Neurology Asia 2025; 30(4) : 995 – 1008

Prognostic value of the TyG-AIP-BMI Composite Index (TabCI) for long-term survival in Ischemic stroke patients: A comprehensive analysis based on MIMIC-IV ICU Data

[1]Yinqin Hu, [1]Yongming Liu, [2]Chenghao Wang, [3]Jiwei Cheng, [4]Junxiong Li

[1]Department of Cardiology, Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China; [2]Jiangxi University of Traditional Chinese Medicine, Nanchang Jiangxi, China; [3]Department of Neurology, Putuo Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China; [4]Huadong Hospital Affiliated to Fudan University, Shanghai China

Abstract

Background & Objective: Insulin resistance-induced metabolic disorders play a crucial role in exacerbating ischemic stroke. This study aims to explore the association between TyG-AIP-BMI Composite Index (TabCI) and long-term mortality risk in severe ischemic stroke patients. *Methods:* Data from the Medical Information Mart for Intensive Care IV (MIMIC-IV 2.2) database were accessed to retrieve data of ischemic stroke patients. Patients were stratified into four groups based on TabCI quartiles. The study assessed the primary outcome of 180-day all-cause mortality and secondary outcomes including 90-day and 1-year ACM. Kaplan-Meier curves were used to compare outcomes across groups, and lasso regression analysis was employed to select covariates. Multivariable Cox proportional hazards regression models and restricted cubic splines (RCS) were used to explore the association between TabCI and these outcomes. Interaction and subgroup analyses were conducted to validate the stability of results. Results: A total of 1,141 severe ischemic stroke patients were included, with a mean age of 69 years (interquartile range [IQR]: 59-79), and 565 participants (49.5%) were male. Kaplan-Meier analysis indicated significantly lower long-term survival rates in patients in Q1 and Q3 compared to those in Q2 and Q4. Cox proportional hazards regression analysis adjusted for covariates showed a statistically significant increase in 180-day mortality risk in TabCI quartiles, with Q2 and Q4 groups also exhibiting increased risks at 90 days and 1 year. Additionally, RCS analysis revealed a gradual L-shaped correlation between TabCI and 90-day and 180-day all-cause mortality, with a smooth U-shaped trend observed for 1-year mortality, demonstrating significant non-linearity. Subgroup analysis further indicated an inverse correlation between TabCI and long-term mortality risk in non-Caucasian patients and those using aspirin, as well as negative correlations in TabCI among patients not receiving CRRT for 90-day and 180-day mortality.
Conclusion: TabCI may serve as an exploratory marker for stratifying long-term risk among severe ischemic stroke patients; however, its clinical predictive efficacy remains limited and requires further validation in larger, prospective studies.

Keywords: Ischemic stroke, TyG, triglyceride, glucose, MIMIC-IV

INTRODUCTION

Stroke is a leading cause of death and disability worldwide. In China, the lifetime risk and disease burden of stroke are as high as 39.3%, ranking highest globally.[1] Ischemic stroke, comprising 81.9% of all strokes, is the predominant type.[2] Large hemisphere ischemic stroke leads to early neurological deficits, progressing to consciousness impairment and rapid onset of brain herniation, known as malignant middle cerebral artery infarction (MMI).[3] MMI has a mortality rate of 60.9% to 78%, often resulting in severe neurological disabilities even for survivors.[3-5] Early prognosis of these patients aids clinicians in providing targeted treatments.

Address correspondence to: Jiwei Cheng, MD, Department of Neurology, Putuo Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China. Tel: 86-13818606517, Email: chengjiwei1@126.com; Junxiong Li, MD. Huadong Hospital Affiliated to Fudan University, Shanghai China. Tel: 86-19921311556, Email: 19921311556@163.com

Date of Submission: 12 September 2025; Date of Acceptance: 15 September 2025

https://doi.org/10.54029/2025pks

Insulin resistance, characterized by decreased insulin sensitivity, is a pivotal mechanism in disrupted glucose and lipid metabolism, crucial in the pathogenesis of type 2 diabetes and cardiovascular diseases.[6] Additionally, insulin resistance is implicated in oxidative stress, inflammatory responses, and neuronal damage.[7] These pathological changes are all related to the progression of ischemic stroke. Triglyceride-Glucose Index (TyG), a recently studied biomarker of insulin resistance, not only reflects the level of insulin resistance in patients but also predicts cardiovascular outcomes.[8] Recent studies have combined TyG with Body Mass Index (BMI) into an index aimed at enhancing the accuracy of predicting cardiovascular events.[9-11] Recent research indicates that the Atherogenic Index of Plasma (AIP), calculated based on the ratio of triglycerides to high-density lipoprotein, is an independent risk factor for cardiovascular events.[12] However, studies to date have focused on individual or paired combinations of these indices, without confirmation of a combined index incorporating all three. The TabCI (TyG-AIP-BMI Composite Index) combines triglycerides, glucose, BMI, and HDL-c into a single metric designed to integrate lipid and glucose metabolism with obesity status. This study aims to explore the TabCI correlation with long-term mortality in patients with severe ischemic stroke, aiming to provide a theoretical basis for reliable assessment tools in the long-term follow-up and stratified management of high-risk stroke patients.

METHODS

Source of data

This retrospective study utilized data from the publicly accessible Medical Information Mart for Intensive Care IV database (MIMIC-IV, version 2.2).MIMIC-IV is an enhanced version of its predecessor, MIMIC-III, featuring updated data and modifications to some table structures. The dataset comprises clinical information from over 190,000 unique hospitalized patients at Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts, spanning from 2008 to 2019. The database provides comprehensive details on patient demographics, vital signs, medications, laboratory tests, surgical procedures, diagnoses, treatment plans, and survival outcomes. Access to this data involved completion of the National Institutes of Health (NIH) Human Research Participant Protection training and passing the Collaborative Institutional Training Initiative (CITI) exam (ID: 13371165). Because the database does not contain any protected health information and patients remain anonymous, a waiver of informed consent was obtained.

Study design and population

This study focused on ischemic stroke patients admitted for the first time to the intensive care unit (ICU).We identified a cohort of 2,770 stroke patients using the search term "Cerebral infarction" in the International Classification of Diseases, 9th and 10th revisions (ICD-9 and ICD-10). Exclusion criteria were established to ensure data accuracy and relevance: (1) Lack of data on triglycerides (TG), fasting blood glucose (FBG), high-density lipoprotein cholesterol (HDL-c), body mass index (BMI), height, or weight on the first day of ICU admission; (2) Patients under 18 years of age; (3) ICU stay less than 24 hours; (4) Patients with multiple ICU admissions for stroke, considering data from the first admission only; (5) Lack of primary outcome indicators (survival status at 90 days, 180 days, and 1 year). Based on these criteria and quartiles of the composite index TabCI including TyG, AIP, and BMI, 1,141 patients were selected and categorized into four groups for further analysis (Figure 1).

Data extraction

In the baseline table, the Shapiro–Wilk test was used to assess the normality of continuous variables. Variables with a normal distribution are presented as mean ± standard deviation (SD), while those with a skewed distribution are presented as median [interquartile range (IQR)]. Continuous variables were compared using Student's t-test or Mann–Whitney Utest, as appropriate. Categorical variables are presented as frequencies and percentages and were compared using the Pearson's chi-square test or Fisher's exact test.

To explore the internal structure of the TabCI components (triglycerides, glucose, HDL-C, and BMI), principal component analysis (PCA) was conducted. The number of retained components was determined based on eigenvalues greater than 1 and visual inspection of the scree plot. Component loadings were examined to interpret the dominant metabolic patterns captured by each principal component.

Kaplan–Meier (K-M) survival curves were used to assess time-to-event outcomes stratified by TabCI deciles. Predictor variables were selected using the least absolute shrinkage and selection

operator (LASSO) with 10-fold cross-validation to identify variables associated with 90-day, 180-day, and 1-year mortality. These variables were then entered into Cox proportional hazards models. Three models were constructed: Model 1 was unadjusted; Model 2 adjusted for age, diastolic blood pressure (DBP), heart rate (HR), and respiratory rate (RR); and Model 3 further adjusted for atrial fibrillation, coronary heart disease, diabetes, myocardial infarction, alteplase, cilostazol, clopidogrel, tirofiban, mechanical ventilation (MV), APSIII, and SAPSII scores.

TabCI was also examined as a continuous variable using restricted cubic spline (RCS) models to assess potential nonlinear associations with outcomes. When nonlinear relationships were observed, inflection points were identified using recursive algorithms. Subgroup analyses and interaction tests were performed across key clinical strata, including age (≤65 vs. >65 years), sex, race/ethnicity, coronary artery disease, diabetes mellitus, hypertension, myocardial infarction, aspirin, cilostazol, clopidogrel, tirofiban, continuous renal replacement therapy (CRRT), and MV.

Outcomes

This study focuses on assessing all-cause mortality outcomes among stroke patients in the MIMIC-IV database over varying time intervals. The primary endpoint was defined as long-term all-cause mortality at 180 days, with secondary endpoints at 90 days and 1 year.

Typ-AIP-BMI Composite Index calculation

TyG is calculated using the formula: Ln[FBG (mg/dL) × TG (mg/dL) / 2].AIP is calculated as: log(TG / HDL-c).BMI is calculated using the formula: weight (kg) / (height (m))^2 (kg/m^2).

