Advances in Precision Medicine, 2026, Volume 11, Issue 6
https://bbwpublisher.com/journal/APM
Online ISSN: 2424-9106
Print ISSN: 2424-8592

When Mild Is Not Benign: Predicting Early Neurological Deterioration in Mild-to-Moderate Acute Ischemic Stroke

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Abstract: *Introduction:* Screening of Factors Influencing Early Neurological Deterioration in Patients with Mild-to-Moderate Ischemic Stroke, Construction of a Predictive Model, and Evaluation of Its Performance. *Methods:* Retrospective data of patients with mild to moderate acute ischemic stroke diagnosed in Guangdong Second Provincial General Hospital from January 2017 to June 2023 were analyzed. The cohort was divided into the early neurological deterioration (END, with a quantity of 205) group and the non-END group (with a quantity of 929). LASSO regression analysis was used to find key predictive features related to END. A nomogram was constructed using R software, and the prediction performance was evaluated through ROC curves, calibration plots, and decision curve analysis (DCA), and stability testing was carried out through five - fold cross - validation. *Results:* A total of 1, 134 patients with mild to moderate acute ischemic stroke were included, among whom 205 experienced early neurological deterioration. LASSO regression identified six independent factors affecting the occurrence of early neurological deterioration: BMI, admission systolic blood pressure, history of diabetes, ADL score, ASPECT score, and treatment methods. A dynamic nomogram model was constructed based on these risk factors. ROC curves, calibration curves, and decision curves indicated that the model has good predictive performance, and fivefold cross-validation further confirmed that the model is highly robust. *Conclusion:* We analyzed and identified 6 independent risk factors for END, namely BMI, admission systolic blood pressure, history of diabetes, ADL score, ASPECTS score, and treatment methods. The nomogram constructed based on these factors has an acceptable predictive performance in the study population.

Keywords: Acute ischemic stroke; Early neurological deterioration; Nomogram

Online publication: June 26, 2026

1. Introduction

Stroke is the second leading cause of death and the third leading cause of disability worldwide [1], with acute

ischemic stroke (AIS) accounting for approximately 80% of all cases [2]. Minor ischemic strokes (National Institutes of Health Stroke Scale [NIHSS] ≤ 5) alone account for over half of all AIS cases and are often underestimated due to initially mild symptoms [3], yet up to 30% of such patients develop disability within 90 days [3]—a figure that escalates substantially across the moderate-severity range [4], where functional dependence without timely intervention is common. Approximately one-third of all AIS patients classified as non-severe by NIHSS at admission ultimately experience lasting disability, directly challenging the prevailing assumption that mild initial presentation reliably predicts a benign clinical course [3]. Together, patients with mild-to-moderate AIS (NIHSS ≤ 15) [5] constitute the numerically dominant subgroup in daily stroke practice, yet this population bears a substantial and systematically underappreciated burden—one for which individualized, evidence-based risk stratification tools remain conspicuously lacking.

Within this population, early neurological deterioration (END)—defined END as an increase of ≥ 2 points in NIHSS score within 7 days of admission [6]—is the most consequential in-hospital complication and the clearest manifestation of the gap between a patient's apparent (presenting) and actual (evolving) severity. The frequency of END varies between 5% and 40% of stroke patients depending on assessment methods and inclusion criteria [7], and its prognostic weight is unambiguous: of studies reporting associations between END and clinical outcome, 95% found worse outcomes at 90 days or hospital discharge in patients who experienced END [8]. The pathophysiology is multifactorial, encompassing hemodynamic instability, infarct progression, hemorrhagic transformation, cerebral edema, and neuroinflammation. The highest incidence of END occurs within 24 hours after admission [9], precisely the window in which individualized risk stratification could most meaningfully alter clinical management. Yet existing END prediction models have been derived predominantly from heterogeneous AIS cohorts spanning all severity levels, or from treatment-specific subgroups heavily weighted toward severe deficits and large vessel occlusion; dedicated models developed and validated exclusively for mild-to-moderate AIS (NIHSS ≤ 15) remain scarce [5], leaving this numerically dominant population without a reliable, population-specific risk stratification tool.

To address this gap, this study aimed to identify independent risk factors for END in a large cohort of patients with mild-to-moderate AIS and to construct a dynamic nomogram integrating variables routinely obtainable—providing a practical, individualized risk stratification tool to support early clinical decision-making in this underserved population.

