

Original Article

Tenecteplase combined with nicergoline improves neurological, endothelial function and short-term prognosis in AACI patients

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Received May 12, 2026; Accepted June 25, 2026; Epub September 15, 2026; Published September 30, 2026

Abstract: Objective: To explore the efficacy of tenecteplase combined with nicergoline in acute atherosclerotic cerebral infarction (AACI), and screen risk indicators for poor prognosis. Methods: A total of 368 AACI patients were enrolled and randomly allocated into a training set (n=258) and a validation set (n=110) at a 7:3 ratio. Each set was subdivided into control group (tenecteplase thrombolysis + basic treatment) and combination group (additional oral nicergoline for 14 days). National Institutes of Health Stroke Scale (NIHSS), Barthel Index (BI), serum nitric oxide (NO), and endothelin-1 (ET-1) were measured before and after treatment. Patients were followed up for 3 months to record mRS, prognosis and adverse events. Independent risk factors were screened by multivariate logistic regression, a nomogram was constructed, and its predictive efficiency was evaluated by receiver operating characteristic (ROC) curve analysis. Results: No significant baseline differences were observed between the two treatment groups within the training set ($P>0.05$). After treatment, in the training set, the combination group had lower NIHSS score, ET-1 level, 3-month poor prognosis rate, mRS score and adverse event incidence, with higher BI and NO levels than the control group (all $P<0.05$). An NIHSS ≥ 3.5 , BI < 76.5 , ET-1 ≥ 57.34 ng/L and NO < 49.29 $\mu\text{mol/L}$ were identified as independent risk factors for poor prognosis. The nomogram demonstrated good calibration in both cohorts. ROC curve analysis showed that the combined model incorporating all 4 indicators had superior predictive performance compared with any single index in both cohorts. Conclusion: Tenecteplase combined with nicergoline can improve neurological and vascular endothelial function, reduce adverse events, and improve short-term prognosis of AACI patients. The 4 indicators are independent predictors for poor prognosis, with better efficiency in combined detection.

Keywords: Tenecteplase, nicergoline, acute atherosclerotic cerebral infarction, neurological function, vascular endothelial function

Introduction

Acute cerebral infarction is a prevalent acute cerebrovascular disorder and the leading cause of cerebrovascular-related disability and mortality among Chinese adults [1]. As a frequent subtype, acute atherosclerotic cerebral infarction (AACI) is characterized by cerebral arterial stenosis or occlusion followed by brain tissue hypoxic-ischemic necrosis, which severely impairs patient prognosis [2]. Intravenous thrombolysis serves as the first-line intervention within 4.5 hours of symptom onset, as prompt reperfusion can salvage vulnerable ischemic

penumbral tissue [3, 4]. Tenecteplase, a third-generation recombinant tissue plasminogen activator, exhibits superior fibrin selectivity, longer half-life, convenient dosing, and fewer hemorrhagic complications than conventional alteplase [5]. Nonetheless, standalone thrombolysis merely recanalizes obstructed vessels and fails to suppress subsequent pathological cascades including ischemia-reperfusion injury, endothelial dysfunction and microcirculatory disturbance. Many patients still suffer unsatisfactory neurological recovery despite successful vascular recanalization [6]. Accordingly, targeted adjunctive medications alongside stand-

ard thrombolysis are required to alleviate vascular injury and optimize neurological prognosis.

Vascular endothelial dysfunction is central to the initiation and progression of atherosclerosis. Abnormal expression of nitric oxide (NO) and endothelin-1 (ET-1) exacerbates vasospasm and microcirculatory disorders, ultimately aggravating cerebral damage [7, 8]. Inflammation also contributes significantly to atherosclerotic plaque rupture and post-infarction ischemia-reperfusion injury, with elevated C-reactive protein (CRP) closely correlating with disease severity [9]. As a semisynthetic ergot alkaloid derivative, nicergoline improves cerebral perfusion, nourishes neurons, regulates endothelial function and suppresses inflammation, rendering it a promising adjunct agent for cerebrovascular disorders [10, 11]. Numerous clinical trials have explored monotherapy with tenecteplase, yet relevant clinical evidence remains scarce regarding the efficacy of tenecteplase combined with nicergoline in ameliorating neurological and endothelial function as well as predicting prognosis among AACI patients.

Accordingly, this study enrolled patients with AACI to explore the clinical value of combination therapy with tenecteplase and nicergoline, analyze the correlation between detected indexes and neurological recovery, and evaluate their predictive performance for poor prognosis, so as to provide evidence for individualized clinical management.