The TyG-AIP-BMI Composite Index (TabCI) is a composite index based on TyG, AIP, and BMI, calculated as: log((TG * glucose * BMI) / (2*HDL-c)).

Statistical analysis

In the baseline table, Shapiro-Wilk test was used to assess continuous variables. Variables conforming to normal distribution are presented as mean ± SD, while those not conforming are presented as median [interquartile range (IQR)]. Continuous variables were compared using Student's t-test or Mann-Whitney test, depending on their distribution. Categorical variables were presented as frequencies and percentages. Significant differences were assessed using Pearson's chi-square test or Fisher's exact test.

Kaplan-Meier (K-M) curves were used to assess time-to-event outcomes stratified by TabCI. Variables were selected using Least Absolute Shrinkage and Selection Operator (LASSO) with 10-fold cross-validation to identify predictors associated with 1-year, 90-day, and 180-day outcomes. Variables selected through LASSO analysis were included in Cox regression to examine the relationship between TabCI and 1-year, 90-day, and 180-day mortality rates. Final model variables were chosen considering event data availability. Model 1 was unadjusted, while Model 2 adjusted for age + DBP + hr + rr, and Model 3 further adjusted for age + DBP + hr + rr + atrial fibrillation + coronary heart disease + diabetes + myocardial infarction + alteplase + cilostazol + clopidogrel + tirofiban + mv + apsiii + sapsii. Additionally, TabCI was examined as a continuous variable using restricted cubic splines (RCS) to elucidate its relationship with the risk of outcome variables. In cases of nonlinear correlation, recursive algorithm identified the inflection point of TabCI with long-term all-cause mortality. Stratified analyses and interaction tests were performed based on age (≤65 years or >65 years)(In previous studies, around 65 years of age was identified as a stratification threshold or critical cutoff for the clinical severity of stroke patients to distinguish the heterogeneity of disease severity.[13]), gender, race/ethnicity, coronary artery disease, type 2 diabetes mellitus (2-DM), hypertension (HTN), myocardial infarction, aspirin, cilostazol, clopidogrel, tirofiban, CRRT, and MV. All statistical analyses were conducted using R software (version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics of study individuals

In this study, out of the 2,770 stroke patients listed in the MIMIC-IV database, 1,141 individuals met the inclusion criteria after screening and were subsequently analyzed (the screening process is depicted in Figure 1).

The mean age of included participants was 69 years (IQR: 59-79). There were 565 male patients, constituting 49.5% of the total, and 749 Caucasian patients, accounting for 65.6%

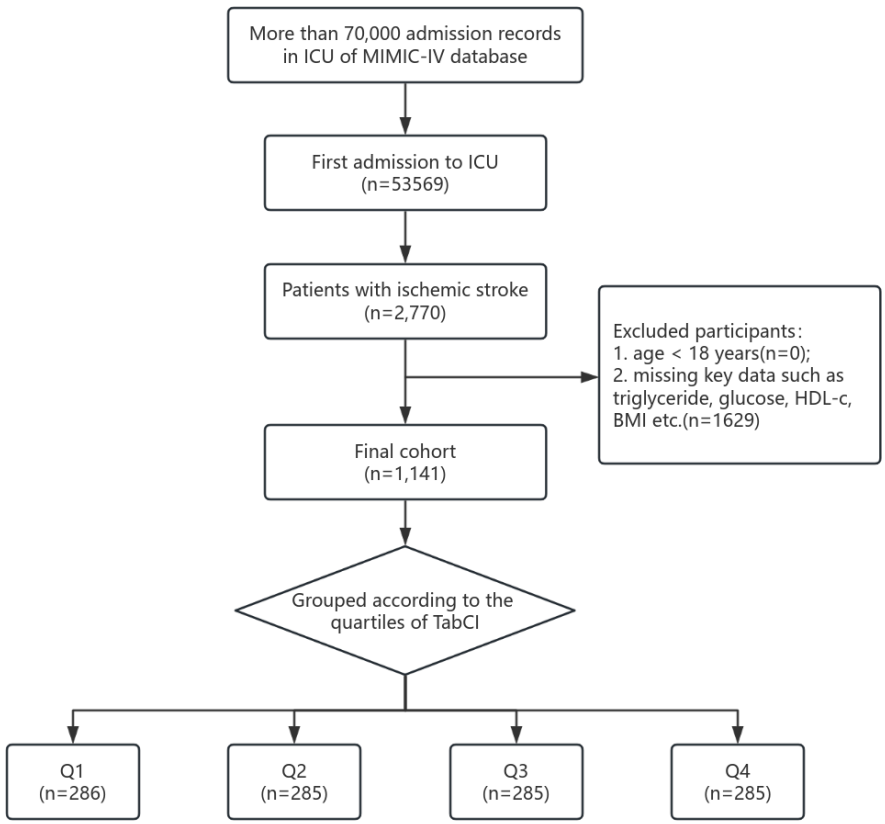


Figure 1. Study flowchart

*A total of 2,770 patients were diagnosed with ischemic stroke. MIMIC-IV: Medical Information Mart for Intensive Care IV; ICU: Intensive Care Unit; HDL-c: High-density lipoprotein cholesterol; BMI: Body Mass Index.

of the total. Participants were categorized into four groups based on quartiles of TabCI at enrollment: Q1 with 286 participants, Q2 with 285 participants, Q3 with 285 participants, and Q4 with 285 participants. Baseline characteristics (Table 1) indicate varying TabCI levels across the four groups: Q1, 7.27 (IQR: 6.99-7.5); Q2, 8.06 (IQR: 7.89-8.23); Q3, 8.7 (IQR: 8.54-8.9); and Q4, 9.71 (IQR: 9.35-10.1).

Principal Component Analysis (PCA) results

PCA revealed that the first two principal components (PC1 and PC2) accounted for 60.6% of the total variance (PC1: 37.2%; PC2: 23.4%), while three components cumulatively explained 82.3% of the variance. The scree plot suggested that two to three components were sufficient to capture the majority of information. (Figure S1A)

The loading matrix indicated that PC1 was mainly influenced by TG (–0.585), glucose (–0.483), and HDL-C (0.521), reflecting a lipid–glucose metabolic axis. PC2 was primarily driven by BMI (0.753) and HDL-C (0.485), indicating a body composition-related dimension. (Table S1) These components suggest distinct underlying metabolic structures that may relate to TabCI grouping and mortality risk.

A PCA biplot further revealed partial separation among TabCI quartiles along PC1 and PC2, supporting the hypothesis that TabCI may reflect latent metabolic clustering associated with clinical outcomes.

In addition, a heatmap visualizing the pairwise relationships among TabCI components (Fig. S1B) demonstrated clear inter-variable trends, such as a positive correlation between HDL-C and TG, and a negative association between BMI and glucose, reinforcing the distinct metabolic dimensions identified in the PCA.

Correlation between TabCI index and clinical outcomes in stroke patients

All variables from the baseline table were included in a LASSO regression analysis, followed by ten-fold cross-validation, resulting in λ value of 0.02100445 (Figure 4). Ultimately, 15

