ongoing neurological monitoring, integrating END risk prediction models into nursing practice could enhance early risk identification, support timely escalation of care, and promote safer, more effective patient management.

In addition, several examination and laboratory indicators—such as fasting plasma glucose (FPG), white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), and systolic blood pressure (SBP)—were identified as independent predictors of END. One possible reason FPG affects END is that it can exacerbate anaerobic glycolysis, leading to intracellular acidosis in brain tissue and resulting in new infarctions in hypoperfused brain areas. WBC counts likely play a significant role in

Table 3 Summary of standardized predictive factors for early neurological deterioration after intravenous thrombolysis in acute ischemic stroke patients

Standardized Predictive Factors of END	Number of Included Studies Reporting the Factor	OR (95%CI)
Baseline/Admission/Post-thrombolysis NIHSS score	9	1.050 (1.021,1.080)
Blood glucose-related indicators (Hyperglycemia, fasting plasma glucose, HbA1c)	7	1.196 (1.088, 1.304)
White blood cell (WBC) count	6	1.089 (1.029,1.148)
Neutrophil-to-lymphocyte ratio	6	1.563 (0.907,2.218)
Systolic blood pressure/ Diastolic blood pressure	5	1.016 (1.009,1.024)
Arterial stenosis/lesions (Carotid artery stenosis, Severe stenosis of responsible vessel, Large artery disease, Important perforator artery disease)	4	0.443 (0.044, 0.842)
D-dimmer	4	3.574 (1.646,5.503)
Atrial fibrillation	3	-
Age	3	-
Body mass index	3	-
Hyperdense middle cerebral artery sign positive	3	-
Lymphocyte-related indicators (Lymphocyte percentage, Lymphocyte count, Lymphocyte-to-monocyte ratio)	3	-
Platelet-related ratios (Platelet-to-lymphocyte ratio, Platelet-to-neutrophil ratio)	3	-
Smoking history	2	-
Previous stroke history, Transient ischemic attack	2	-
Coagulation-related indicators (Thrombin time, Prothrombin time)	2	-
Liver/kidney function indicators (Creatinine, Alanine transaminase)	2	-
Cardiac muscle-related indicators (Creatine kinase-MB, Lactate dehydrogenase)	2	-
Prognostic nutritional index	1	-
Lipoprotein	1	-
Monocyte-to-high density lipoprotein ratio	1	-
TOAST classification	1	-
Occlusion site	1	-
Thrombus length	1	-
Mean platelet volume	1	-
Serum albumin	1	-
Hemoglobin	1	-
Swallowing function score	1	-
Antiplatelet therapy	1	-
Urokinase use	1	-
Gender	1	-
Homocysteine	1	-
Low ASPECTS score	1	-

the occurrence of END by releasing various inflammatory substances that participate in the clotting process, predisposing patients to thrombus formation. Excessive WBC aggregation can simultaneously hinder the recovery of cerebral blood flow after IVT [21]. A high NLR indicates that the proinflammatory activity of neutrophils may surpass the regulatory function of lymphocytes, creating an environment conducive to uncontrolled peripheral inflammation spreading to a vulnerable brain [37]. Given that these metabolic, inflammatory, and hemodynamic indicators are routinely monitored in clinical practice, nurses play a pivotal role in early risk detection and ongoing patient surveillance. Integrating END risk prediction tools into nursing workflows may support

proactive risk stratification, guide timely escalation of care, and facilitate targeted interventions such as glucose control, blood pressure optimization, and inflammatory risk monitoring—ultimately contributing to improved neurological outcomes and patient safety.