Methods

Study subjects

A total of 368 inpatients with TOAST-defined large-artery atherosclerotic cerebral infarction who were treated at our center from March 2022 to March 2025 were enrolled. Patients were randomly allocated into a training set (n=258) and a validation set (n=110) at a 7:3 ratio. The training set was further divided into a control group (n=148) and a combination group (n=110) according to therapeutic schedules, and the validation set was split into 60 control cases and 50 combination cases correspondingly. This study was approved by the institutional ethics committee of Yulin Hospital of Traditional Chinese Medicine.

Inclusion criteria: Patients were classified as large-artery atherosclerotic stroke following TOAST criteria; intracranial hemorrhage was ruled out by cranial CT/MRI, and cervical or intracranial CTA/MRA confirmed $\geq 50\%$ luminal stenosis of the relevant large arteries; patients with other TOAST subtypes, including cardioembolic, small-vessel, and undetermined-cause stroke, were excluded; the interval from symptom onset to thrombolysis was within 4.5 hours, satisfying the indication for intravenous thrombolysis; complete clinical data were available and 3-month follow-up could be accomplished.

Exclusion criteria: Pre-existing intracranial hemorrhage, coagulation disorders or any contraindication to thrombolysis; severe dysfunction of the heart, liver, kidney and other vital organs; previous cerebral infarction with residual severe neurological deficits; confirmed allergy to tenecteplase or nicergoline; patients lost to follow-up or dying from unrelated causes during follow-up.

Treatment regimens

All patients received routine basic treatment for acute cerebral infarction, including blood pressure, blood glucose and lipid control, antiplatelet and neuroprotective therapy, as well as fluid and electrolyte balance maintenance. Besides the above management, the control group was administered tenecteplase at 0.25 mg/kg, capped at a maximum single dose of 25 mg via intravenous bolus over 5-10 seconds. The combination group took the same thrombolytic regimen plus oral nicergoline 20 mg twice daily. All patients started thrombolysis within 4.5 hours after stroke onset, with a total treatment period of 14 days.

Observation indicators

Primary indicators: (1) Prognostic indicators: The modified Rankin Scale (mRS) scores of all patients were recorded during the 3-month follow-up, and the prognostic outcomes were evaluated. An mRS score ≤ 2 was defined as a good prognosis, while an mRS score > 2 was defined as a poor prognosis.

(2) Adverse reactions: The occurrence of adverse reactions in both groups during treatment was collected, and the incidence of adverse reactions was calculated, including

bleeding, dizziness, nausea and abnormal liver function.

Secondary indicators: (1) Baseline data: Baseline data of patients in both groups were collected, including gender, age, body mass index (BMI), time from symptom onset to thrombolysis, underlying diseases (hypertension, type 2 diabetes mellitus, hyperlipidemia, coronary heart disease) and infarction site.

(2) Neurological function and activities of daily living: The National Institutes of Health Stroke Scale (NIHSS) scores and Barthel Index (BI) scores of patients in both groups were collected before treatment and at 3 months after treatment. The NIHSS was used to assess the degree of neurological deficit, with higher scores indicating more severe deficits; the Barthel Index was applied to evaluate patients' activities of daily living, with higher scores representing better functional ability.

(3) Vascular endothelial function indicators: Serum levels of vascular endothelial function indicators (NO and ET-1) were measured before treatment and at 14 days after treatment. Fasting peripheral venous blood samples were collected, and the concentrations of NO and ET-1 were determined using enzyme-linked immunosorbent assay (ELISA).

Statistical analysis

All statistical analyses were performed using SPSS 26.0. Normally distributed measurement data were expressed as mean $\pm$ standard deviation (SD) and compared using the independent-samples t-test; ordinal data were presented as median (interquartile range) [M (P_{25} , P_{75})], with intergroup comparisons performed using the Mann-Whitney U test. Categorical data were expressed as case number (percentage) [n (%)] and compared using the χ^2 test. Multivariate logistic regression was used to screen independent risk factors for poor prognosis. A nomogram was developed, and receiver operating characteristic (ROC) curve analysis was performed to calculate the area under the curve (AUC), sensitivity and specificity for model performance assessment. The training set (n=258) was used for intergroup efficacy comparison and model establishment, while the validation set (n=110) was only applied to externally validate the nomogram and ROC rather

than plotted for efficacy indicators; all relevant efficacy data of the validation set were fully described in the results section to prevent selective reporting. A two-tailed P value <0.05 was defined as statistically significant.