Table 1: Baseline characteristics and outcomes by quartiles of TabCI

	ALL N=1141	Q1 N=286	Q2 N=285	Q3 N=285	Q4 N=285	P value
Status_90d	0.24 (0.43)	0.29 (0.45)	0.22 (0.42)	0.27 (0.44)	0.20 (0.40)	0.047
Time_90d	90.0 [90.0;90.0]	90.0 [67.6;90.0]	90.0 [90.0;90.0]	90.0 [61.3;90.0]	90.0 [90.0;90.0]	0.051
Status_180d	0.30 (0.46)	0.35 (0.48)	0.26 (0.44)	0.34 (0.47)	0.26 (0.44)	0.015
Time_180d	180 [97.4;180]	180 [67.6;180]	180 [147;180]	180 [61.3;180]	180 [170;180]	0.015
Status_1year	0.37 (0.48)	0.40 (0.49)	0.29 (0.46)	0.41 (0.49)	0.37 (0.48)	0.013
Time_1year	365 [97.4;365]	365 [67.6;365]	365 [147;365]	365 [61.3;365]	365 [170;365]	0.015
Age	69.0 [59.0;79.0]	71.0 [58.0;80.0]	72.0 [61.0;80.0]	69.0 [62.0;81.0]	66.0 [56.0;73.0]	<0.001
Bmi	27.9 [24.4;32.6]	24.2 [20.7;27.7]	27.6 [24.8;30.8]	29.0 [25.5;33.4]	31.4 [27.3;35.7]	<0.001
Gender:						<0.001
Male	565 (49.5%)	106 (37.1%)	141 (49.5%)	141 (49.5%)	177 (62.1%)	
Female	576 (50.5%)	180 (62.9%)	144 (50.5%)	144 (50.5%)	108 (37.9%)	
Weight	74.0 [62.0;88.0]	62.0 [52.0;74.0]	75.0 [66.0;86.0]	75.0 [64.0;90.0]	84.0 [68.0;100]	<0.001
Marital_status:						<0.001
Single	320 (28.0%)	82 (28.7%)	58 (20.4%)	70 (24.6%)	110 (38.6%)	
Divorced/ Widowed	255 (22.3%)	77 (26.9%)	82 (28.8%)	59 (20.7%)	37 (13.0%)	
Married	566 (49.6%)	127 (44.4%)	145 (50.9%)	156 (54.7%)	138 (48.4%)	
Race:						<0.001
White	749 (65.6%)	163 (57.0%)	179 (62.8%)	207 (72.6%)	200 (70.2%)	
No White	392 (34.4%)	123 (43.0%)	106 (37.2%)	78 (27.4%)	85 (29.8%)	
DBP	130 [120;145]	130 [118;144]	132 [120;148]	132 [120;143]	132 [120;145]	0.39
SBP	76.0 [67.0;82.0]	75.0 [64.0;82.0]	78.0 [70.0;82.0]	75.0 [68.0;82.0]	76.0 [64.5;85.0]	0.456
HR	83.0 [73.0;97.0]	82.0 [67.0;96.0]	83.0 [73.0;97.0]	83.0 [73.0;94.0]	86.0 [75.0;101]	0.037
RR	19.0 [15.0;22.0]	18.0 [15.0;22.0]	18.0 [15.0;21.0]	19.0 [16.0;22.0]	20.0 [17.0;22.0]	0.002
ALT	20.0 [15.0;31.0]	18.0 [13.0;26.0]	20.0 [14.0;28.0]	20.0 [15.0;32.8]	25.0 [17.0;36.8]	<0.001
Glucose	113 [96.0;156]	99.0 [89.0;110]	104 [91.0;125]	119 [101;163]	177 [132;273]	<0.001
Hba1c	5.90 [5.40;6.80]	5.60 [5.23;6.00]	5.80 [5.40;6.20]	6.00 [5.50;6.90]	6.90 [6.00;8.80]	<0.001
HDL-c	48.0 [37.0;62.0]	65.0 [53.0;76.0]	52.0 [43.0;62.0]	43.0 [36.0;53.0]	33.0 [28.0;42.0]	<0.001
TG	116 [85.0;168]	72.0 [58.0;87.8]	107 [87.0;125]	137 [107;170]	198 [150;257]	<0.001
AF	1141 (100%)	286 (100%)	285 (100%)	285 (100%)	285 (100%)	.
Coronary heart disease:						<0.001
No	584 (51.2%)	182 (63.6%)	155 (54.4%)	128 (44.9%)	119 (41.8%)	
Yes	557 (48.8%)	104 (36.4%)	130 (45.6%)	157 (55.1%)	166 (58.2%)	
Diabetes:						<0.001
No	569 (49.9%)	212 (74.1%)	177 (62.1%)	127 (44.6%)	53 (18.6%)	
Yes	572 (50.1%)	74 (25.9%)	108 (37.9%)	158 (55.4%)	232 (81.4%)	
Hyperlipidemia	1141 (100%)	286 (100%)	285 (100%)	285 (100%)	285 (100%)	.
Hypertension						0.032
No	323 (28.3%)	94 (32.9%)	63 (22.1%)	86 (30.2%)	80 (28.1%)	
Yes	818 (71.7%)	192 (67.1%)	222 (77.9%)	199 (69.8%)	205 (71.9%)	
Myocardial infarction						<0.001
No	765 (67.0%)	210 (73.4%)	206 (72.3%)	186 (65.3%)	163 (57.2%)	
Yes	376 (33.0%)	76 (26.6%)	79 (27.7%)	99 (34.7%)	122 (42.8%)	
Stroke	1141 (100%)	286 (100%)	285 (100%)	285 (100%)	285 (100%)	.
Alteplase						0.812
No	865 (75.8%)	217 (75.9%)	221 (77.5%)	216 (75.8%)	211 (74.0%)	
Yes	276 (24.2%)	69 (24.1%)	64 (22.5%)	69 (24.2%)	74 (26.0%)	

Aspirin						0.132
No	104 (9.11%)	34 (11.9%)	29 (10.2%)	21 (7.37%)	20 (7.02%)	
Yes	1037 (90.9%)	252 (88.1%)	256 (89.8%)	264 (92.6%)	265 (93.0%)	
Cilostazol						<0.001
No	1125 (98.6%)	286 (100%)	285 (100%)	283 (99.3%)	271 (95.1%)	
Yes	16 (1.40%)	0 (0.00%)	0 (0.00%)	2 (0.70%)	14 (4.91%)	
Clopidogrel						0.001
No	694 (60.8%)	186 (65.0%)	181 (63.5%)	183 (64.2%)	144 (50.5%)	
Yes	447 (39.2%)	100 (35.0%)	104 (36.5%)	102 (35.8%)	141 (49.5%)	
Tirofiban						0.011
No	1137 (99.6%)	286 (100%)	285 (100%)	285 (100%)	281 (98.6%)	
Yes	4 (0.35%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (1.40%)	
CRRT						0.047
No	1071 (93.9%)	267 (93.4%)	276 (96.8%)	268 (94.0%)	260 (91.2%)	
Yes	70 (6.13%)	19 (6.64%)	9 (3.16%)	17 (5.96%)	25 (8.77%)	
MV						0.001
No	589 (51.6%)	162 (56.6%)	162 (56.8%)	144 (50.5%)	121 (42.5%)	
Yes	552 (48.4%)	124 (43.4%)	123 (43.2%)	141 (49.5%)	164 (57.5%)	
APS III	38.0 [28.0;51.0]	38.0 [29.0;53.0]	36.0 [26.0;45.0]	38.0 [28.0;51.0]	41.0 [31.0;51.0]	0.015
GCS	15.0 [14.0;15.0]	15.0 [14.0;15.0]	15.0 [14.0;15.0]	15.0 [14.0;15.0]	15.0 [15.0;15.0]	0.008
OASIS	29.0 [24.0;36.0]	30.0 [26.0;37.0]	30.0 [24.0;35.0]	30.0 [24.0;36.0]	28.0 [24.0;35.0]	0.032
SAPS II	33.0 [26.0;41.0]	32.0 [26.0;39.8]	34.0 [27.0;41.0]	33.0 [26.0;41.0]	34.0 [27.0;42.0]	0.557
SIRS	2.00 [1.00;3.00]	2.00 [1.00;3.00]	2.00 [2.00;3.00]	2.00 [1.00;3.00]	2.00 [2.00;3.00]	0.149
SOFA	3.00 [2.00;6.00]	3.00 [1.00;5.00]	3.00 [2.00;5.00]	3.00 [2.00;6.00]	4.00 [2.00;6.00]	0.073
TyG	8.96 (0.76)	8.19 (0.34)	8.65 (0.31)	9.10 (0.34)	9.88 (0.65)	<0.001
TabCI	8.37 [7.75;9.08]	7.27 [6.99;7.50]	8.06 [7.89;8.23]	8.70 [8.54;8.90]	9.71 [9.35;10.1]	<0.001

Bmi: body mass Index; DBP: diastolic blood pressure; SBP: systolic pressure; HR: heart rate; RR: respiratory rate; ALT: alanine aminotransferase; Hba1c: Hemoglobin; HDL-c: High-density lipoprotein cholesterol; TG: triglycerides; AF: Atrial fibrillation; CRRT: continuous renal replacement therapy; MV: mechanical ventilation; APSIII: acute physiology score-III; GCS: glasgow Coma Scale; OASIS: oxford acute severity of illness score; SAPSII: simplified Acute Physiology Score II; SIRS: systemic Inflammatory Response Syndrome; SOFA: sequential organ failure estimate; TyG: triglyceride-glucose index; TabCI: TyG-AIP-BMI Composite Index;

prognostically relevant covariates were selected, including age, DBP, heart rate, respiratory rate, atrial fibrillation, coronary heart disease, diabetes, myocardial infarction, alteplase use, cilostazol use, clopidogrel use, tirofiban use, mechanical ventilation, APACHE III score, and SAPS II score.

To explore the independent effect of TabCI on long-term all-cause mortality in stroke patients, we employed three Cox proportional hazards regression models (Table 2). Model 1 was unadjusted for covariates, Model 2 adjusted for age, DBP, heart rate, and respiratory rate, and Model 3 further adjusted for age, DBP, heart rate, respiratory rate, atrial fibrillation, coronary heart disease, diabetes, myocardial infarction, alteplase use, cilostazol use, clopidogrel use, tirofiban use, mechanical ventilation, APACHE III score, and SAPS II score.

In Model 3, we observed that the hazard ratios (HRs) and 95% confidence intervals (CIs) for TabCI predicting all-cause mortality at 90 days, 180 days, and 1 year were 0.74 (0.64-0.86), 0.77 (0.68-0.88), and 0.85 (0.76-0.95) respectively, with corresponding P-values of <0.001, <0.001, and 0.004 (Table 2).

Using the lowest quartile of TabCI (Q1) as reference, the hazard ratios (HRs) and 95% CIs for Q2/Q3/Q4 predicting 180-day all-cause mortality were 0.55 (0.39-0.76), 0.72 (0.52-0.99), and 0.47 (0.33-0.68) respectively, with corresponding P-values of <0.001, 0.041, and <0.001, indicating statistically significant differences.

