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Association between the triglyceride-glucose index and poor prognosis in patients undergoing endovascular therapy across glucose metabolic status groups

wei deng
China-Japan Union Hospital of Jilin University
Zhengqiao Bao
Xiangyang No.1 People's Hospital, Hubei University of Medicine
Jun Han
Xiangyang No.1 People's Hospital, Hubei University of Medicine
Peiyang Zhou
Xiangyang No.1 People's Hospital, Hubei University of Medicine
Guangxian Nan
China-Japan Union Hospital of Jilin University
Yanli Sun
sunyl3312@163.com
Xiangyang No.1 People's Hospital, Hubei University of Medicine

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Abstract

Background

This study aimed to investigate the association between the triglyceride-glucose (TyG) index and poor prognosis in acute ischemic stroke (AIS) patients undergoing endovascular therapy (EVT), and to further evaluate this association across glucose metabolic status groups.

Methods

This multicenter retrospective cohort study included AIS patients who underwent EVT between September 2018 and January 2024. Patients were categorized into tertiles according to the TyG index: T1 (TyG ≤ 8.51), T2 (8.51 < TyG ≤ 9.20), and T3 (TyG > 9.20). Glucose metabolic status was classified as normal glucose regulation (NGR), prediabetes mellitus (Pre-DM), or diabetes mellitus (DM). The primary outcome was poor prognosis, defined as a modified Rankin Scale (mRS) score ≥ 3 at 90 days.

Results

Among 789 patients included in the final analysis, 438 (55.5%) had poor prognosis at 90 days. The TyG index was independently associated with poor prognosis in the overall cohort, both as a continuous variable (OR = 1.65; 95% CI 1.32–2.07; *P* < 0.001) and when comparing the T3 group with the T1 group (OR = 2.04; 95% CI 1.36–3.05; *P* = 0.001). In analyses stratified by glucose metabolic status, the association was significant in the NGR and DM groups, but not in the Pre-DM group; the highest proportion of poor prognosis was observed in the DM group (266/417, 63.8%). Glucose metabolic status did not significantly modify this association. Restricted cubic spline analysis showed a positive linear association between the TyG index and poor prognosis in the overall cohort. Adding the TyG index to the basic clinical model modestly improved prognostic discrimination and risk reclassification.

Conclusion

The TyG index was independently associated with 90-day poor prognosis after EVT, and this association was not significantly modified by glucose metabolic status, although patients with DM had the highest proportion of poor prognosis. Further validation in larger cohorts is warranted.

Introduction

Stroke remains one of the leading causes of death and long-term disability worldwide, and acute ischemic stroke (AIS) accounts for nearly 85% of all stroke cases [1, 2]. Among patients with AIS, large vessel occlusion (LVO) represents a particularly severe subtype and is responsible for a substantial proportion of disease burden [3]. Since the pivotal randomized trials published in 2015, endovascular therapy (EVT) has become the standard of care for eligible patients with LVO [4–8]. Nevertheless, improved devices, workflow optimization, and higher rates of successful reperfusion have not fully translated into favorable functional outcomes, and a considerable

proportion of patients remain disabled after EVT [9]. Identifying simple metabolic markers that can be obtained early after admission may therefore help improve risk stratification and guide post-procedural management.

Insulin resistance (IR) has been increasingly recognized as a key metabolic contributor to cardiovascular and cerebrovascular disease [10, 11]. The triglyceride-glucose (TyG) index, derived from fasting glucose and triglyceride levels, has emerged as a simple and readily available surrogate marker of IR [12]. Growing evidence links an elevated TyG index to cerebrovascular risk and adverse stroke outcomes. Bian et al. [13] reported that the TyG index predicted ischemic stroke risk, particularly in individuals with normal glucose regulation (NGR) or prediabetes mellitus (Pre-DM). A recent meta-analysis further showed that a higher TyG index was associated with adverse stroke outcomes, including stroke recurrence and mortality [11]. In addition, the TyG index has been associated with carotid plaque instability, especially among patients with diabetes mellitus (DM) [14], and with in-hospital or intensive care unit mortality in patients with ischemic stroke [15, 16].

Evidence regarding the prognostic role of the TyG index in patients with LVO undergoing EVT remains limited, particularly across glucose metabolic status groups. Lee et al. [17] first reported an association between a higher TyG index and poor outcomes after reperfusion therapy. More recently, Sun et al. [18] found that elevated TyG index was associated with worse clinical outcomes after EVT in a single-center retrospective cohort. However, whether this association differs according to glucose metabolic status remains unclear. Therefore, in this multicenter retrospective cohort study, we investigated the association between the TyG index and poor prognosis after EVT, with particular emphasis on differences across NGR, Pre-DM, and DM groups.

Methods

Study population

This multicenter retrospective cohort study enrolled patients with anterior-circulation AIS who underwent EVT at six stroke centers in China between September 2018 and January 2024. The study was approved by the Human Research Ethics Committee of Xiangyang No.1 People's Hospital (No. 2025KY058), and the requirement for written informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki. Eligible patients were aged 18 years or older, had AIS caused by large vessel occlusion, and received EVT. Patients were excluded if they had a prestroke modified Rankin Scale (mRS) score ≥ 2, missing fasting plasma glucose or HbA1c data, or were lost to 90-day follow-up.