Results

Baseline data of the training set and validation set

As shown in **Table 1**, there were no significant differences between the training and validation sets in age, sex, onset-to-thrombolysis time, BMI, hypertension, T2DM, hyperlipidemia, coronary heart disease, or infarct location (all $P>0.05$).

Baseline data of both groups

Similarly, in the training set, there were no significant differences between the combination and control groups in age, sex, onset-to-thrombolysis time, BMI, hypertension, T2DM, hyperlipidemia, coronary heart disease, or infarct location (all $P>0.05$). Shown in **Table 2**.

Neurological function and activities of daily living in both groups

There were no significant differences in NIHSS (**Figure 1A**) or BI (**Figure 1B**) between the two groups before treatment ($P>0.05$). After treatment, NIHSS scores decreased and the BI scores increased in both groups; however, the combination group had significantly lower significantly lower NIHSS scores and higher BI scores than the control group (both $P<0.001$).

Vascular endothelial function indicators in both groups

There were no significant differences in ET-1 (**Figure 2A**) or NO (**Figure 2B**) between the two groups before treatment ($P>0.05$). After treatment, ET-1 levels decreased and NO levels increased in both groups; however, the combination group had significantly lower ET-1 levels and significantly higher NO levels than the control group ($P<0.001$).

mRS scores and prognostic outcomes of both groups

As shown in **Table 3**, all 368 patients were followed up for 3 months. The results showed that the poor prognosis rate of the combination

Table 1. Comparison of baseline data between the training and validation sets [n (%), $\bar{x} \pm s$]

	Training set (n=258)	Validation set (n=110)	t/χ^2	P
Age (yr)	58.55 $\pm$ 3.59	58.57 $\pm$ 3.35	0.050	0.960
Gender			1.581	0.209
Male	148 (57.4)	55 (50.0)		
Female	110 (42.6)	55 (50.0)		
Time from onset to thrombolysis (h)	2.80 $\pm$ 0.31	2.84 $\pm$ 0.34	1.100	0.272
BMI (kg/m ²)	22.58 $\pm$ 2.0	22.53 $\pm$ 1.77	0.227	0.821
Hypertension			0.847	0.357
Yes	190 (73.6)	86 (78.2)		
No	68 (26.4)	24 (21.8)		
Type 2 diabetes mellitus			0.037	0.848
Yes	80 (31.0)	33 (30.0)		
No	178 (69.0)	77 (70.0)		
Hyperlipidemia			0.590	0.442
Yes	146 (56.6)	67 (60.9)		
No	112 (43.4)	43 (39.1)		
Hyperlipidemia			0.200	0.655
Yes	51 (19.8)	24 (21.8)		
No	207 (80.2)	86 (78.2)		
Infarction site			0.467	0.494
Anterior circulation	203 (78.7)	90 (81.8)		
Posterior circulation	55 (21.3)	20 (18.2)		

Notes: BMI: body mass index.

Table 2. Comparison of baseline data between the combination and control groups [n (%), $\bar{x} \pm s$]

	Combination group (n=110)	Control group (n=148)	t/χ^2	P
Age (yr)	58.64 $\pm$ 4.04	58.58 $\pm$ 3.29	0.131	0.896
Gender			0.985	0.321
Male	67 (60.9)	81 (54.7)		
Female	43 (39.1)	67 (45.3)		
Time from onset to thrombolysis (h)	2.79 $\pm$ 0.32	2.80 $\pm$ 0.29	0.262	0.794
BMI (kg/m ²)	22.57 $\pm$ 1.99	22.59 $\pm$ 1.82	0.084	0.933
Hypertension			0.731	0.393
Yes	84 (76.4)	106 (71.6)		
No	26 (23.6)	42 (28.4)		
Type 2 diabetes mellitus			0.719	0.398
Yes	31 (28.2)	49 (33.1)		
No	79 (71.8)	99 (66.9)		
Hyperlipidemia			0.152	0.657
Yes	65 (59.1)	91 (61.5)		
No	45 (40.9)	57 (38.5)		
Hyperlipidemia			0.753	0.386
Yes	19 (17.3)	32 (21.6)		
No	91 (82.7)	116 (78.4)		
Infarction site			0.567	0.452
Anterior circulation	89 (80.9)	114 (77.0)		
Posterior circulation	21 (19.1)	34 (23.0)		

Notes: BMI: body mass index.