2. Methods

2.1. Study population

This retrospective study enrolled consecutive patients with mild-to-moderate acute ischemic stroke (NIHSS ≤ 15) admitted to Guangdong Second Provincial General Hospital from January 2017 to June 2023. The study protocol was approved by the institutional ethics committee (No. 2025-KY-KZ-310-01) and was conducted in accordance with the Declaration of Helsinki.

Inclusion criteria were as follows: (1) age ≥ 18 years old; (2) symptom onset to admission ≤ 72 hours; (3) NIHSS score ≤ 15; (4) clinical diagnosis of AIS according to the Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke 2018.

Exclusion criteria included: (1) unknown time of symptom onset; (2) history of thyroid disease, malignant tumor, hematologic disease, or severe cardiac, hepatic, or renal disease.

2.2. Data collection

Clinical data collected included demographic characteristics, medical history, onset-to-admission time, admission blood pressure, Activities of Daily Living (ADL) score assessed by the Barthel Index [10], Alberta Stroke Program Early CT Score (ASPECTS) [11], NIHSS score, Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification [12], treatment modalities, and laboratory parameters. NIHSS scores were assessed at admission, 1–3 days, and 7 days after admission. Fasting blood samples for C-reactive protein (CRP), white blood cell, neutrophil, lymphocyte, monocyte, and platelet counts were obtained within 24 hours of admission.

2.3. Outcome measurement

The primary outcome was early neurological deterioration (END), defined as an increase in NIHSS score of ≥ 2 points within 7 days after admission [6].

2.4. Statistical analysis

Use R (Windows 4.5.2) to analyze all statistical data, use multiple imputation to handle missing data, and use LASSO regression to screen candidate variables. Incorporate (Sel vars) into multivariate logistic regression analysis to explore the independent risk factors for END. Based on the independent risk factors, construct a nomogram prediction model using the R software package. Evaluate the prediction performance of the nomogram using ROC, calibration curves, and decision curve analysis (DCA). All statistical tests were two-tailed; a *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 1134 patients were included, of whom 205 cases (18.08%) had END and 929 cases (81.92%) did not. Baseline characteristics are shown in **Table 1**. Significant between-group differences were observed in body mass index (BMI), diabetes history, admission systolic blood pressure (aSBP), admission NIHSS score, ADL score, ASPECTS, TOAST classification, treatment methods, and absolute neutrophil count (all $P < 0.05$).

Table 1. Baseline characteristics of the study population between the END group and non-END group

Characteristics	END group (n=205)	non-END group(n=929)	*P*-value
Age, y	56.0 (50.0, 66.0)	59.0 (51.0, 68.0)	0.206
Male, n (%)	146 (71.2)	657 (70.7）	0.99
BMI	25.1 (23.4, 27.7)	24.2 (22.0, 26.4)	< 0.001*
Hypertension, n(%)	138(67.3)	563 (60.6)	0.201
Diabetes, n(%)	66 (32.2)	211 (22.7)	0.017*
Coronary Heart Disease, n(%)	11 (5.4)	62 (6.7)	0.788
Stroke or TIA, n(%)	24 (11.7)	134 (14.2)	0.642
Smoke(n, %)	95 (46.3)	430 (46.3)	1
Time from onset to hospitalization, h	12.0 (5.00, 26.0)	12.5 (4.00, 31.0)	0.998
Systolic blood pressure on admission, mmHg	150 (136, 170)	146 (132, 162)	0.009*
Diastolic blood pressure on admission, mmHg	89.0 (80.0, 98.0)	87.0 (78.0, 98.0)	0.117
NIHSS on admission	4 (2, 6)	3(2, 4)	< 0.001*