Data collection and definitions

Clinical data for AIS patients were obtained from electronic medical records. Baseline variables included age, sex, vascular risk factors, including hypertension, diabetes, hyperlipidemia, atrial fibrillation, and smoking, as well as systolic blood pressure (SBP) and diastolic blood pressure (DBP) at admission. Venous blood samples were obtained in the early morning after admission after at least 8 hours of fasting. Laboratory measurements included triglycerides (TG), fasting plasma glucose (FPG), glycated hemoglobin A1c (HbA1c), crea, urea, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C). The TyG index was calculated as follows: TyG index = Ln [TG (mg/dL) × FPG (mg/dL) / 2] [12]. Glucose metabolic status was defined according to the American Diabetes Association criteria [19]. Diabetes mellitus (DM) was defined as a history of diabetes, use of

glucose-lowering medications, FPG ≥ 7.0 mmol/L, or HbA1c ≥ 6.5%. Prediabetes mellitus (Pre-DM) was defined as FPG 5.6–6.9 mmol/L or HbA1c 5.7%–6.4% in the absence of DM. Normal glucose regulation (NGR) was defined as FPG < 5.6 mmol/L and HbA1c < 5.7%, without a history of diabetes. The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) was used to assess early ischemic changes in the middle cerebral artery territory on baseline computed tomography [20]. Stroke etiology was classified as large artery atherosclerosis, cardioembolism, or other causes according to the Trial of Org 10172 in Acute Stroke Treatment criteria [21]. Large vessel occlusion was defined as occlusion of the internal carotid artery or the M1 or M2 segment of the middle cerebral artery. Poor prognosis was defined as an mRS score ≥ 3 at 90 days. The 90-day mRS score was assessed during scheduled outpatient visits or through telephone-based mRS assessment conducted by trained research nurses or neurologists [22].

Statistical analysis

Statistical analyses were performed using R version 4.4.2 (R Foundation for Statistical Computing) and SPSS version 27.0 for Windows. A two-sided P value < 0.05 was considered statistically significant. Missing baseline data were minimal and were handled using multiple imputation, as described in the Supplementary Material. Continuous variables were presented as mean ± standard deviation or median with interquartile range, according to their distribution, and were compared using Student's t test, one-way analysis of variance, Mann–Whitney U test, or Kruskal–Wallis test, as appropriate. Categorical variables were summarized as counts and percentages and compared using the chi-square test or Fisher's exact test.

Binary logistic regression models were used to evaluate the association between the TyG index and poor prognosis, with odds ratios (ORs) and 95% confidence intervals (CIs) reported. Covariates were selected based on univariate associations with poor prognosis and established clinical relevance. Multivariable models were adjusted for age, sex, smoking, atrial fibrillation, hypertension, baseline National Institutes of Health Stroke Scale (NIHSS) score, ASPECTS, intravenous thrombolysis (IVT), onset to puncture time, TOAST etiology, and occlusion location. Analyses were further stratified by glucose metabolic status, including NGR, Pre-DM, and DM. The interaction between the TyG index and glucose metabolic status was assessed by adding multiplicative interaction terms to the logistic regression models, and P for interaction was calculated using likelihood ratio tests. Restricted cubic spline analysis was performed to evaluate the dose-response association between the TyG index and poor prognosis, with tests for overall association and non-linearity. The spline models were adjusted for the same covariates as the multivariable logistic regression models.

To assess the incremental predictive value of the TyG index, we compared a basic model with the basic model plus the TyG index. Model discrimination was evaluated using the C statistic, and changes in discrimination were assessed using the change in C statistic. Risk reclassification was evaluated using continuous net reclassification improvement and integrated discrimination improvement. Receiver operating characteristic curves were generated using predicted probabilities from the corresponding logistic regression models. Subgroup analyses were performed according to age, sex, hypertension, history of diabetes, atrial fibrillation, IVT, and onset to puncture time. Sensitivity analyses were conducted after excluding patients without successful reperfusion to examine the robustness of the main findings.

Results

Baseline characteristics

- Of 1,475 patients screened, 789 met the eligibility criteria and were included in the final analysis (Fig. 1). The median age was 69 years, and 440 patients (55.8%) were male. At 90 days, 351 patients (44.5%) had good prognosis, whereas 438 patients (55.5%) had poor prognosis. Compared with patients with good prognosis, those with poor prognosis were older and more likely to have atrial fibrillation, hypertension, and diabetes. They also had higher levels of SBP, TG, FPG, HbA1c, TyG index, urea, and baseline NIHSS, but lower ASPECTS (all $P < 0.05$; Table 1). Patients were further categorized into tertiles according to the admission TyG index: T1 (≤ 8.51, n = 263), T2 (8.51–9.20, n = 263), and T3 (> 9.20, n = 263). Compared with patients in the T1 group, those in the T3 group were younger and more likely to have hypertension and diabetes. Increasing TyG tertiles were associated with higher levels of TG, FPG, HbA1c, TC, and LDL-C, as well as a higher proportion of poor prognosis (Table S1).

Table 1
Baseline characteristics of patients with good and poor prognosis.