Demographic, clinical, and imaging-related factors—including advanced age, higher body mass index (BMI), concomitant atrial fibrillation (AF), and a positive hyperdense middle cerebral artery sign (HMCAS)—were associated with an increased risk of END. These factors likely reflect underlying vascular vulnerability, cardioembolic burden, and the severity of large-vessel occlusion, all of which predispose patients to rapid neurological decline. Additionally, smoking history, previous stroke, prolonged

Table 4 PROBAST results of included studies

Author(year)	Study type	ROB				Applicability			Overall	
		Participants	Predictors	Outcome	Analysis	Participants	Predictors	Outcome	ROB	Applicability
Bian, Li (2021)	A	-	+	+	-	+	+	+	-	+
Deng, Yong (2024)	B	-	?	?	-	?	?	?	-	+
Hu, Yanfang (2021)	B	-	?	?	-	?	?	?	-	-
Li, Bin (2022)	B	-	?	-	-	?	?	?	-	+
Lv, Zhe (2023)	B	-	?	-	-	?	?	?	-	+
Xu, Shouquan (2023)	B	-	?	?	-	?	?	?	-	+
Yuan, Changhong (2021)	A	-	?	?	-	?	?	?	-	+
Zhang, mei (2022)	A	-	?	-	-	?	?	?	-	+
Gao, Yuan (2023)	B	?	?	-	-	?	?	?	-	+
Jin, Huijuan (2023)	B	-	?	?	-	?	?	?	-	+
Li, Ning (2024)	B	-	?	-	-	?	?	?	-	+
Luo, Bang (2024)	B	-	?	?	-	?	?	?	-	+
Seners, P. (2021)	B	-	?	?	-	?	?	?	-	-
Tian, Tian (2023)	B	?	?	+	-	+	+	+	-	+
Wang, Mei (2023)	B	-	?	?	-	?	?	?	-	+
Wen, Rui (2024)	B	-	?	?	-	?	?	?	-	+
Yang, Huan (2023)	B	-	?	-	-	?	?	?	-	+
Zhu, Bifeng (2024)	A	?	?	?	-	?	?	?	-	+

PROBAST Prediction model Risk Of Bias Assessment Tool, ROB risk of bias

A indicates "development only"; B indicates "development and validation in the same publication". + indicates low ROB/low concern regarding; - indicates high ROB/high concern regarding application; ? Indicates unclear ROB/under concern regarding applicability

onset-to-treatment time (OTT), and extended onset-to-needle time (ONT) were significantly linked to END, underscoring the critical roles of cumulative vascular risk and timely reperfusion therapy in neurological outcomes. Collectively, these findings reinforce the multifactorial nature of END and highlight the need for a more nuanced and integrative approach to risk assessment. Given the complex interplay among patient characteristics, vascular pathology, treatment timeliness, and inflammatory and metabolic status, comprehensive and dynamic risk prediction tools are essential to support individualized clinical decision-making.

This meta-analysis highlights several implications for clinical practice and future research. The relatively high pooled AUC suggests that existing models have potential for predicting END in patients with acute ischemic stroke after intravenous thrombolysis. However, substantial heterogeneity and high risk of bias, along with the predominance of Chinese populations, limit the reliability and generalizability of these findings. Future studies should focus on improving methodological quality, including adequate sample size estimation, standardized handling of missing data, and robust external validation. Standardization of END definitions and outcome measures is also essential to enhance comparability across studies. Furthermore, integrating key clinical, laboratory, and imaging predictors, particularly through machine learning and multimodal data may improve predictive performance. Such advancements could facilitate early

risk stratification, support personalized clinical decision-making, and ultimately improve neurological outcomes.

Limitations

This review has several potential limitations. First, most of the included studies were conducted in China, which may limit the generalizability of the prediction models to Western populations. It is essential for future research to develop risk prediction models for END in diverse populations. Second, due to differences in reporting transparency and methodology among the included studies, it is difficult to recommend one predictive model over another. Therefore, more rigorous methodologies and greater transparency in reporting are needed in future research.

Conclusion

This review includes 18 studies encompassing 18 models. The pooled area under the curve (AUC) of 15 validated models was 0.87 (95% CI: 0.84–0.91), indicating a moderate level of discrimination. According to PROBAST, all included studies were found to have a high risk of bias. Currently, prediction models for END in acute ischemic stroke patients do not meet PROBAST standards. Therefore, future prediction model development should involve larger sample sizes and more rigorous research designs. Although existing END prediction models demonstrate moderate discrimination, nurse-centered risk assessment tools and standardized monitoring protocols