Secondary outcomes showed that for 90-day all-cause mortality, the hazard ratios were 0.61 (0.43-0.88), 0.73 (0.51-1.04), and 0.45 (0.29-0.68) with corresponding P-values of 0.009, 0.085, and <0.001. For 1-year all-cause mortality, the hazard ratios were 0.56 (0.41-0.77), 0.77 (0.57-1.03), and 0.57 (0.41-0.78) with corresponding P-values of <0.001, 0.076, and <0.001. Results indicated

Table 2: Multivariable Cox proportional hazard models for long-term all-cause mortality

Variable	Model I HR	95% CI	P-value	Model II HR	95% CI	P-value	Model III HR	95% CI	P-value
90-d mortality									
TabCI	0.9	0.80-1.01	0.071	0.84	0.73-0.95	0.007	0.74	0.64-0.86	<0.001
Q1									
Q2	0.74	0.53-1.02	0.068	0.68	0.47-0.96	0.03	0.61	0.43-0.88	0.009
Q3	0.94	0.69-1.29	0.7	0.91	0.65-1.27	0.6	0.73	0.51-1.04	0.085
Q4	0.66	0.47-0.93	0.017	0.61	0.42-0.9	0.011	0.45	0.29-0.68	<0.001
180-d mortality									
TabCI	0.92	0.83-1.02	0.11	0.86	0.76-0.96	0.01	0.77	0.68-0.88	<0.001
Q1									
Q2	0.68	0.51-0.92	0.013	0.60	0.44-0.84	0.002	0.55	0.39-0.76	<0.001
Q3	0.96	0.72-1.27	0.8	0.89	0.66-1.20	0.5	0.72	0.52-0.99	0.041
Q4	0.69	0.51-0.94	0.017	0.63	0.45-0.88	0.007	0.47	0.33-0.68	<0.001
1-year mortality									
TabCI	1.01	0.92-1.11	0.8	0.97	0.87-1.07	0.5	0.85	0.76-0.95	0.004
Q1									
Q2	0.68	0.51-0.91	0.008	0.62	0.46-0.84	0.002	0.56	0.41-0.77	<0.001
Q3	1.05	0.81-1.36	0.7	0.98	0.74-1.29	0.9	0.77	0.57-1.03	0.076
Q4	0.88	0.67-1.14	0.3	0.83	0.62-1.11	0.2	0.57	0.41-0.78	<0.001

statistical significance for all groups except Q3 in 90 days and 1 year. These findings were consistent with Kaplan-Meier curve analysis, showing that stroke patients with TabCI indices in the ranges of (7.75-8.37) and (9.08-13.1) faced higher long-term all-cause mortality risks compared to those in the ranges of (5.88-7.75) and (8.37-9.08) (Table 2).

The detection of nonlinear relationships

RCS analysis reveals a gradual L-shaped relationship between TabCI and all-cause mortality at 90 and 180 days among stroke patients. The presence of a threshold effect is evident from the graph, indicating that beyond a certain TabCI threshold, the risk of death does not significantly increase with further TabCI elevation. Conversely, a gradual U-shaped relationship is observed in 1-year all-cause mortality, suggesting that both low and high TabCI levels increase the risk of death at 1 year. Specifically, significant nonlinearity is observed only in the RCS curve for 1-year all-cause mortality, with P nonlinear = 0.0035 and P overall = 0.105 (Figure 5C).However, similar significant trends were not observed in the RCS curves for 90-day and 180-day all-cause mortality among stroke patients (90 days: P nonlinear = 0.227, P overall = 0.083; 180 days: P nonlinear = 0.127, P overall = 0.08), as shown in Figures 5A and 5B.

Main results

Kaplan-Meier curves indicated changes in all-cause mortality (ACM) across quartiles of TabCI at 90 days, 180 days, and 1 year (Figure 4). Importantly, there was no discernible trend of positive or negative correlation between long-term survival rates and quartiles of TabCI, whether for the primary outcome of 180-day mortality risk or secondary outcomes at 90 days or 1 year. However, patients in the Q1 and Q3 groups exhibited significantly lower long-term survival rates compared to those in the Q2 and Q4 groups, with corresponding p-values of 0.049 for the primary outcome at 180 days and 0.015 and 0.014 for the secondary outcomes at 90 days and 1 year, respectively (Figure 4).

To better elucidate the underlying trends, patients were stratified into ten groups based on deciles of the TabCI. ACM was assessed at 90 days, 180 days, and 1 year, with the grouping details presented in Table S2. At the 1-year follow-up, patients in the Q4 (7.87–8.12) and Q5 (8.13–8.37) groups exhibited significantly higher survival rates compared to other deciles (P = 0.046). However, no statistically significant differences were observed in mortality at 90 or 180 days (P > 0.05) (Figure 5).

Subsequently, we assessed the clinical predictive performance of TabCI for mortality using receiver operating characteristic (ROC)

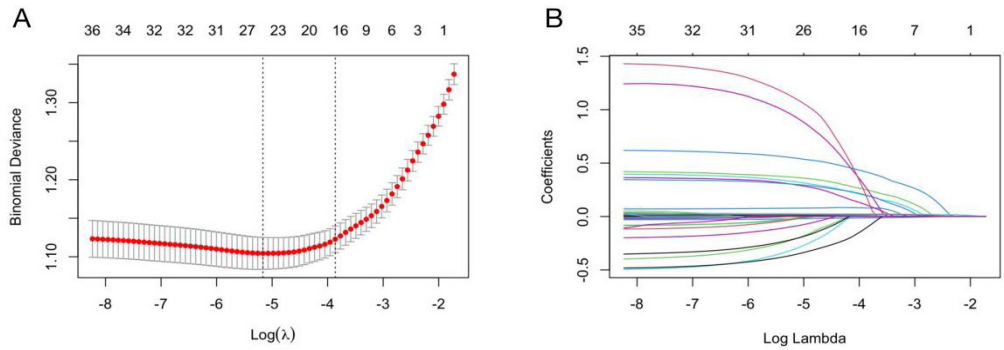


Figure 2. Lasso regression results
A. Cross-validation curve; B. Lasso coefficient path

curves. However, the area under the curve (AUC) values indicated limited predictive ability: AUC for primary outcome at 180 days was 0.543, and for secondary outcomes, AUC was 0.541 at 90 days and 0.561 at 1 year (Figure 6). Then, We grouped the participants based on the quartiles of TabCI and observed the predictive effects of these four groups on long-term mortality events (Figure S2). Moreover, patients were also stratified into deciles based on the TabCI score to evaluate the clinical predictive performance of each group in relation to mortality. The corresponding results are presented in Figure S3 and Table S3.

Notably, compared to the traditional TyG index, the TabCI index shows a slight advantage in predicting long-term all-cause mortality in stroke patients. The AUC values for the TyG index in predicting long-term all-cause mortality are as follows: 90 days: 0.506; 180 days: 0.505; 1 year: 0.482 (Figure S4).

Subgroup analysis

Subgroup analyses and interaction tests were conducted based on age (≤65 years or >65 years), gender, ethnicity, coronary heart disease, type 2 diabetes, hypertension, myocardial infarction, aspirin use, cilostazol use, clopidogrel use, tirofiban use, CRRT (continuous renal replacement therapy), and MV (mechanical ventilation) (Figure 7).

The study findings reveal a significant association between lower mortality risk in subgroups of non-white stroke patients and TabCI, with HR (95% CI) of 0.68 (0.55-0.84) at 90 days, 0.75 (0.63-0.9) at 180 days, and 0.79 (0.67-0.94) at 1 year. Conversely, higher mortality rates in subgroups of white stroke patients are associated with TabCI, with HR (95% CI) of 1.04 (0.9-1.19) at 90 days, 1.03 (0.91-1.17) at 180 days, and 1.14 (1.02-1.27) at 1 year, all statistically significant (90 days [P<0.001], 180 days [P=0.001], 1 year [P=0.006]).

Interestingly, higher TabCI scores were significantly associated with increased mortality among stroke patients without pre-existing hyperlipidemia, with hazard ratios of 1.24 (95% CI: 1.03–1.50) at 90 days, 1.16 (95% CI: 0.96–1.41) at 180 days, and 1.22 (95% CI: 1.02–1.46) at 1 year. In contrast, higher TabCI scores were associated with lower mortality in the subgroup of stroke patients with hyperlipidemia, with hazard

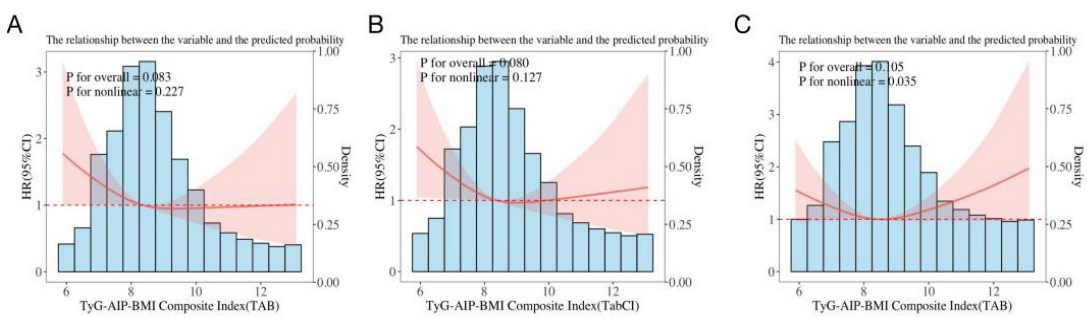


Figure 3. RCS curves for patients with severe ischemic stroke
A. Relationship between TabCI and 90-day mortality risk; B. Relationship between TabCI and 180-day mortality risk; C. Relationship between TabCI and 1-year mortality risk;