Age (years)	**Total (n = 789)**	**Good prognosis (n = 351)**	**Poor prognosis (n = 438)**	***P*-value**
	69 (59–76)	**66 (56–73)**	**71 (63–78)**	**< 0.001**
Male (n, %)	440 (55.8)	224 (63.8)	216 (49.3)	< 0.001
Smoking history (n, %)	179 (22.7)	87 (24.8)	92 (21.0)	0.240
Atrial fibrillation (n, %)	323 (40.9)	129 (36.8)	194 (44.3)	0.039
Hypertension (n, %)	463 (58.7)	183 (52.1)	280 (63.9)	0.001
Hyperlipidemia (n, %)	152 (19.3)	58 (16.5)	94 (21.5)	0.098
Diabetes (n, %)	190 (24.1)	66 (18.8)	124 (28.3)	0.003
SBP (mmHg)	145 (127–161)	142 (126–159)	146 (128–166)	0.040
DBP (mmHg)	83 (74–94)	82 (73–92)	84 (74–96)	0.103
Laboratory examination				
TG (mmol/L)	1.18 (0.81–1.85)	1.12 (0.78–1.66)	1.25 (0.83–2.05)	0.012
FPG (mmol/L)	6.93 (5.81–8.7)	6.48 (5.6–7.8)	7.31 (6.04–9.23)	< 0.001
TyG index	8.78 (8.38–9.41)	8.65 (8.29–9.26)	8.93 (8.44–9.57)	< 0.001
HbA1c (%)	5.90 (5.60–6.40)	5.80 (5.5–6.22)	5.95 (5.6–6.5)	0.009
Crea (umol/L)	70.9 (57-89.6)	70 (56-86.6)	71 (57.8–92)	0.144
Urea (mmol/L)	5.8 (4.7–7.4)	5.8 (4.4–7.3)	5.9 (4.9–7.6)	0.025
TC (mmol/L)	4.27 (3.56–5.05)	4.25 (3.62-5.0)	4.28 (3.5–5.07)	0.784
LDL-C (mmol/L)	2.49 (1.9–3.1)	2.49 (2.02–3.09)	2.49 (1.86–3.11)	0.265
NIHSS	16 (12–19)	14 (11–18)	17 (14–20)	< 0.001
ASPECTS	7 (6–9)	8 (7–9)	7 (5–8)	< 0.001
Local anesthesia (n, %)	619 (78.5)	269 (76.6)	350 (79.9)	0.306

SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; FPG, fasting plasma glucose; TyG, triglyceride-glucose index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; IVT, intravenous thrombolysis; LAA, large artery atherosclerosis; CE, cardiac embolism; ICA, internal carotid artery; M1, M1 segment of the middle cerebral artery; M2, M2 segment of the middle cerebral artery; NGR, normal glucose regulation; Pre-DM, prediabetes mellitus; DM, diabetes mellitus.

Age (years)	Total (n = 789)	Good prognosis (n = 351)	Poor prognosis (n = 438)	*P*-value
	69 (59–76)	**66 (56–73)**	**71 (63–78)**	**< 0.001**
IVT (n, %)	119 (15.1)	46 (13.1)	73 (16.7)	0.197
TOAST etiology (n, %)				0.469
LAA	305 (38.7)	132 (37.6)	173 (39.5)	
CE	397 (50.3)	175 (49.9)	222 (50.7)	
Others	87 (11.0)	44 (12.5)	43 (9.8)	
Occlusion location (n, %)				< 0.001
ICA	191 (24.2)	58 (16.5)	133 (30.4)	
M1	500 (63.4)	246 (70.1)	254 (58.0)	
M2	98 (12.4)	47 (13.4)	51 (11.6)	
Time metrics (min)				
Onset to door time	220 (110–407)	195 (90–400)	240 (120–410)	0.096
Onset to puncture time	324 (217–531)	310 (210–523)	335 (222–535)	0.329
Onset to recanalization time	401 (290–631)	385 (280–620)	425 (299–641)	0.061

SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; FPG, fasting plasma glucose; TyG, triglyceride-glucose index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; IVT, intravenous thrombolysis; LAA, large artery atherosclerosis; CE, cardiac embolism; ICA, internal carotid artery; M1, M1 segment of the middle cerebral artery; M2, M2 segment of the middle cerebral artery; NGR, normal glucose regulation; Pre-DM, prediabetes mellitus; DM, diabetes mellitus.

- According to glucose metabolic status, 70 patients (8.9%) were classified as NGR, 302 (38.3%) as Pre-DM, and 417 (52.8%) as DM. TG, FPG, HbA1c, and TyG index differed significantly across the three groups (all $P < 0.001$; Figure S1). The proportion of poor prognosis was higher in the Pre-DM and DM groups than in the NGR group, and hypertension and female sex were more common in the DM group (Table S2).

Association between the TyG index and poor prognosis

- Binary logistic regression analyses were performed to evaluate the association between the TyG index and poor prognosis in the overall cohort. In the adjusted model, the TyG index was independently associated with poor prognosis when analyzed as a continuous variable (OR = 1.65; 95% CI 1.32–2.07; $P < 0.001$). When the TyG index was analyzed as tertiles, patients in the T3 group had a significantly higher risk of poor prognosis than those in the T1 group after adjustment (OR = 2.04; 95% CI 1.36–3.05; $P = 0.001$), whereas the association was not significant in the T2 group (OR = 1.37; 95% CI 0.93–2.02; $P = 0.116$). A significant

trend across TyG tertiles was also observed in both the unadjusted and adjusted models (both *P* for trend ≤ 0.001; Table 2).

Table 2
Association between the TyG index and poor prognosis.