Characteristics	END group (n=205)	non-END group(n=929)	*P*-value
ADL Score	55.0 (35.0, 85.0)	75.0 (55.0, 95.0)	< 0.001*
ASPECT Score	8 (7, 9)	9 (8, 9)	< 0.001*
TOAST classification			0.005*
Large-artery atherosclerosis, n (%)	124(60.5)	385 (41.4)	
Cardioembolic, n (%)	9 (4.4)	25 (2.7)	
Small-artery occlusion,n (%)	67 (32.7)	487 (52.4)	
Other etiology, n (%)	5 (2.4)	27 (3.0)	
Undetermined etiology,n (%)	0 (0)	5 (0.5)	
Treatment Methods			< 0.001*
Medication, n (%)	119 (58.0)	680 (73.2)	
Arterial thrombolysis, n(%)	11 (5.4)	15 (1.6)	
Endovascular thrombectomy, n (%)	58 (28.2)	88 (9.5)	
Intravenous Thrombolysis, n (%)	6 (2.9)	114 (12.3)	
Thrombolysis and Endovascular thrombectomy, n (%)	11 (5.4)	32 (3.4)	
CRP(mg/L)	3.10 (0.70, 8.60)	2.60 (0.30, 6.60)	0.404
White blood cell, 10^9/L	8.28 (6.72, 10.1)	7.88 (6.44, 9.51)	0.154
Platelet, 10^9/L	243 (201, 288)	237 (200, 280)	0.545
Neutrophil, 10^9/L	5.72 (4.39, 7.53)	5.18 (4.02, 6.73)	0.013*
Monocyte, 10^9/L	0.47 (0.35, 0.57)	0.46 (0.36, 0.59)	0.926
Lymphocyte, 10^9/L	1.77 (1.34, 2.13)	1.82 (1.35, 2.34)	0.343

Note: *$P < 0.05$ indicates statistically significant differences.

3.2. LASSO regression for variable selection

All baseline variables were included in the LASSO regression analysis. Six variables associated with END were ultimately selected: BMI, aSBP, ADL Score, ASPECTS, diabetes and treatment methods. The variable selection path plot and cross-validation results are presented in **Figure 1A** and **Figure 1B**, respectively.

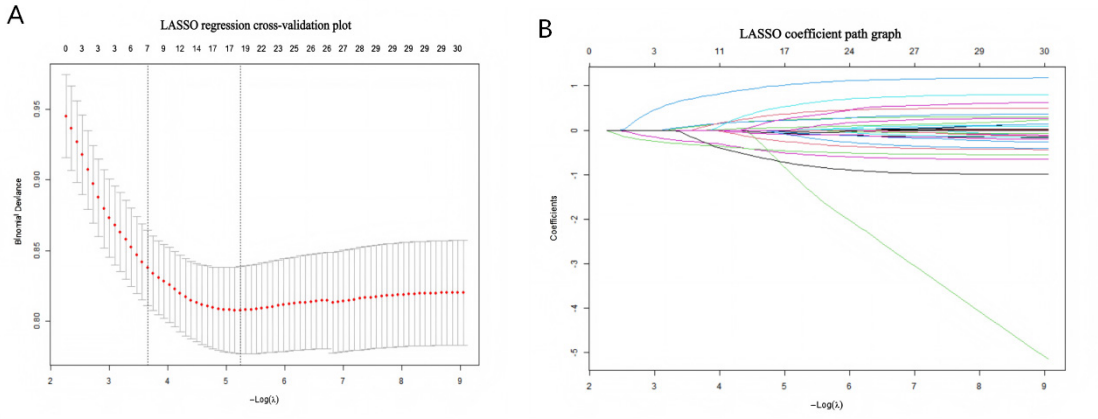

Figure 1. LASSO regression analysis: The variable selection path plot and cross-validation results.

(A) LASSO regression cross-validation plot for screening predictors of END in mild-to-moderate AIS. The y-axis shows binomial deviance, and the x-axis is −log(λ). Vertical dotted lines mark the optimal λ val-

ues based on minimum deviance and 1-SE rules; numbers above the curve represent the count of retained variables at each λ. (

B) LASSO coefficient path plot for predictor selection of END in mild-to-moderate AIS. The x-axis is −log(λ), the y-axis denotes regression coefficients of candidate variables, and each colored line represents the coefficient trajectory of a single predictor across different regularization intensities. Values at the top of the plot indicate the number of variables with non-zero coefficients at each −log(λ) position.

3.3. Multivariate logistic regression analysis

The six variables identified by LASSO were entered into multivariate logistic regression. BMI, aSBP, ADL Score, ASPECTS, diabetes and treatment methods confirmed as independent risk factors for END in patients with mild-to-moderate AIS (all $P < 0.05$). Detailed results are shown in **Table 2**.