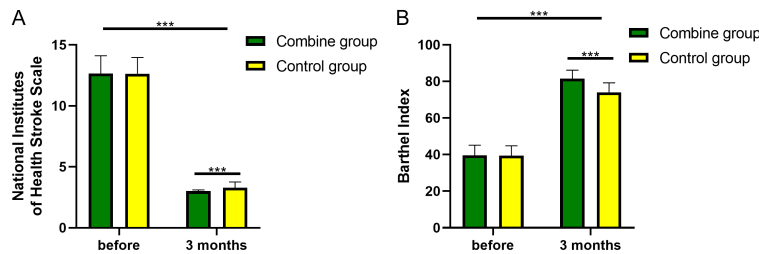


Figure 1. Comparison of neurological deficit and activities of daily living between the two groups before and after treatment. A. Changes in NIHSS scores before treatment and 3 months after treatment; B. Changes in BI scores before treatment and 3 months after treatment. Notes: *** $P < 0.001$ vs. the same group before treatment. NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index.

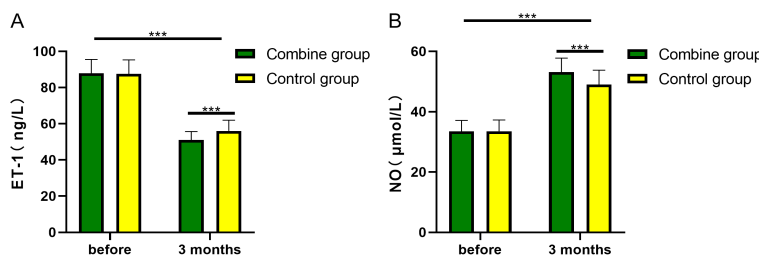


Figure 2. Comparison of vascular endothelial function indexes between the two groups before and after treatment. A. Changes in ET-1 levels before treatment and 14 days after treatment; B. Changes in NO levels before treatment and 14 days after treatment. Notes: *** $P < 0.001$ vs. the same group before treatment. NO: nitric oxide; ET-1: endothelin-1.

Table 3. Comparison of mRS scores and prognostic outcomes between the combination and control groups

	Combination group (n=110)	Control group (n=148)	t/χ^2	P
mRS	2.0 (2.0, 2.5)	3.0 (2.5, 3.0)	5.962	<0.001
Prognosis			6.384	0.012
Good prognosis	91 (82.7)	102 (68.9)		
Poor prognosis	19 (17.3)	46 (31.1)		

Notes: mRS: modified Rankin Scale.

group was 17.3% (19/110), significantly lower than 31.1% (46/148) in the control group ($P = 0.012$), and mRS score was significantly lower than that of control group ($P < 0.001$).

Incidence of adverse reactions in both groups

As shown in **Table 4**, within 3 months of treatment, the incidence of adverse reactions in the combination group was 8.2% (9/110), significantly lower than 18.2% (27/148) in control group ($P = 0.021$).

Univariate analysis of factors influencing patient prognosis

As shown in **Table 5**, there were no significant differences between the poor prognosis group and the favorable prognosis group in age, sex, onset-to-thrombolysis time, BMI, hypertension, T2DM, hyperlipidemia, coronary heart disease, or infarct location ($P > 0.05$). However, the poor prognosis group had significantly higher NIHSS score and ET-1 level at 3 months after treatment, and significantly lower BI scores and NO levels at 3 months after treatment (all $P < 0.001$).

Multivariate logistic regression analysis of factors influencing patient prognosis

Variables that showed significant differences in univariate analysis were selected for further analysis, and cutoff values for NIHSS, BI, ET-1 and NO were determined (**Table 6**). Multivariate logistic regression analysis (**Table 7**) showed that NIHSS ≥ 3.5 , BI < 76.5 , ET-1 ≥ 57.34 ng/L, and NO < 49.29 μmol/L were independent risk factors for poor prognosis.