Variable	Event, n (%)	Unadjusted analysis		Adjusted analysis*	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
TyG	438 (55.5)	1.64 (1.35–2.00)	< 0.001	1.65 (1.32–2.07)	< 0.001
T1	126 (47.9)	Reference		Reference	
T2	144 (54.8)	1.29 (0.92–1.82)	0.140	1.37 (0.93–2.02)	0.116
T3	168 (63.9)	1.91 (1.35–2.71)	< 0.001	2.04 (1.36–3.05)	0.001
P for trend			< 0.001		0.001

OR, odds ratio; CI, confidence interval; TyG, triglyceride-glucose index; *Adjusted for age, sex, smoking, atrial fibrillation, hypertension, National Institutes of Health Stroke Scale, Alberta Stroke Program Early Computed Tomography Score, intravenous thrombolysis, onset to puncture time, TOAST etiology, and occlusion location.

Association between the TyG index and poor prognosis according to glucose metabolic status

Binary logistic regression analyses were performed after stratification by glucose metabolic status. In the adjusted model, the TyG index as a continuous variable was significantly associated with poor prognosis in the NGR group (OR = 8.37; 95% CI 1.99–54.12; *P* = 0.011) and the DM group (OR = 1.46; 95% CI 1.06–2.03; *P* = 0.021), but not in the Pre-DM group (OR = 1.38; 95% CI 0.88–2.18; *P* = 0.164). When analyzed as tertiles, the proportion of poor prognosis increased across TyG tertiles in the NGR group, from 38.6% in T1 to 47.4% in T2 and 57.1% in T3; after adjustment, the T3 group had a higher risk than the T1 group (OR = 23.93; 95% CI 1.52–377.74; *P* = 0.024; *P* for trend = 0.019). No significant associations across TyG tertiles were observed in the Pre-DM or DM groups after adjustment. The interaction between glucose metabolic status and the TyG index was not statistically significant, either as a continuous variable or as tertiles in the adjusted models (*P* for interaction = 0.123 and 0.094, respectively; Table 3).

Table 3
Association between the TyG index and poor prognosis according to glucose metabolic status.

Variable	Glucose metabolic status	Event, n (%)	Unadjusted analysis		*P* for interaction	Adjusted analysis*		*P* for interaction
			OR (95% CI)	*P*-value		OR (95% CI)	*P*-value	
TyG continuous					0.798			0.123
	NGR	30 (42.9)	1.77 (0.84–3.93)	0.142		8.37 (1.99–54.12)	0.011	
	Pre-DM	142 (47.0)	1.33 (0.91–1.96)	0.149		1.38 (0.88–2.18)	0.164	
	DM	266 (63.8)	1.43 (1.09–1.90)	0.01		1.46 (1.06–2.03)	0.021	
TyG tertiles					0.265			0.094
T1	NGR	17 (38.6)	Reference			Reference		
T2		9 (47.4)	1.43 (0.48–4.23)	0.519		3.72 (0.68–20.44)	0.13	
T3		4 (57.1)	2.12 (0.42–10.65)	0.363		23.93 (1.52–377.74)	0.024	
P for trend				0.307			0.019	
T1	Pre-DM	68 (47.9)	Reference			Reference		
T2		48 (41.7)	0.78 (0.47–1.28)	0.325		0.83 (0.47–1.45)	0.509	
T3		26 (57.8)	1.49 (0.76–2.93)	0.249		1.61 (0.74–3.53)	0.231	
P for trend				0.563			0.472	
T1	DM	40 (54.1)	Reference			Reference		

OR, odds ratio; CI, confidence interval; TyG, triglyceride-glucose index; NGR, normal glucose regulation; Pre-DM, prediabetes mellitus; DM, diabetes mellitus; *Adjusted for age, sex, smoking, atrial fibrillation, hypertension, National Institutes of Health Stroke Scale, Alberta Stroke Program Early Computed Tomography Score, intravenous thrombolysis, onset to puncture time, TOAST etiology, and occlusion location.

Variable	Glucose metabolic status	Event, n (%)	Unadjusted analysis		*P* for interaction	Adjusted analysis*		*P* for interaction
			OR (95% CI)	*P*-value		OR (95% CI)	*P*-value	
T2		88 (66.7)	1.70 (0.95–3.05)	0.074		1.77 (0.91–3.43)	0.092	
T3		138 (65.4)	1.61 (0.94–2.75)	0.084		1.79 (0.96–3.35)	0.069	
P for trend				0.155			0.115	

OR, odds ratio; CI, confidence interval; TyG, triglyceride-glucose index; NGR, normal glucose regulation; Pre-DM, prediabetes mellitus; DM, diabetes mellitus; *Adjusted for age, sex, smoking, atrial fibrillation, hypertension, National Institutes of Health Stroke Scale, Alberta Stroke Program Early Computed Tomography Score, intravenous thrombolysis, onset to puncture time, TOAST etiology, and occlusion location.

Restricted cubic spline analysis adjusted for the same covariates as the multivariable logistic regression models demonstrated a significant positive association between the TyG index and poor prognosis in the overall cohort (*P* for overall < 0.001), without evidence of non-linearity (*P* for non-linearity = 0.794). However, this association was not statistically significant within the NGR, Pre-DM, or DM groups (*P* for overall = 0.061, 0.180, and 0.080, respectively), and no significant non-linear associations were detected across these groups (all *P* for non-linearity > 0.05; Fig. 2).