Table 2. Multivariate analysis of END in patients with mild-to-moderate acute ischemic strok

Variable	β	SE	Z value	OR	95%CI	*P* value
BMI	0.0793	0.0231	3.4323	1.0826	1.0350-1.1334	< 0.001
Systolic blood pressure on admission	0.0122	0.0035	3.4349	1.0123	1.0053-1.0194	< 0.001
ADL Score	-0.0161	0.0035	-4.5704	0.9840	0.9772-0.9908	< 0.001
ASPECT Score	-0.3589	0.0724	-4.9548	0.6985	0.6052-0.8044	< 0.001
Diabetes	0.4708	0.1849	2.5466	1.6013	1.1108-2.2952	0.01
Medication	1.1338	0.4409	2.5715	3.1075	1.4160-8.2146	0.01
Arterial thrombolysis	2.2045	0.4636	4.7554	9.0658	3.9161-24.8229	< 0.001
Endovascular thrombectomy	1.8770	0.6230	3.0130	6.5340	1.9715-23.2897	0.002
Thrombolysis and Endovascular thrombectomy	1.2183	0.5697	2.1385	3.3816	1.1327-10.9209	0.03

3.4. Construction of the Nomogram

Based on the coefficients derived from multivariate logistic regression, a dynamic nomogram was constructed to predict individual END probability in patients with mild-to-moderate AIS (**Figure 2**). The nomogram is publicly accessible at: https://ycmx1.shinyapps.io/DynNomapp/.

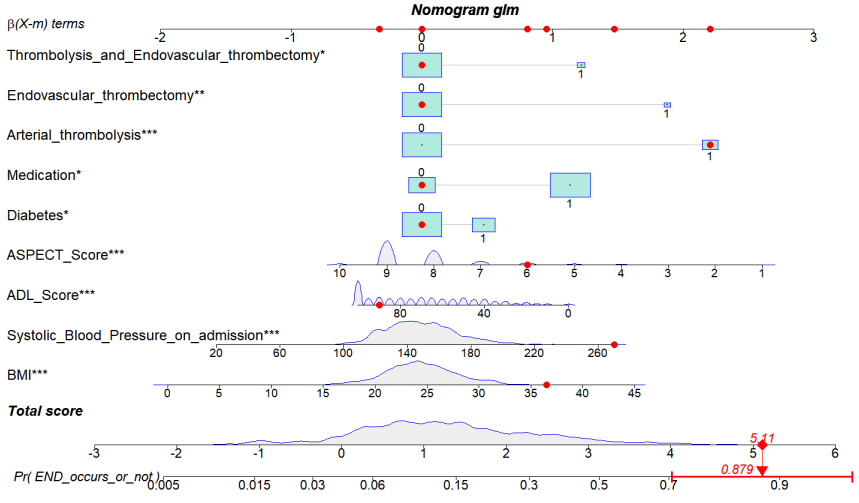

Figure 2. Nomogram for predicting END in patients with mild-to-moderate AIS.

3.5. Model predictive performance

The receiver operating characteristic (ROC) curve (**Figure 3A**) showed that the area under the curve (AUC) of the prediction model was 0.773 (95% CI: 0.738–0.808), indicating good discriminative ability. The calibration curve (**Figure 3B**) showed close agreement between predicted and observed probabilities, confirming satisfactory calibration. Decision curve analysis (DCA) (**Figure 3C**) revealed the net clinical benefit across threshold probabilities of 0–0.4, particularly within 0–0.2, supporting the model's practical decision-making value.