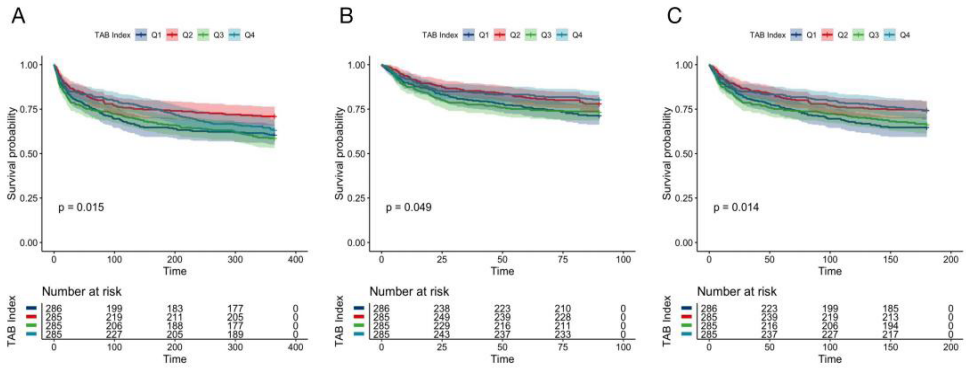


Figure 4. Kaplan-Meier survival analysis curves for patients with severe ischemic stroke
A. Cumulative incidence of death at 90 days; B. Cumulative incidence of death at 180 days; C. Cumulative incidence of death at 1 year

ratios of 0.79 (95% CI: 0.69–0.91) at 90 days, 0.85 (95% CI: 0.75–0.96) at 180 days, and 0.95 (95% CI: 0.85–1.05) at 1 year. These findings were statistically significant at all time points (90 days: P < 0.001; 180 days: P = 0.005; 1 year: P = 0.012).

Regarding aspirin use, significant associations are observed between TabCI and lower mortality rates in subgroups of stroke patients receiving aspirin antiplatelet therapy, with HR (95% CI) of 0.86 (0.76–0.98) at 90 days, 0.88 (0.79–0.98) at 180 days, and 0.97 (0.88–1.07) at 1 year. Conversely, higher mortality rates in subgroups of stroke patients not receiving aspirin antiplatelet therapy are associated with TabCI, with HR (95% CI) of 1.25 (0.9-1.73) at 90 days, 1.34 (0.99-1.83) at 180 days, and 1.42 (1.06-1.91) at 1 year, all statistically significant (90 days [P=0.029], 180 days [P=0.007], 1 year [P=0.008]).

Additionally, among stroke patients not receiving CRRT treatment, TabCI significantly reduces the risk of death at 90 days and 180 days, with HR (95% CI) of 0.83 (0.73–0.95, P=0.007) and 0.88 (0.78–0.98, P=0.032), respectively. Notably, among stroke patients not receiving CRRT treatment, lower TabCI does not significantly benefit 1-year mortality risk (HR 0.99, 95% CI 0.9–1.1, P=0.412), indicating no statistically significant effect.

DISCUSSION

This study introduces a novel index, TabCI, combining TyG, AIP, and BMI for the first time, and explores its correlation with long-term mortality risk in severe ischemic stroke patients.

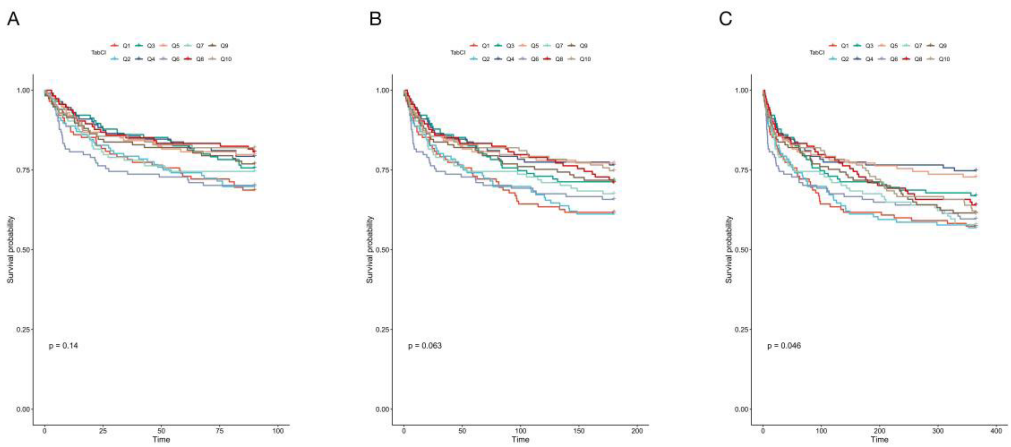


Figure 5. Kaplan–Meier survival curves across TabCI deciles in patients with severe ischemic stroke
A. Cumulative incidence of death at 90 days; B. Cumulative incidence of death at 180 days; C. Cumulative incidence of death at 1 year

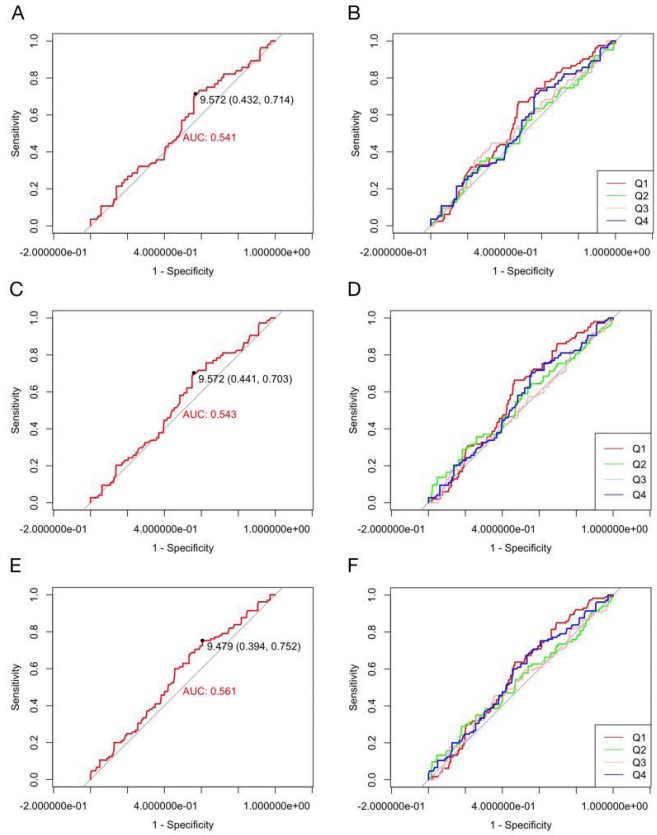
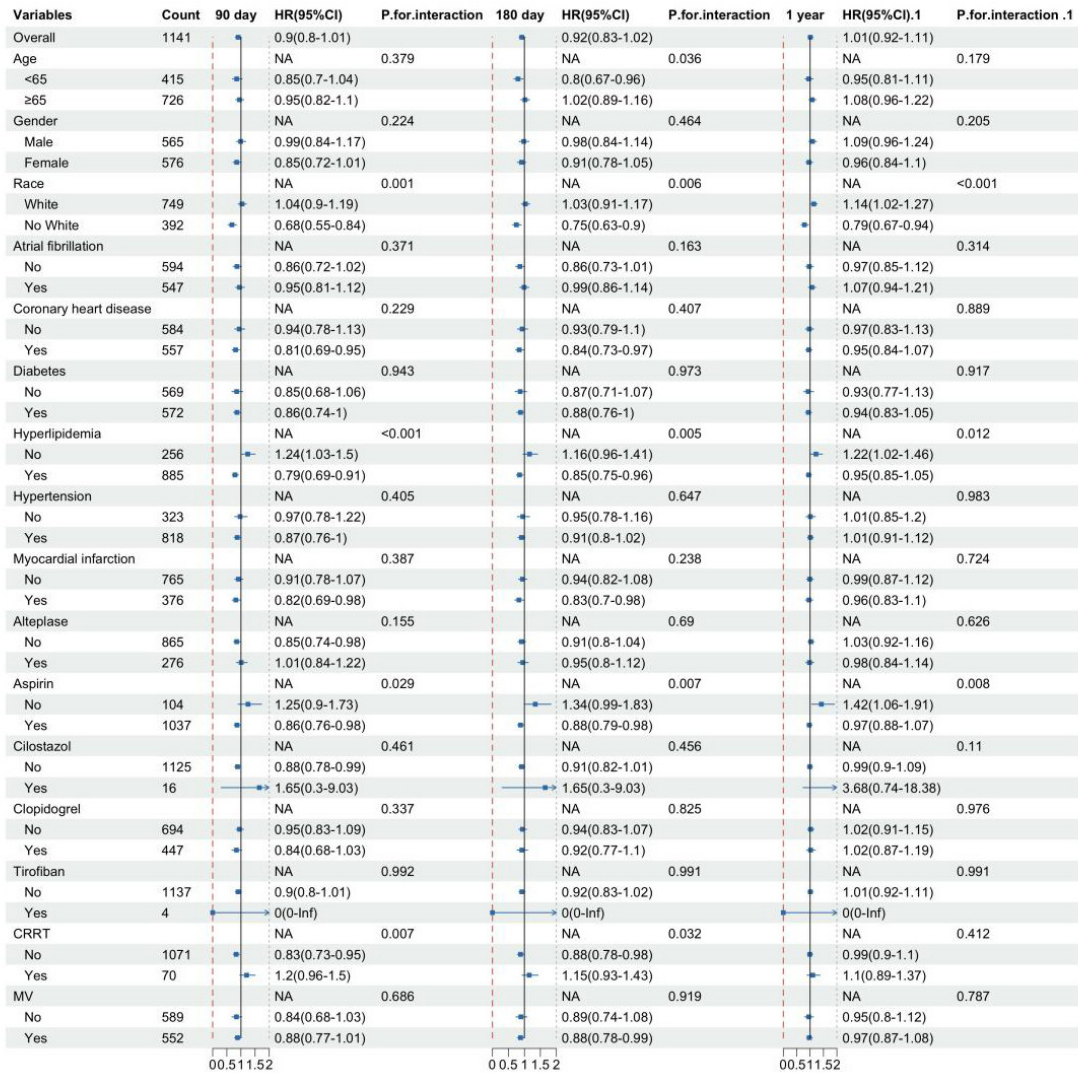