The predictive value of the TyG index for poor prognosis

The incremental predictive value of the TyG index was assessed by comparing the basic model with the basic model plus the TyG index (Table 4; Figure S2). In the overall cohort, adding the TyG index improved the C statistic from 0.747 to 0.761 (*P* = 0.029), with significant improvements in NRI (0.238; 95% CI 0.084–0.396; *P* = 0.002) and IDI (0.021; 95% CI 0.006–0.043; *P* = 0.002). Across glucose metabolic status subgroups, the improvement appeared most pronounced in the NGR group, where the C statistic increased from 0.792 to 0.860 (*P* = 0.037), accompanied by significant improvements in NRI and IDI. No significant improvement in the C statistic or NRI was observed in the Pre-DM or DM groups, although IDI was significantly improved in the DM group and showed borderline improvement in the Pre-DM group.

Table 4
Discrimination and reclassification performance of the TyG index for predicting poor prognosis.

Model	C statistic Estimate (95% CI)	*P*-value	NRI(continuous) Estimate (95% CI)	*P*-value	IDI Estimate (95% CI)	*P*-value
Overall						
Basic model	0.747 (0.713–0.781)		Reference		Reference	
Basic model + TyG	0.761 (0.728–0.794)	0.029	0.238 (0.084–0.396)	0.002	0.021 (0.006–0.043)	0.002
NGR						
Basic model	0.792 (0.683–0.900)		Reference		Reference	
Basic model + TyG	0.860 (0.771–0.949)	0.037	0.750 (0.040–2.000)	0.044	0.117 (0.002–0.466)	0.016
Pre-DM						
Basic model	0.724 (0.668–0.780)		Reference		Reference	
Basic model + TyG	0.727 (0.671–0.783)	0.646	0.048 (-0.153–0.307)	0.569	0.006 (0.000–0.032)	0.050
DM						
Basic model	0.762 (0.715–0.809)		Reference		Reference	
Basic model + TyG	0.771 (0.725–0.816)	0.210	0.184 (-0.043–0.417)	0.106	0.010 (0.000–0.038)	0.022

NRI, Net Reclassification Improvement; IDI, Integrated Discrimination Improvement

Subgroup and sensitivity analyses

Subgroup and interaction analyses showed that the association between the TyG index and poor prognosis was generally consistent across prespecified subgroups (Fig. 4). A higher TyG index was associated with increased odds of poor prognosis in most subgroups, including both age groups, both sexes, patients with or without hypertension, patients with or without atrial fibrillation, and patients with onset to puncture time ≤ 360 min. The association was not statistically significant among patients with a history of diabetes or those receiving IVT. No significant interactions were observed across any prespecified subgroup variables (all *P* for interaction > 0.05).

After excluding patients without successful reperfusion, the association between the TyG index and poor prognosis remained robust. In the overall cohort, higher TyG index was independently associated with poor prognosis as both a continuous variable and tertiles, with a significant trend across tertiles (Table S3). Stratified analyses showed significant associations in the NGR and DM groups, but not in the Pre-DM group. A significant

interaction was observed for the continuous TyG index across glucose metabolic status groups, whereas the interaction for TyG tertiles was not significant (Table S4).

Discussion

In this multicenter retrospective cohort study of AIS patients undergoing EVT, a higher TyG index was independently associated with an increased risk of 90-day poor prognosis and showed a positive linear relationship with adverse outcomes. Stratified analyses suggested significant associations in patients with NGR and DM, but not in those with Pre-DM; however, glucose metabolic status did not significantly modify this association. Adding the TyG index to a basic model provided modest improvement in prognostic discrimination and risk reclassification, suggesting that the TyG index may serve as a simple marker for post-EVT risk stratification.

The prognostic relevance of the TyG index has been increasingly reported across cardiovascular and cerebrovascular populations. In patients with coronary artery disease, higher TyG index values have been associated with adverse cardiovascular events [23, 24]. Similar associations have also been observed in cerebrovascular disease, where the TyG index has been linked to an increased risk of vascular restenosis after revascularization [25]. Beyond ischemic events, Yang et al. [26] reported a positive association between the TyG index and all-cause mortality in patients with intracerebral hemorrhage, while Huang et al. [27] suggested its potential utility for mortality risk assessment in critically ill patients with hemorrhagic stroke. Together, these findings support the TyG index as a clinically accessible metabolic marker with potential prognostic value across a broad spectrum of vascular diseases.

The prognostic role of the TyG index in AIS patients undergoing EVT remains insufficiently defined. In this multicenter cohort, a higher TyG index was independently associated with poor prognosis after EVT, consistent with previous studies linking the TyG index to adverse stroke outcomes [11, 15–18]. The association was evident when TyG was analyzed both as a continuous variable and as tertiles, and restricted cubic spline analysis showed a positive linear relationship in the overall cohort. Moreover, adding the TyG index to a basic model modestly improved prognostic discrimination and risk reclassification. These findings suggest that the TyG index, as a simple and readily available metabolic marker, may help refine post-EVT risk stratification.

The mechanisms linking an elevated TyG index to poor prognosis after EVT are likely multifactorial. As a surrogate marker of IR, the TyG index may reflect metabolic disturbances that adversely affect cerebrovascular homeostasis. IR and compensatory hyperinsulinemia can disrupt insulin signaling in vascular endothelial cells and reduce vascular endothelial growth factor expression [28, 29]. IR may also impair nitric oxide bioavailability and increase reactive oxygen species production, leading to endothelial dysfunction, impaired vasomotor regulation, and weakened cerebrovascular autoregulation [30, 31]. These changes may reduce the brain's capacity to compensate for acute ischemic injury. In addition, a higher TyG index reflects a combined burden of hyperglycemia and hypertriglyceridemia. Hyperglycemia can promote inflammation and oxidative stress, accelerate neuronal injury in the ischemic penumbra, disrupt the blood–brain barrier, and increase the risk of hemorrhagic transformation [32, 33]. IR may further enhance platelet activation, tissue factor expression, and thrombin generation, thereby promoting thrombosis and microvascular dysfunction [34]. Collectively, these mechanisms may contribute to more severe vascular injury and poorer recovery in patients with a higher TyG

index. Further experimental and clinical studies are needed to clarify the biological pathways underlying this association.