Nomogram analysis of both sets

Nomogram analysis of the training set indicated that NIHSS was the strongest indicator, contributing most significant to risk prediction, NO was the second most significant correlated indicator, while BI and ET-1 had relatively weaker contributions (**Figure 3A**). The slope of the calibration curve was close to 1, indicating good diagnostic efficacy of the model (**Figure 3B**). Nomogram analysis of the validation set confirmed the above results: NIHSS was the most significant indicator, NO was the second most significant one, and BI and ET-1 had minor contributions to risk prediction (**Figure 3C**). In addition, the slope of

Table 4. Comparison of incidence of adverse reactions between the combination and control groups [n (%)]

Group	n	Bleeding	Dizziness	Nausea	Abnormal liver function	Incidence of adverse reactions
Combination group	110	1 (0.9)	2 (1.8)	5 (4.5)	1 (0.9)	9 (8.2)
Control group	148	9 (6.1)	8 (5.4)	8 (5.4)	2 (1.4)	27 (18.2)
χ^2						5.320
<i>P</i>						0.021

Table 5. Univariate analysis of risk factors for poor prognosis in AACI patients [n (%), $\bar{x} \pm s$]

	Poor prognosis group (n=65)	Good prognosis group (n=193)	<i>t</i> / χ^2	<i>P</i>
Age (yr)	58.54±3.50	58.55±3.62	0.019	0.985
Gender			0.440	0.507
Male	35 (53.8)	113 (58.5)		
Female	30 (46.2)	80 (41.5)		
Time from onset to thrombolysis (h)	2.84±0.28	2.79±0.32	1.123	0.263
BMI (kg/m ²)	22.58±1.98	22.51±2.01	0.244	0.808
Hypertension			0.482	0.488
Yes	50 (76.9)	140 (72.5)		
No	15 (23.1)	53 (27.5)		
Type 2 diabetes mellitus			0.069	0.793
Yes	21 (32.3)	59 (30.6)		
No	44 (67.7)	134 (69.4)		
Hyperlipidemia			0.456	0.500
Yes	37 (56.9)	119 (61.7)		
No	28 (43.1)	74 (38.3)		
Hyperlipidemia			0.172	0.679
Yes	14 (21.5)	37 (19.2)		
No	51 (78.5)	156 (80.8)		
Infarction site			0.160	0.689
Anterior circulation	50 (76.9)	153 (79.3)		
Posterior circulation	15 (23.1)	40 (20.7)		
3 months NIHSS	3.52±0.50	3.06±0.23	10.035	<0.001
3 months BI	72.58±5.20	78.81±5.63	7.862	<0.001
3 months ET-1 (ng/L)	58.46±5.71	52.33±5.22	7.995	<0.001
3 months NO (μmol/L)	46.78±4.23	52.11±4.68	8.130	<0.001

Notes: BMI: body mass index; NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.

the calibration curve of the validation set was also close to 1, which further verified the favorable diagnostic efficacy of the model (**Figure 3D**).

ROC curve analysis of both sets

The results of ROC curve analysis are presented in **Table 8** and **Figure 4**. ROC curve analysis of TS (**Figure 4A**) showed that NIHSS, BI, ET-1

and NO exhibited favorable diagnostic efficacy for prognosis, and the combined detection of these indicators exhibited superior diagnostic efficacy to any single indicator alone. The results of the validation set (**Figure 4B**) were consistent with those of training set: each of the four indicators had good prognostic diagnostic efficacy, and the combined detection achieved better diagnostic performance than single indicator detection.

Table 6. Assignment table

Influencing Factors	Assignment
Prognostic outcome (Y)	0: Good prognosis 1: Poor prognosis
NIHSS (X1)	0: <3.5 1: ≥3.5
BI (X2)	0: ≥76.5 1: <76.5
ET-1 (X3)	0: <57.34 ng/L 1: ≥57.34 ng/L
NO (X4)	0: ≥49.29 μmol/L 1: <49.29 μmol/L

Notes: NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.

Discussion

AACI is caused by cerebral atherosclerotic stenosis or occlusion that leads to ischemic cerebral necrosis, and represents a major cause of stroke-associated disability and mortality [12]. Clinically, tenecteplase is widely adopted for thrombolysis due to its high fibrin selectivity, prolonged half-life, simple administration and relatively low hemorrhagic risk [13, 14]. Nevertheless, tenecteplase monotherapy only recanalizes occluded vessels and cannot prevent subsequent pathological changes such as ischemia-reperfusion injury, endothelial impairment, and microcirculatory dysfunction [15]. Our retrospective analysis of AACI subjects revealed that combined treatment with tenecteplase and nicergoline significantly improved neurological and endothelial function, decreased adverse event rates and ameliorated patient prognosis. Higher NIHSS scores, lower BI values, elevated ET-1 and reduced NO levels were confirmed as independent risk factors for poor clinical outcomes.