Figure 6. Receiver operating characteristic (ROC) curves for severe ischemic stroke patients
A. Prediction of 90-day mortality risk by TabCI; B. Prediction of 90-day mortality risk by quartile groups of TabCI; C. Prediction of 180-day mortality risk by TabCI; D. Prediction of 180-day mortality risk by quartile groups of TabCI; E. Prediction of 1-year mortality risk by TabCI; F. Prediction of 1- year mortality risk by quartile groups of TabCI

TyG was initially identified as a pathophysiological marker for obesity, metabolic syndrome, and insulin resistance in diabetes.[8] Insulin resistance is closely associated with stroke and serves as an independent predictor of stroke onset and progression in hospitalized patients.[14,15] Recently, TyG has been reported as a clinical prognostic indicator for cardiovascular disease incidence and mortality risk.[16] This index primarily incorporates fasting glucose and serum triglycerides, two key laboratory indicators closely associated with stroke incidence and progression. Blood glucose levels are associated with multiple pathological changes leading to stroke, such as arteriosclerosis and microcirculatory disturbances.[17] Analysis of multicenter RCT data from Solitaire Flow Restoration With Intention for Thrombectomy (SWIFT) indicates that participants with baseline serum glucose levels >7.8 mmol/L (140 mg/dL) have a higher risk of functional deterioration at 3 months.[18] Meanwhile, higher serum glucose was also a predictor of adverse outcomes at three months after ischemic stroke.[19] The relationship between TGs and ischemic stroke has been extensively studied, and a large body of evidence indicates that hypertriglyceridemia is a risk factor for ischemic stroke, and the multifactor-adjusted hazard ratio (HR) and 95% confidence interval (CI) for ischemic stroke are 1.07 (95%CI, 95%CI) for every 1 mmol/l increase in triglycerides. 1.05 to 1.09).[20] Combining TyG with obesity metrics such as Body Mass Index (BMI), Waist Circumference (WC), and Waist-to-Height Ratio (WtHR) significantly enhances the accuracy of insulin assessment.[21]

This study categorized subjects into four groups based on TabCI quartiles and examined their long-term mortality rates. Our Kaplan-Meier survival analysis revealed no significant correlation between TabCI quartiles and long-term survival rates at 90 days, 180 days, or 1 year. However, notably, patients in Q1 and Q3 exhibited significantly lower long-term survival rates compared to those in Q2 and Q4 at these



Variables	Count	90 day	HR(95%CI)	P.for.interaction	180 day	HR(95%CI)	P.for.interaction	1 year	HR(95%CI).1	P.for.interaction .1
Overall	1141		0.9(0.8-1.01)			0.92(0.83-1.02)			1.01(0.92-1.11)	
Age			NA	0.379		NA	0.036		NA	0.179
<65	415		0.85(0.7-1.04)			0.8(0.67-0.96)			0.95(0.81-1.11)	
≥65	726		0.95(0.82-1.1)			1.02(0.89-1.16)			1.08(0.96-1.22)	
Gender			NA	0.224		NA	0.464		NA	0.205
Male	565		0.99(0.84-1.17)			0.98(0.84-1.14)			1.09(0.96-1.24)	
Female	576		0.85(0.72-1.01)			0.91(0.78-1.05)			0.96(0.84-1.1)	
Race			NA	0.001		NA	0.006		NA	<0.001
White	749		1.04(0.9-1.19)			1.03(0.91-1.17)			1.14(1.02-1.27)	
No White	392		0.68(0.55-0.84)			0.75(0.63-0.9)			0.79(0.67-0.94)	
Atrial fibrillation			NA	0.371		NA	0.163		NA	0.314
No	594		0.86(0.72-1.02)			0.86(0.73-1.01)			0.97(0.85-1.12)	
Yes	547		0.95(0.81-1.12)			0.99(0.86-1.14)			1.07(0.94-1.21)	
Coronary heart disease			NA	0.229		NA	0.407		NA	0.889
No	584		0.94(0.78-1.13)			0.93(0.79-1.1)			0.97(0.83-1.13)	
Yes	557		0.81(0.69-0.95)			0.84(0.73-0.97)			0.95(0.84-1.07)	
Diabetes			NA	0.943		NA	0.973		NA	0.917
No	569		0.85(0.68-1.06)			0.87(0.71-1.07)			0.93(0.77-1.13)	
Yes	572		0.86(0.74-1)			0.88(0.76-1)			0.94(0.83-1.05)	
Hyperlipidemia			NA	<0.001		NA	0.005		NA	0.012
No	256		1.24(1.03-1.5)			1.16(0.96-1.41)			1.22(1.02-1.46)	
Yes	885		0.79(0.69-0.91)			0.85(0.75-0.96)			0.95(0.85-1.05)	
Hypertension			NA	0.405		NA	0.647		NA	0.983
No	323		0.97(0.78-1.22)			0.95(0.78-1.16)			1.01(0.85-1.2)	
Yes	818		0.87(0.76-1)			0.91(0.8-1.02)			1.01(0.91-1.12)	
Myocardial infarction			NA	0.387		NA	0.238		NA	0.724
No	765		0.91(0.78-1.07)			0.94(0.82-1.08)			0.99(0.87-1.12)	
Yes	376		0.82(0.69-0.98)			0.83(0.7-0.98)			0.96(0.83-1.1)	
Alteplase			NA	0.155		NA	0.69		NA	0.626
No	865		0.85(0.74-0.98)			0.91(0.8-1.04)			1.03(0.92-1.16)	
Yes	276		1.01(0.84-1.22)			0.95(0.8-1.12)			0.98(0.84-1.14)	
Aspirin			NA	0.029		NA	0.007		NA	0.008
No	104		1.25(0.9-1.73)			1.34(0.99-1.83)			1.42(1.06-1.91)	
Yes	1037		0.86(0.76-0.98)			0.88(0.79-0.98)			0.97(0.88-1.07)	
Cilostazol			NA	0.461		NA	0.456		NA	0.11
No	1125		0.88(0.78-0.99)			0.91(0.82-1.01)			0.99(0.9-1.09)	
Yes	16		1.65(0.3-9.03)			1.65(0.3-9.03)			3.68(0.74-18.38)	
Clopidogrel			NA	0.337		NA	0.825		NA	0.976
No	694		0.95(0.83-1.09)			0.94(0.83-1.07)			1.02(0.91-1.15)	
Yes	447		0.84(0.68-1.03)			0.92(0.77-1.1)			1.02(0.87-1.19)	
Tirofiban			NA	0.992		NA	0.991		NA	0.991
No	1137		0.9(0.8-1.01)			0.92(0.83-1.02)			1.01(0.92-1.11)	
Yes	4		0(0-Inf)			0(0-Inf)			0(0-Inf)	
CRRT			NA	0.007		NA	0.032		NA	0.412
No	1071		0.83(0.73-0.95)			0.88(0.78-0.98)			0.99(0.9-1.1)	
Yes	70		1.2(0.96-1.5)			1.15(0.93-1.43)			1.1(0.89-1.37)	
MV			NA	0.686		NA	0.919		NA	0.787
No	589		0.84(0.68-1.03)			0.89(0.74-1.08)			0.95(0.8-1.12)	
Yes	552		0.88(0.77-1.01)			0.88(0.78-0.99)			0.97(0.87-1.08)	

Figure 7. Forest plot of subgroup analysis of TabCI and long-term mortality risk in patients with severe ischemic stroke

time points. This suggests higher survival rates among severe ischemic stroke patients when TabCI ranges between 7.89-8.23 and 9.35-10.1.In contrast to traditional TyG index, we conducted ROC curve analyses using overall TabCI and quartiles to further explore its diagnostic efficacy for predicting long-term survival rates in severe ischemic stroke patients. Although TabCI did not demonstrate high specificity in predicting long-term survival, its AUC was slightly higher than that of TyG. However, this marginal improvement lacks statistical significance, and therefore should be interpreted with caution. Further studies with appropriate statistical comparisons are required to validate whether TabCI offers a clinically meaningful advantage over TyG. This superiority may be attributed to TabCI's integration with the Atherogenic Index of Plasma (AIP).The AIP is a novel biomarker in today's era of cardiovascular disease, proven to be positively associated with the risk of cardiovascular disease mortality.[22] Our TabCI index combines the TyG index with two other metabolic markers, thereby enhancing the accuracy of prognosis diagnosis for cardiovascular disease patients to some extent.