In the present study, patients undergoing EVT were stratified into NGR, Pre-DM, and DM groups according to glucose metabolic status. The association between the TyG index and poor prognosis was observed in the NGR and DM groups, but not in the Pre-DM group. Although the point estimate appeared larger in the NGR group, formal interaction testing did not show significant effect modification by glucose metabolic status; therefore, this subgroup finding should be interpreted cautiously. This pattern is partly consistent with previous studies suggesting that the TyG index may have stronger prognostic value in individuals without diabetes than in those with diabetes [15, 27]. This paradox may be explained by reverse causality, where the diagnosis of comorbidities leads to timely treatment or healthier lifestyle choices, thereby improving prognosis despite an elevated risk of poor prognosis [35]. The null finding in the Pre-DM group is also noteworthy. Although previous studies have linked the TyG index to carotid plaque instability and ischemic stroke risk in individuals with Pre-DM [13, 14], evidence regarding its prognostic role after EVT remains limited. Our findings suggest that the prognostic implications of the TyG index may vary across glucose metabolic status groups, but further studies with larger subgroup samples are needed to confirm these results.

This study has several limitations. First, although this was a multicenter study, its retrospective and observational design precludes causal inference. Second, the sample size of the NGR subgroup was relatively small, which may have limited statistical power and contributed to the imprecision of subgroup estimates. Third, the TyG index was used as a surrogate marker of IR and may not fully capture the complexity of IR. Direct measurements, such as the hyperinsulinemic-euglycemic clamp or homeostatic model assessment, may provide more accurate assessments but are less feasible in routine clinical practice. Fourth, survival bias related to early fatal events cannot be completely excluded. Finally, the study population consisted exclusively of Chinese patients, which may limit the generalizability of our findings to other ethnic and geographic populations. Further prospective studies with larger and more diverse cohorts are warranted.

In summary, the TyG index was independently associated with poor prognosis in AIS patients undergoing EVT and provided modest incremental prognostic value beyond a basic model. Although glucose metabolic status did not significantly modify this association, patients with DM had the highest proportion of poor prognosis, and stratified analyses suggested associations in the NGR and DM groups. Further prospective studies are needed to validate these findings.

Declarations

Ethics approval and consent to participate

The Xiangyang No.1 People's Hospital Human Research Ethics Committee approved this study (No. 2025KY058), waiving the requirement for written informed consent.

Consent for publication

Not Applicable.

Conflicts of interest disclosure

All authors declare no conflict of interest.

Sources of Funding

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Clinical trial number

Not applicable.

Basic model

age, sex, smoking, atrial fibrillation, hypertension, National Institutes of Health Stroke Scale, Alberta Stroke Program Early Computed Tomography Score, intravenous thrombolysis, onset to puncture time, TOAST etiology, and occlusion location.

Author Contribution

G.X. N. and W. D. conducted the literature review and conceived the study. G.X. N., Y.L. S., and W. D. were responsible for the planning, design, and execution of the study. W. D. supervised and coordinated the project and wrote the initial manuscript draft. P.Y. Z., Z.Q. B., and J. H. contributed to data acquisition, processing, and analysis. This manuscript complies with all instructions to authors. The authorship requirements have been met and the final manuscript was approved by all authors. This manuscript has not been published elsewhere and is not under consideration by another journal.

Acknowledgements

Not Applicable.

Data Availability

Availability of data and materialsThe datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Figures