The present results are in line with previous research from Warach et al. [16] and Hu et al. [17], showing that combination treatment facilitates neurological recovery and improves patients' activities of daily living. Mechanistically, tenecteplase induces vascular recanalization and rapid cerebral reperfusion to lay a foundation for neurological recovery [18]. Nicergoline dilates cerebral vasculature, thereby boosting perfusion and endothelial metabolism. It also accelerates NO production, suppresses ET-1 expression, restores endothelial homeostasis, and relieves vasospasm, collectively reducing

secondary cerebral injury [19]. Furthermore, its anti-inflammatory effect alleviates ischemia-reperfusion-triggered inflammation and protects vascular endothelium as well as neurons, supporting neural repair from multiple pathways and improving long-term functional recovery [20]. The synergistic effect of tenecteplase's revascularization and nicergoline's microcirculation-regulating and neuroprotective effects yields more remarkable improvements in neurological function and daily performance.

Endothelial dysfunction is a crucial pathological driver of neurological deficits, impaired daily living and adverse clinical outcomes [21, 22]. As an endogenous vasodilator with antiplatelet activity, NO antagonizes the potent vasoconstrictive effect of ET-1. Imbalanced secretion of the two mediators worsens vasospasm and microcirculatory disturbance, further exacerbating cerebral ischemic damage [23, 24]. Our findings confirm that combined therapy reinforces endothelial protection and improves neurological function. Mechanistically, tenecteplase restores cerebral perfusion to relieve persistent ischemic injury to endothelial cells [25]. Nicergoline directly acts on endothelial cells, upregulates endothelial nitric oxide synthase to stimulate NO synthesis and inhibit ET-1 release, thus alleviating vasospasm, correcting microcirculation and reducing secondary brain damage [26]. Compared with monotherapy, the combined strategy achieves vascular recanalization while preserving endothelial structure and function.

Three-month follow-up revealed lower mRS scores, a lower rate of poorer prognosis, and a lower incidence of adverse events in the combination group compared with the control group, consistent with findings reported by Huo et al. [27]. These data indicate that adjunct nicergoline improves clinical outcomes and enhances treatment safety following tenecteplase thrombolysis. Mechanistically, ischemia-reperfusion after cerebral infarction disrupts blood-brain barrier (BBB) integrity and represents a key contributor to post-thrombolytic intracranial hemorrhage. Nicergoline stabilizes BBB structure by optimizing cerebral microcirculation and alleviating endothelial edema, thereby limiting extravasation of plasma and thrombolytic agents. High-dose tenecteplase tends to induce excessive systemic fibrinolysis and raise

Table 7. Multivariate logistic regression analysis of independent risk factors for poor prognosis in AACI patients

Influencing Factors	β	Std. Error	Wald χ^2	P	OR	95% CI	
						Lower	Upper
NIHSS ≥ 3.5	1.854	0.462	16.131	0.000	6.383	2.583	15.771
BI < 76.5	1.053	0.402	6.851	0.009	2.866	1.303	6.305
ET-1 ≥ 57.34 ng/L	0.966	0.412	5.489	0.019	2.627	1.171	5.895
NO < 49.29 μ mol/L	1.144	0.400	8.189	0.004	3.140	1.434	6.874

Notes: NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.