Furthermore, this study examined the association between TabCI levels and all-cause mortality at 90 days, 180 days, and 1 year. An L-shaped association was observed at 90 and 180 days, suggesting that lower TabCI levels were associated with a modestly increased risk of short-term mortality. For 1-year mortality, however, a

U-shaped trend emerged, indicating increased mortality risk at both low and high ends of the TabCI spectrum. To further validate this non-linear relationship and assess the potential threshold effect, we conducted sensitivity analyses using tertile and decile-based stratifications of TabCI. The decile-based Kaplan–Meier analysis revealed that patients in the fourth (7.87–8.12) and fifth (8.13–8.37) deciles had the highest 1-year survival rates, with statistically significant differences across deciles (log-rank p = 0.046), while no significant survival differences were observed at 90 or 180 days. Tertile-based grouping did not yield significant results at any timepoint.

These findings suggest that the originally observed non-monotonicity, particularly the lower survival in the Q3 group, may reflect true biological or clinical thresholds rather than simple index instability. Nonetheless, further validation in independent cohorts is needed. Our results highlight the importance of considering non-linear patterns when applying TabCI in clinical settings. These findings suggest a potential association between specific TabCI ranges ((7.87–8.12) and (8.13–8.37)) and improved survival outcomes. While this points to a possible value of TabCI in risk stratification, the current evidence remains preliminary, and further validation is needed before its clinical application as a long-term prognostic marker can be confirmed.

Finally, to gain deeper insights into the impact of TabCI on long-term mortality among critically ill stroke patients, we conducted subgroup analyses adjusting for multiple covariates. We observed a significant association between lower TabCI and increased mortality rates at 180 days, 90 days, and 1 year among non-Caucasian stroke patients who received aspirin intervention. Timely antiplatelet therapy is universally recognized by guidelines to improve neurological outcomes and reduce mortality risks for ischemic stroke patients. Guidelines recommend administering aspirin within 48 hours of ischemic stroke onset, aligning with overall patient benefits.[23] Previous studies have indicated that compared to Caucasians, African-American, Hispanic, and other ethnic/racial groups have a higher compliance rate with fenofibrate oral intake, leading to a greater reduction in triglyceride levels.[24] This suggests higher adherence to treatment regimens among these groups compared to Caucasians. Furthermore, we observed a significant inverse relationship between higher TabCI and reduced 90-day and 180-day mortality risks among stroke patients who did not receive CRRT treatment. Conversely, this trend was reversed in stroke patients who received CRRT, possibly due to renal impairment and the severity of their condition. Renal dysfunction often accompanies metabolic abnormalities, which can exacerbate dyslipidemia and hyperglycemia, thereby increasing adverse cardiovascular events.[25]

It is important to note the limitations of this study. Firstly, it is a single-center retrospective study relying on observational data retrieved from the MIMIC-IV database, which presents challenges in establishing definitive causal relationships. Secondly, the study included a relatively small sample size of only 1141 cases, all of whom were critically ill ischemic stroke patients treated in the United States. To comprehensively evaluate the predictive performance of this index in the real world, exploration among other mild stroke or TIA patients is warranted. Additionally, the inclusion was limited to the United States, with no reported studies on Asians, particularly Chinese individuals. Lastly, our primary outcome measure was long-term all-cause mortality rather than stroke-related mortality, which may be influenced by numerous uncontrollable factors. Despite adjusting for many variables and conducting subgroup analyses, the potential impact of unmeasured confounders cannot be completely ruled out. Future research will involve large-scale longitudinal studies among Chinese and other Asian populations to strengthen the conclusions of this study.

In conclusion, TabCI demonstrated a gradual L-shaped correlation with 90-day and 180-day all-cause mortality, and a flattened U-shaped trend with 1-year mortality among severe ischemic stroke patients. These findings indicate a potential non-linear relationship between TabCI levels and mortality risk, with certain intermediate ranges associated with better survival outcomes.

However, the clinical predictive efficacy of TabCI remains limited, and its potential as a long-term risk stratification marker is not yet conclusive. Although TabCI showed marginally better AUC values compared to TyG, this improvement lacks statistical significance. Therefore, TabCI may serve as an exploratory indicator to assist in risk stratification, but cannot yet be considered a reliable or superior prognostic tool. Further large-scale, multi-center, and prospective studies across diverse populations are warranted to validate its utility and compare its performance against existing markers.

DISCLOSURE

Data availability: All data are publicly available in MIMIC-IV (https://charls.charlsdata.com).

Financial support: This study was supported by: 1. Project of "XingLin Scholars Training" of Chengdu University of Traditional Chinese Medicine (No. YYZX2022170); 2. Training Plan of "100 professionals" of Shanghai Putuo District Central Hospital (No.2022-RCJC-05); 3. Shanghai Putuo District Health System Clinical Characteristic Special Disease Construction Project (No. 2023tszb04); 4. Science and Technology Innovation Project of Putuo District Health System (No. ptkwws202301).

Conflict of interest: None

REFERENCES

1. GBD 2016 Lifetime Risk of Stroke Collaborators, Feigin VL, Nguyen G, Cercy K, et al. Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016. *N Engl J Med* 2018; 379:2429-37. doi: 10.1056/NEJMoa1804492
2. Chen Y, Wright N, Guo Y, *et al*. Mortality and recurrent vascular events after first incident stroke: a 9-year communitybased study of 0·5 million Chinese adults. *Lancet Glob Health* 2020; 8:e580-90. doi: 10.1016/S2214-109X(20)30069-3
3. Zhao J, Su YY, Zhang Y, *et al*. Decompressive hemicraniectomy in malignant middle cerebral artery infarct: a randomized controlled trial enrolling patients up to 80 years old. *Neurocrit Care* 2012;17(2):161-71. doi: 10.1007/s12028-012-9703-3.
4. Jüttler E, Schwab S, Schmiedek P, *et al*. Decompressive surgery for the treatment of malignant infarction of the Middle Cerebral Artery (DESTINY): a randomized, controlled trial. *Stroke* 2007;38(9):2518-25. doi: 10.1161/STROKEAHA.107.485649.
5. Vahedi K, Vicaut E, Mateo J, *et al*. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). *Stroke* 2007;38(9):2506-17. doi: 10.1161/STROKEAHA.107.485235.
6. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol* 2018;17(1):122. doi: 10.1186/s12933-018-0762-4.
7. Ding PF, Zhang HS, Wang J, *et al*. Insulin resistance in ischemic stroke: Mechanisms and therapeutic approaches. *Front Endocrinol* (Lausanne). 2022;13:1092431. doi: 10.3389/fendo.2022.1092431.
8. Hill MA, Yang Y, Zhang L, *et al*. Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism* 2021;119:154766. DOI: 10.1016/j.metabol.2021.154766.
9. Dang K, Wang X, Hu J, *et al*. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003-2018. *Cardiovasc Diabetol* 2024;23(1):8. doi:10.1186/s12933-023-02115-9.
10. Li W, Shen C, Kong W, *et al*. Association between the triglyceride glucose-body mass index and future cardiovascular disease risk in a population with Cardiovascular-Kidney-Metabolic syndrome stage 0-3: a nationwide prospective cohort study. *Cardiovasc Diabetol* 2024;23(1):292. doi:10.1186/s12933-024-02352-6.
11. Li F, Wang Y, Shi B, *et al*. Association between the cumulative average triglyceride glucose-body mass index and cardiovascular disease incidence among the middle-aged and older population: a prospective nationwide cohort study in China. *Cardiovasc Diabetol* 2024;23(1):16. doi:10.1186/s12933-023-02114-w.
12. Qu L, Fang S, Lan Z, *et al*. Association between atherogenic index of plasma and new-onset stroke in individuals with different glucose metabolism status: insights from CHARLS. *Cardiovasc Diabetol* 2024;23(1):215. doi: 10.1186/s12933-024-02314-y.
13. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. *Stroke* 1991;22(3):312-8. doi:10.1161/01.str.22.3.312.
14. Huang Q, Yin L, Liu Z, *et al*. Association of novel lipid indicators with the risk of stroke among participants in Central China: a population-based prospective study. *Front Endocrinol* (Lausanne). 2023;14:1266552. doi: 10.3389/fendo.2023.1266552.
15. Yang Y, Huang X, Wang Y, *et al*. The impact of triglyceride-glucose index on ischemic stroke: a systematic review and meta-analysis. *Cardiovasc Diabetol* 2023;22(1):2. doi: 10.1186/s12933-022-01732-0.
16. Yu H, Tao L, Li Y G, *et al*. Association between triglyceride-glucose index trajectories and carotid atherosclerosis progression. *Cardiovasc Diabetol* 2023; 22(1). DOI:10.1186/s12933-023-01847-y.
17. Sacco S, Foschi M, Ornello R, De Santis F, Pofi R, Romoli M. Prevention and treatment of ischaemic and haemorrhagic stroke in people with diabetes mellitus: a focus on glucose control and comorbidities. *Diabetologia* 2024;67(7):1192-205. doi: 10.1007/s00125-024-06146-z.
18. Kim JT, Jahan R, Saver JL; SWIFT Investigators. Impact of glucose on outcomes in patients treated with mechanical thrombectomy: A post hoc analysis of the Solitaire flow restoration with the Intention for Thrombectomy Study. *Stroke* 2016;47(1):120-7. doi: 10.1161/STROKEAHA.115.010753.
19. Zeinhom MG, Khalil MFE, Kamel IFM, *et al*. Predictors of the unfavorable outcomes in acute ischemic stroke patients treated with alteplase, a multi-center randomized trial. *Sci Rep* 2024;14(1):5960. doi:10.1038/s41598-024-56067-5.
20. Gu X, Li Y, Chen S, *et al*. Association of lipids with ischemic and hemorrhagic stroke: A prospective cohort study among 267,500 Chinese. *Stroke* 2019;50(12):3376-84. doi: 10.1161/STROKEAHA.119.026402.