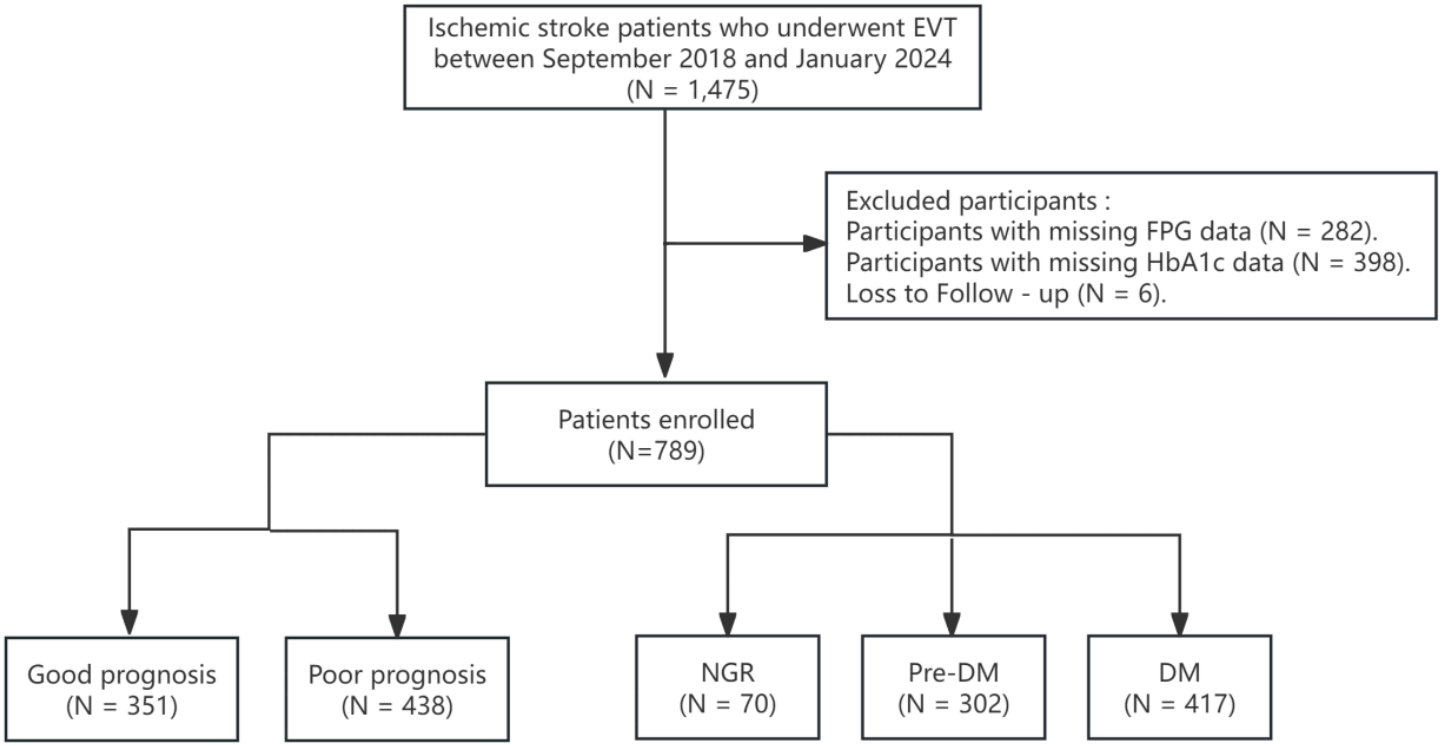


Figure 1

Flowchart of patient selection. This figure presents the enrollment information of patients included in this study. EVT, endovascular therapy; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; NGR, normal glucose regulation; Pre-DM, prediabetes mellitus; DM, diabetes mellitus.