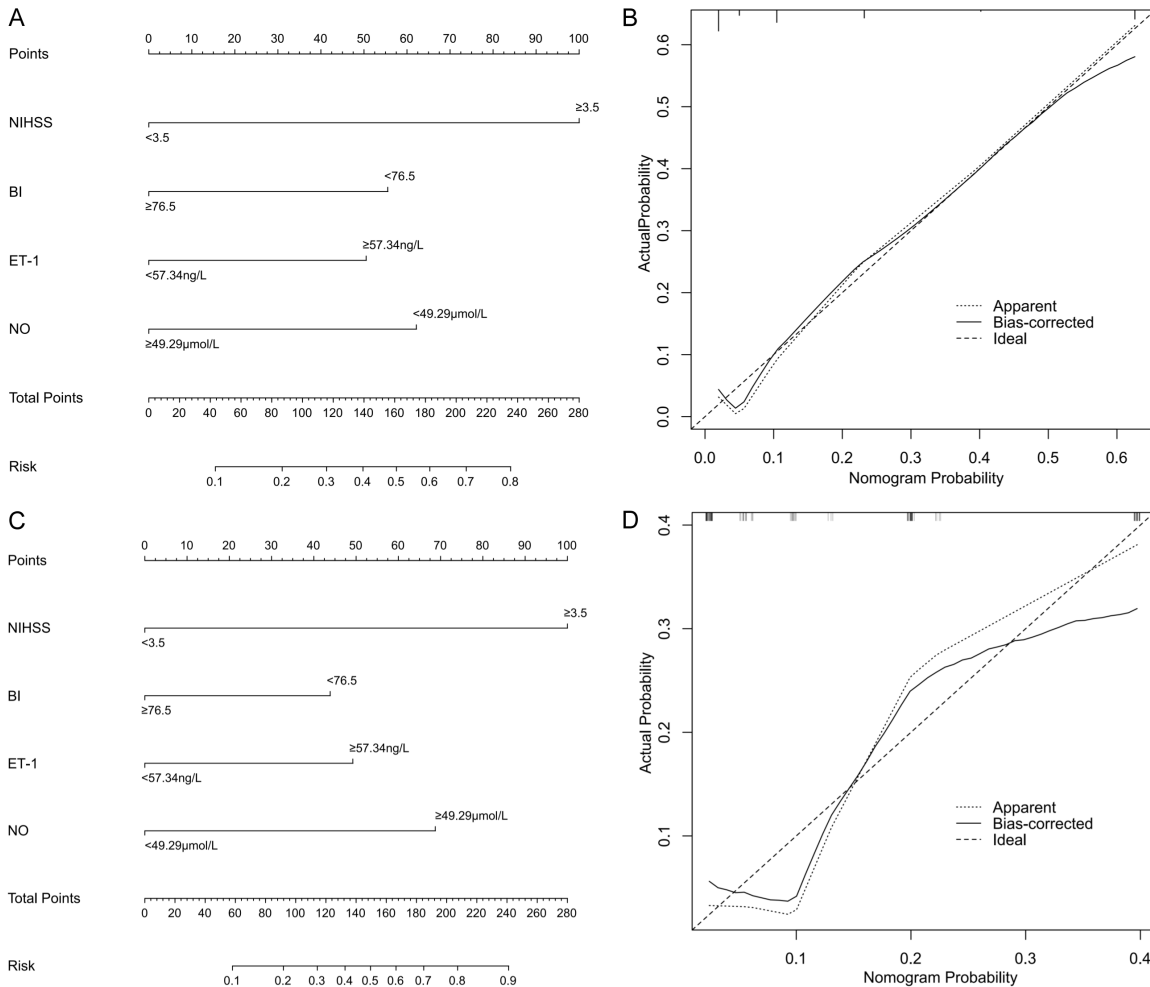


Figure 3. Construction and prognostic performance evaluation of the nomogram model. A. Nomogram in the training set; B. Calibration curve for the Nomogram in the training set; C. Nomogram in the validation set; D. Calibration curve for the Nomogram in the validation set. Notes: NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.

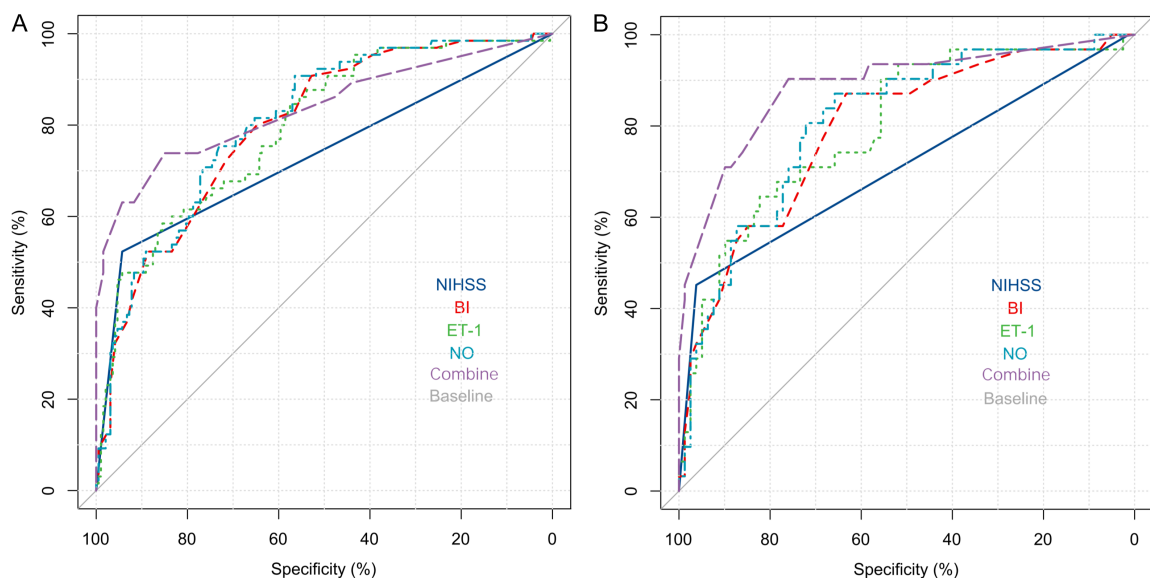
bleeding risk, whereas nicergoline modulates excessive fibrinolytic activity, thereby maintaining coagulation-fibrinolysis homeostasis and preventing microvascular bleeding. In addition, post-ischemic inflammatory infiltration destroys small vessel walls; nicergoline mitigates inflam-