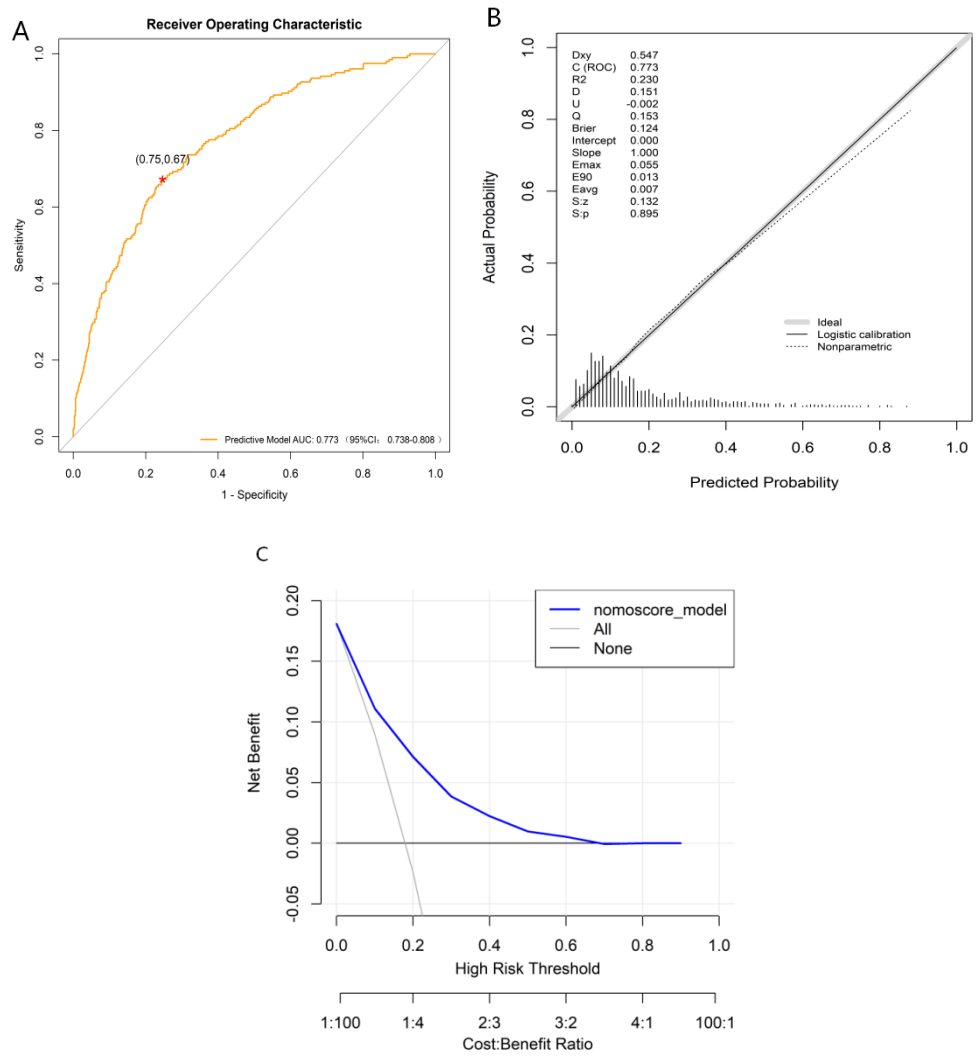

Figure 3. Comprehensive model performance assessment.

(A) ROC curve of the predictive nomogram for early neurological deterioration in mild-to-moderate acute ischemic stroke. The model yielded an AUC of 0.773 (95% CI: 0.738–0.808). The red asterisk indicates the optimal threshold point (specificity = 0.75, sensitivity = 0.67). The diagonal line represents random performance.

(B) Calibration plot for the END prediction nomogram in mild-to-moderate AIS. X-axis: model-predicted probability of early neurological deterioration; Y-axis: observed actual probability. The solid gray line indicates ideal calibration, the solid black line is the logistic calibration fit, and the dotted line is the nonparametric fit.

(C) Decision curve analysis (DCA) for the END predictive nomogram in mild-to-moderate AIS. The x-axis is high-risk threshold probability, the y-axis is net clinical benefit, and the bottom axis displays cost–benefit ratios. The blue curve denotes the nomogram model; the light gray line represents universal intervention for all patients, and the horizontal dark gray line represents no intervention for any patient. The model provides favorable net benefit within a broad threshold range, supporting its clinical application value.

3.6. Model validation

Internal validation was performed using 400 iterations of five-fold cross-validations across seven performance indicators (**Table 3**). The AUC decreased from 0.773 in the training set to 0.760 after validation (ΔAUC = −0.014), indicating stable discriminatory performance. R^2 decreased from 0.230 to 0.192 and the discrimination index from 0.151 to 0.121; both reductions remained within acceptable ranges. The U-test statistic remained close to 0 (post-validation: 0.003) and the Brier score increased marginally from 0.124 to 0.128, confirming high consistency between predicted and observed probabilities. Maximum calibration deviation increased from 0.055 to 0.186 after validation, suggesting some calibration instability at the extremes of the predicted probability distribution; however, overall model performance remained clinically acceptable.