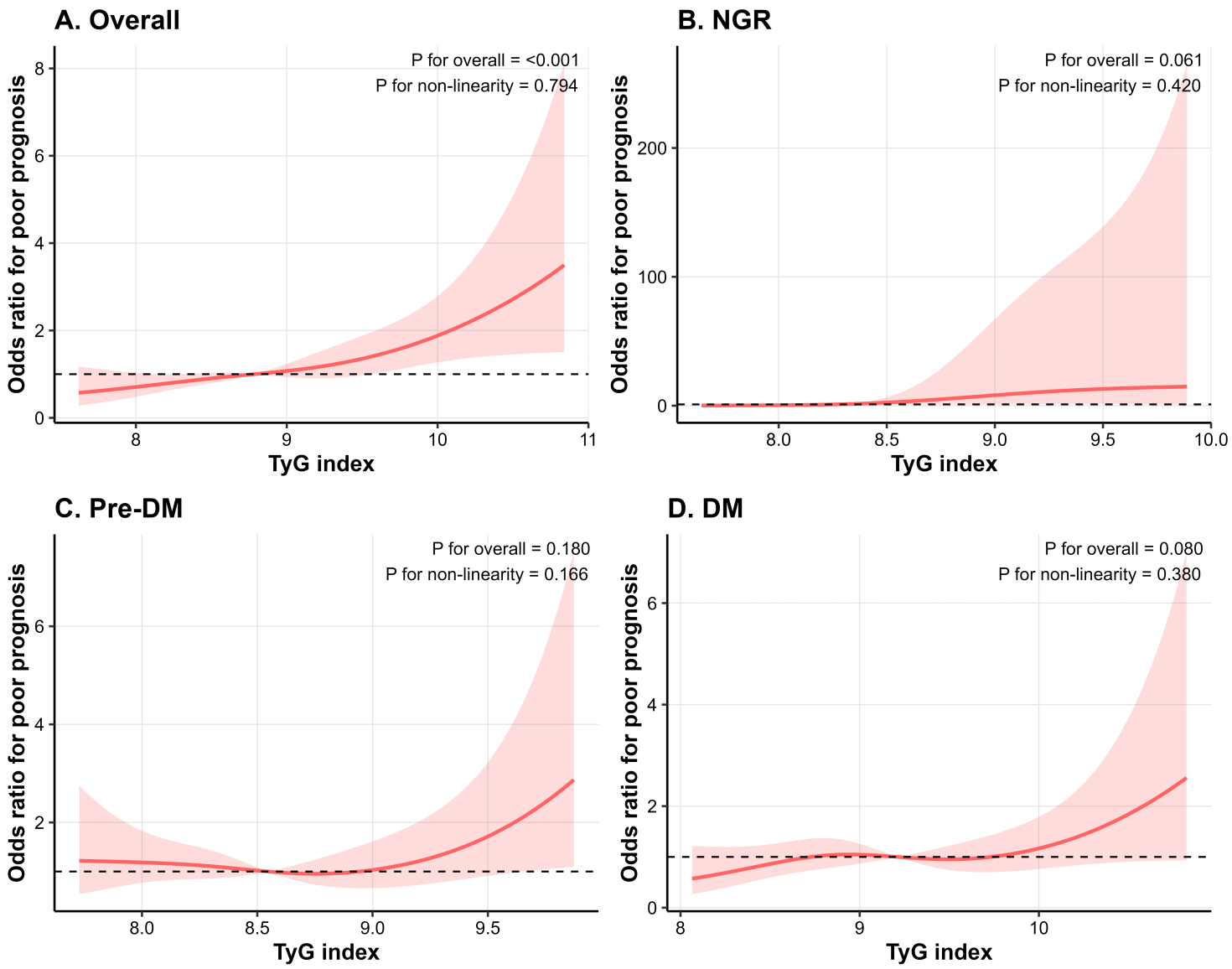


Figure 2

Restricted cubic spline analysis of the association between the TyG index and poor prognosis. A, overall cohort; B, NGR, normal glucose regulation; C, Pre-DM, prediabetes mellitus; D, DM, diabetes mellitus. Adjusted for age, sex, smoking, atrial fibrillation, hypertension, National Institutes of Health Stroke Scale, Alberta Stroke Program Early Computed Tomography Score, intravenous thrombolysis, onset to puncture time, TOAST etiology, and occlusion location.

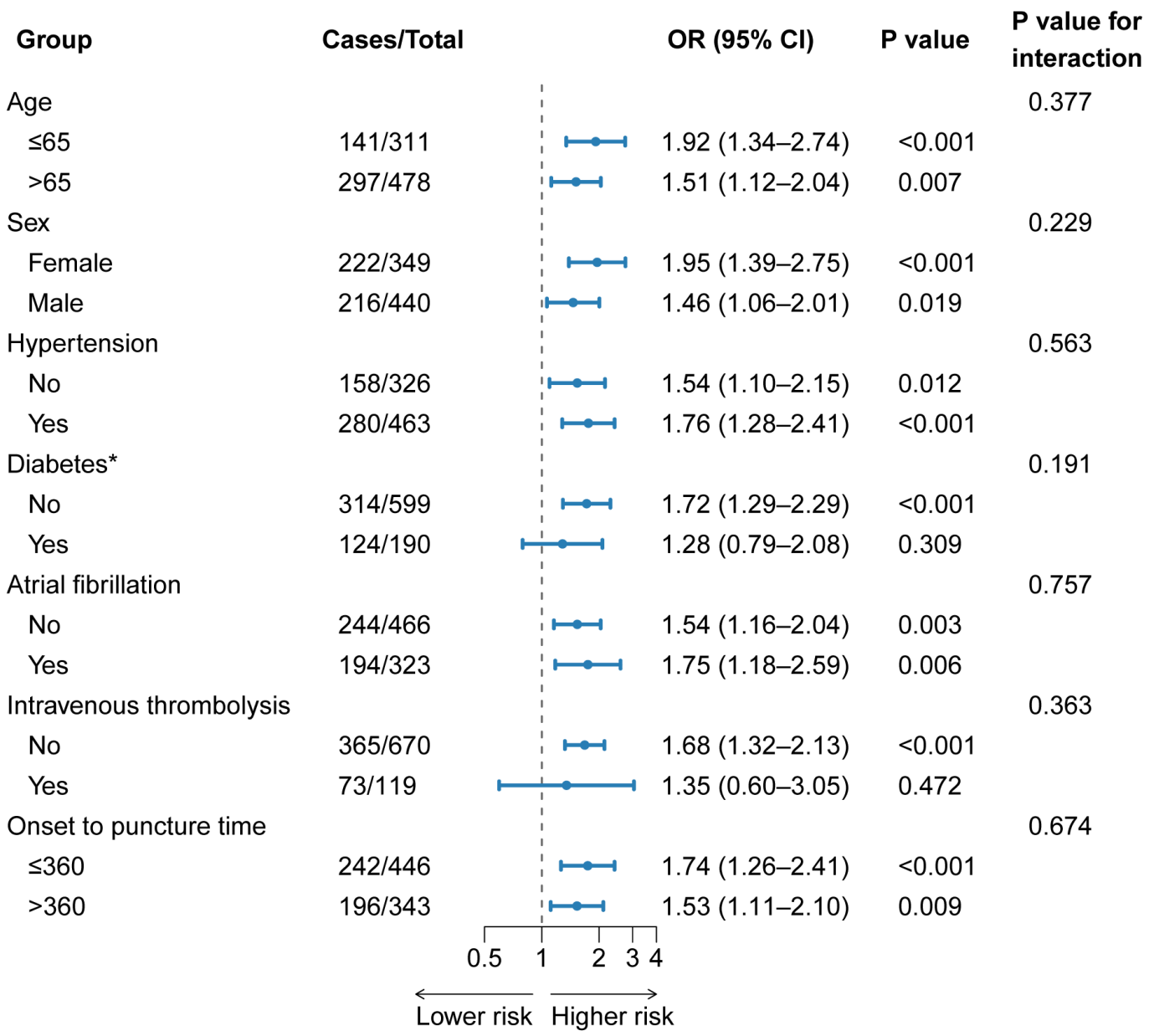


Figure 3

Subgroup and interaction analyses of the association between the TyG index and poor prognosis. Subgroup analyses were performed according to age, sex, hypertension, diabetes, atrial fibrillation, intravenous thrombolysis, and onset-to-puncture time. *Diabetes refers to a history of diabetes. Odds ratios were calculated per 1-unit increase in the TyG index. OR, odds ratio; CI, confidence interval; TyG, triglyceride-glucose index; IVT, intravenous thrombolysis; OPT, onset to puncture time.

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