matory vascular damage and reduces microvascular rupture risk via anti-inflammatory properties [28, 29]. Such multi-target synergies collectively lead to a markedly lower bleeding incidence in patients receiving combination therapy.

Table 8. ROC curve analysis of risk factors for predicting poor prognosis in AACI patients

Group	Factor	AUC	P	95% CI	Sensitivity	Specificity	Youden index	Cut-off value
Training set	NIHSS	0.733	<0.001	0.653-0.813	0.523	0.943	0.466	3.5
	BI	0.798	<0.001	0.732-0.858	0.648	0.800	0.448	76.5
	ET-1	0.795	<0.001	0.732-0.857	0.585	0.855	0.440	57.34 ng/L
	NO	0.807	<0.001	0.749-0.866	0.731	0.754	0.485	49.29 μ mol/L
	Combine	0.836	<0.001	0.770-0.902	0.738	0.85	0.588	-
Validation set	NIHSS	0.710	<0.001	0.590-0.830	0.452	0.962	0.414	3.5
	BI	0.794	<0.001	0.700-0.888	0.633	0.871	0.504	76.5
	ET-1	0.797	<0.001	0.703-0.890	0.645	0.823	0.468	57.34 ng/L
	NO	0.810	<0.001	0.721-0.899	0.658	0.871	0.529	49.29 μ mol/L
	Combine	0.886	<0.001	0.810-0.963	0.903	0.759	0.662	-

Notes: NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.


Figure 4. ROC curves predicting prognosis. A. Training set. B. Validation set. Notes: NIHSS: National Institutes of Health Stroke Scale; BI: Barthel Index; NO: nitric oxide; ET-1: endothelin-1.

Multivariate logistic regression identified NIHSS ≥ 3.5 , BI < 76.5 , ET-1 ≥ 57.34 ng/L and NO < 49.29 μ mol/L as independent risk factors for unfavorable prognosis among AACI patients. The established nomogram demonstrated that NIHSS contributed most strongly to prognostic prediction. ROC analysis demonstrated that each biomarker possessed acceptable predictive ability, and the combined panel yielded significantly better predictive efficiency than individual indicators. Elevated NIHSS denotes severe cerebral ischemic injury and hinders neurological restoration, increasing the risk of poor outcomes [30]. Decreased BI manifests severe neurological and physical impairment that obstructs rehabilitation and

adversely affects long-term prognosis [30]. Abnormal ET-1 and NO concentrations reflect unresolved endothelial damage and persistent microcirculatory disturbance, restricting cerebral perfusion and tissue repair [31, 32]. Combined detection of these four parameters therefore improves prognostic accuracy.

Several limitations of the present study should be noted. First, this single-center retrospective design may be subject to inherent selection bias. Second, follow-up was restricted to 3 months; long-term patient outcomes were not monitored, precluding evaluation of the regimen's sustained efficacy. Third, dosage-related effects were not investigated, hence the opti-

mal nicergoline dosage remains to be determined. Future multi-center, large-sample prospective randomized controlled trials are required to validate our findings and explore different drug dosages. Additional biomarkers including inflammatory and coagulation markers should also be incorporated to refine the prognostic model and facilitate evidence-based clinical management of AACI.

Conclusion

Tenecteplase combined with nicergoline offers prominent clinical benefits for AACI patients. The combination effectively improves neurological and endothelial function, lowers adverse event rates and elevates the 3-month favorable prognosis rate, representing a safe and feasible therapeutic option. NIHSS, BI, ET-1 and NO are independent predictors of unfavorable outcomes, and their combined measurement outperforms single indicators to guide clinical risk stratification and individualized treatment.

Disclosure of conflict of interest

None.

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