Table 3. Performance metrics of the nomogram model evaluated by 400 iterations of fivefold cross-validation

Indication	Modeling Data Value	Calibrated Value	Δ
AUC/C-index	0.773	0.760	-0.014
R^2	0.230	0.192	-0.039
Discrimination_Index(D)	0.151	0.121	-0.030
U.test	-0.002	0.003	0.006
Brier.Score	0.124	0.128	0.004
Maximum.Deviation	0.055	0.186	0.132
Minimum.Deviation	0.007	0.037	0.030

4. Discussion

In this retrospective cohort of 1, 134 patients with mild-to-moderate acute ischemic stroke (AIS; NIHSS ≤ 15), END occurred in 18.1%, confirming that a substantial fraction of ostensibly low-risk strokes deteriorates in hospital. Using least absolute shrinkage and selection operator (LASSO) regression followed by multivariable logistic modeling, we identified six admission-available predictors—body mass index (BMI), admission aSBP, diabetes, ADL score, the ASPECTS, and treatment methods—and combined them into a dynamic, openly accessible nomogram with acceptable and internally stable discrimination (AUC 0.773) and favorable net clinical benefit. The tool addresses a population for which dedicated risk-stratification instruments have been lacking.

Five of these predictors are mechanistically coherent and concordant with prior work. Higher BMI (odds ratio [OR] 1.08 per unit) reflects obesity-related insulin resistance [13] and a prothrombotic, pro-inflammatory state [14], consistent with its established role in ischemic-stroke burden [15]. Elevated aSBP (OR 1.01 per mmHg) acts on impaired cerebral autoregulation and a vulnerable blood–brain barrier, echoing Cui et al. in non-reperfused mild-to-moderate AIS [16]. Diabetes (OR 1.60) impairs vasoreactivity and shifts the coagulation–fibrinolysis balance [17,18], reproducing the associations reported by Dávalos et al. and Tanaka et al. [19,20].

Lower ADL (OR 0.98 per point) marks diminished premorbid reserve, and lower ASPECTS (OR 0.70 per point) a larger ischemic core [21]—both narrowing the clinical margin before deterioration becomes manifest.

The treatment-modality result is counterintuitive: relative to intravenous thrombolysis, medication alone (OR 3.11), intra-arterial thrombolysis (OR 9.07), endovascular thrombectomy (OR 6.53), and bridging therapy (OR 3.38) all carried higher END odds. This should not be read causally. END incidence rose from 5.0% with intravenous thrombolysis to 39.7–42.3% with thrombectomy and intra-arterial thrombolysis, tracking the higher large-artery-atherosclerosis burden (60.5% vs 41.4%) and admission NIHSS of the END group—i.e., confounding by indication, in which modality encodes residual occlusion severity not captured by the other covariates. The pattern accords with the known propensity of mild-presenting large-vessel occlusions managed without timely reperfusion to deteriorate [6]. The variable remains useful for admission-time prediction but is not a causal target.

On 400-iteration five-fold cross-validation, discrimination was stable (ΔAUC −0.014) while calibration drifted at the probability extremes (maximum deviation 0.055 → 0.186), so predictions are most reliable in the mid-range. Decision-curve net benefit spanned threshold probabilities of approximately 0–0.4 (clearest within 0–0.2), matching a low-cost screening application. Unlike prior END models derived from severity-heterogeneous or large-vessel-occlusion–weighted cohorts, this instrument is purpose-built for NIHSS ≤ 15, uses only admission variables, and is deployed as an interactive web nomogram—its principal novelty.

Several limitations apply. The single-center, retrospective design lacks external validation; the treatment-modality association is subject to confounding by indication; the 6.5-year enrollment window spans evolving reperfusion practice; and our END definition (a ≥ 2-point NIHSS rise within seven days) is broader than the 24- to 72-hour or ≥ 4-point thresholds used elsewhere, limiting cross-study comparability. Calibration was also less stable at the probability extremes, and the model omits biomarkers and dynamic imaging (collateral status, perfusion mismatch, serial NIHSS), with missing data handled by multiple imputation and inter-rater agreement of clinical scores not formally quantified.

5. Conclusion

In conclusion, BMI, admission systolic blood pressure, diabetes, ADL score, ASPECTS, and treatment methods were independently associated with END in mild-to-moderate AIS, and an admission-based dynamic nomogram built on them achieved acceptable, stable discrimination. Pending prospective multicenter external validation—and the incorporation of biological and imaging markers to sharpen performance at the risk extremes—the tool offers a practical means of flagging, at the point of admission, the “low-risk” strokes that in fact merit heightened vigilance.

Disclosure statement

The authors declare no conflict of interest.

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