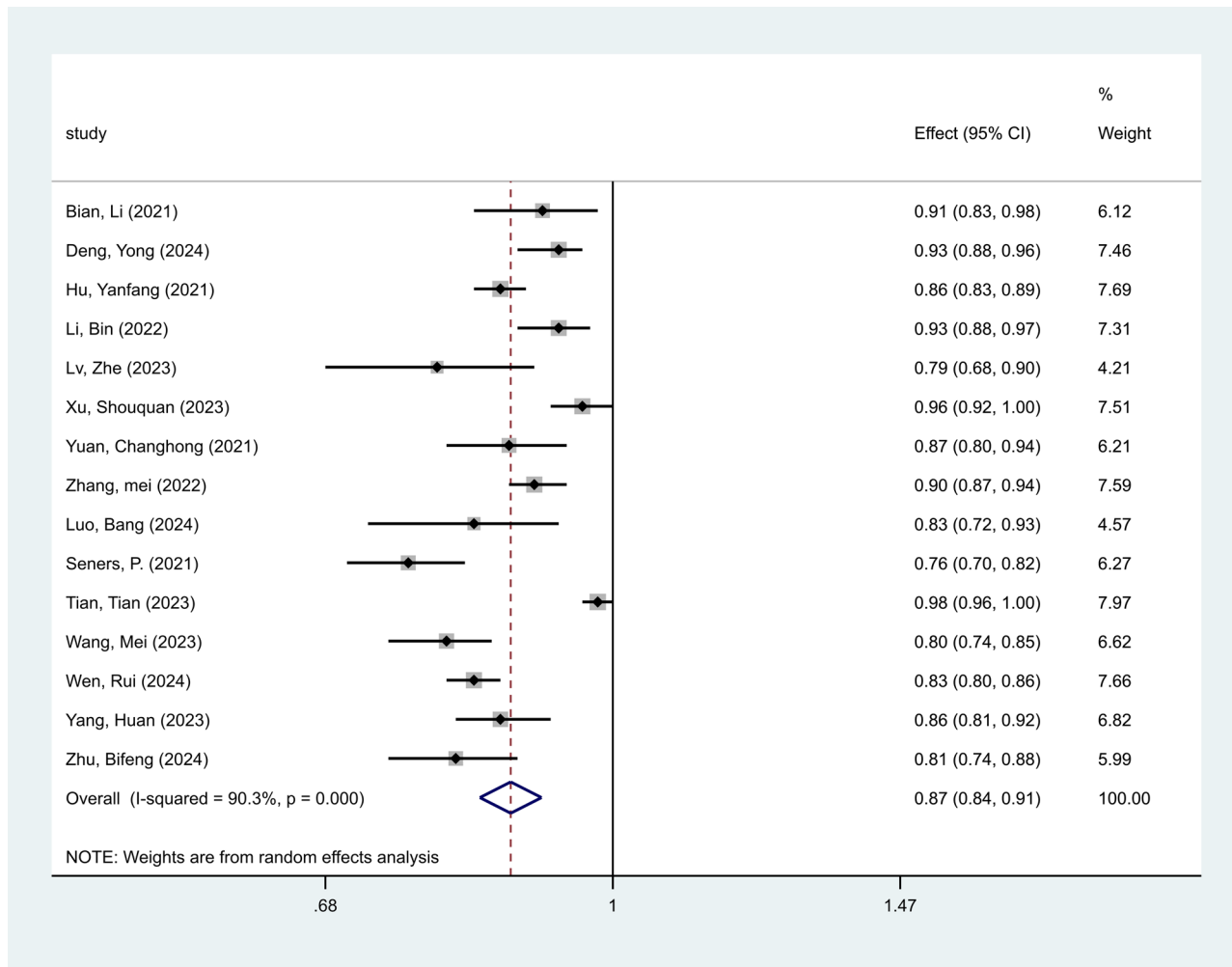


Fig. 2 Forest plot of the random effects meta-analysis of pooled AUC estimates for 15 validation models

are essential to improve early detection and prevention of neurological deterioration.

Supplementary Information

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- Supplementary Material 1.
- Supplementary Material 2.

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Authors' contributions
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Data availability
The data is available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate
Not Applicable.
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Consent for publication
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The authors declare no competing interests.

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