21. Bala C, Gheorghe-Fronea O, Pop D, *et al*. The association between six surrogate insulin resistance indexes and hypertension: A population-based study. *Metab Syndr Relat Disord* 2019;17(6):328-33. doi: 10.1089/met.2018.0122.
22. Rabiee Rad M, Ghasempour Dabaghi G, Darouei B, Amani-Beni R. The association of atherogenic index of plasma with cardiovascular outcomes in patients with coronary artery disease: A systematic review and meta-analysis. *Cardiovasc Diabetol* 2024;23(1):119. doi: 10.1186/s12933-024-02198-y.
23. Jauch EC, Saver JL, Adams HP Jr, *et al*. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44(3):870-947. doi: 10.1161/STR.0b013e318284056a.
24. Cromer SJ, Thaweethai T, Wexler DJ. Racial/ethnic and socioeconomic disparities in achievement of treatment goals within a clinical trial: a secondary analysis of the ACCORD trial. *Diabetologia* 2023;66(12):2261-74. doi: 10.1007/s00125-023-05997-2.
25. Ndumele CE, Neeland IJ, Tuttle KR, *et al*. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: A scientific statement from the American Heart Association. *Circulation* 2023;148(20):1636-64. doi: 10.1161/CIR.0000000000001186.

Supplementary material

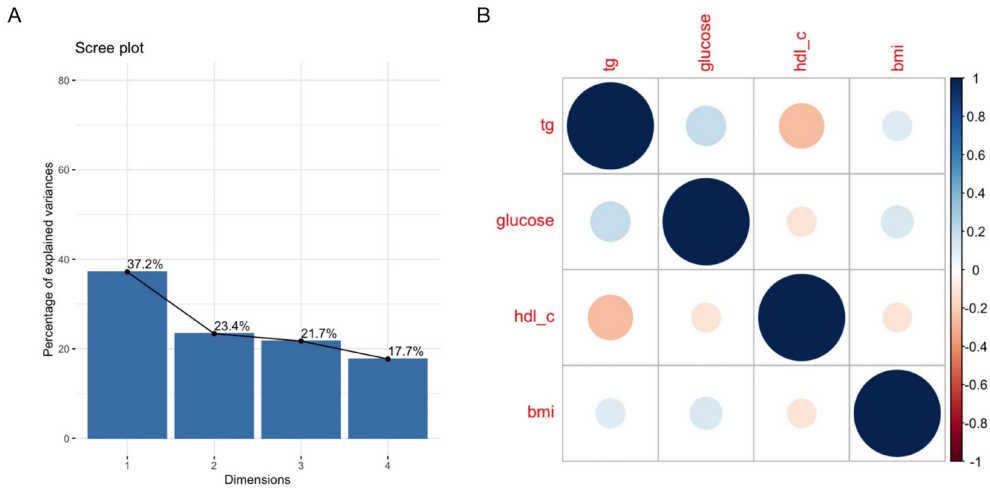


Fig.S1. Scree Plot and Correlation Heatmap of TabCI Components

A.Scree Plot. B. Correlation Heatmap

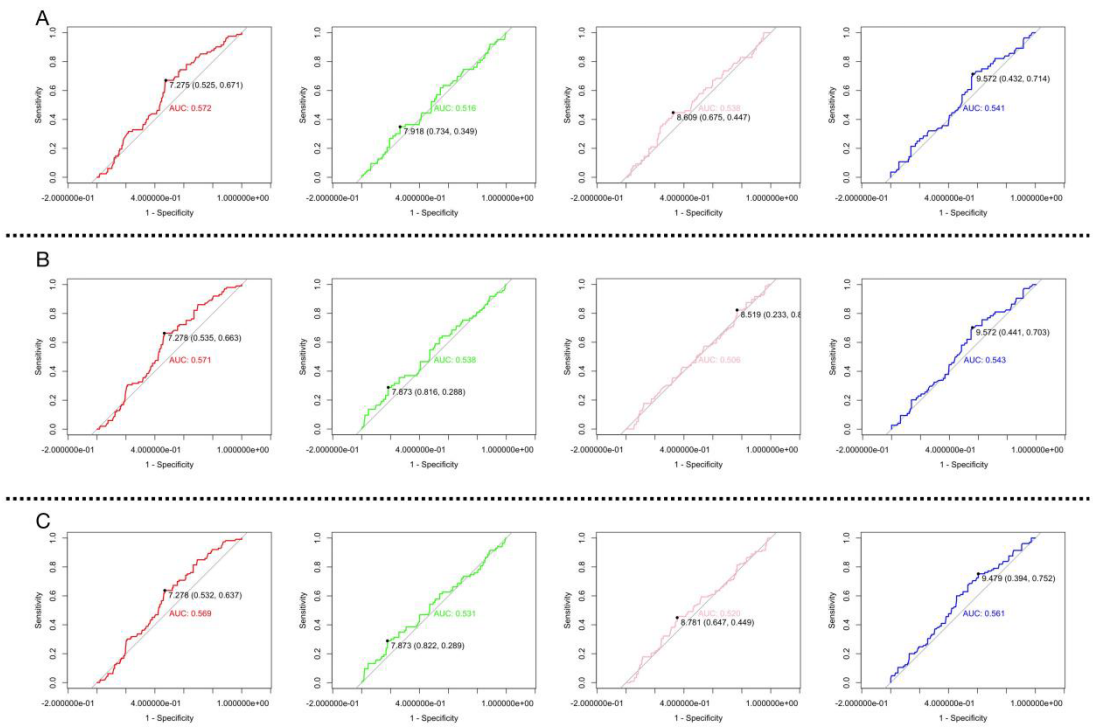


Fig.S2. Receiver operating characteristic (ROC) curve of TabCI in patients with severe ischemic stroke

A.90 days. B. 180 days. C. 1 year

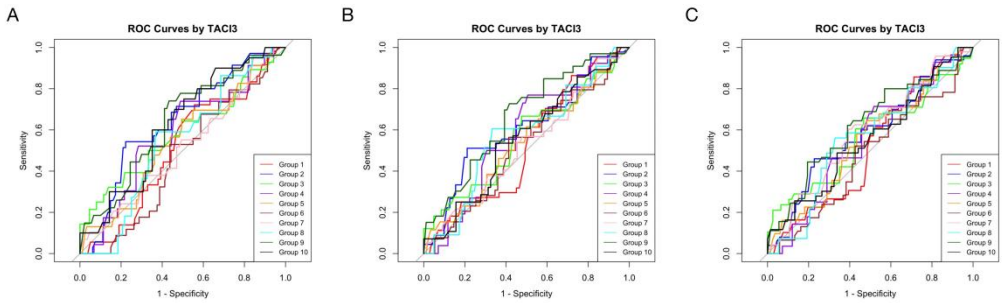


Fig.S3. Receiver operating characteristic (ROC) curve of TabCI in patients with severe ischemic stroke

A.90 days. B. 180 days. C. 1 year

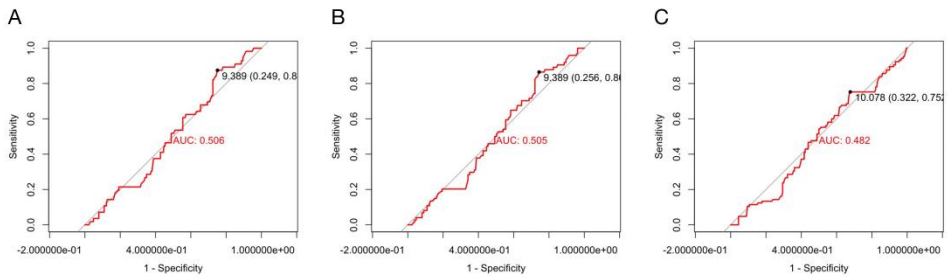


Fig.S4. Receiver operating characteristic (ROC) curve of TyG in patients with severe ischemic stroke

A. 90 days. B. 180 days. C. 1 year