Cardiovascular Diabetology

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Associations of triglyceride glucose-body mass index with short-term mortality in critically ill patients with ischemic stroke

Qingrong Ouyang[1], Lei Xu[1] and Ming Yu[1*]

Abstract

Background The triglyceride glucose-body mass index (TyG-BMI) has been established as a convenient and reliable marker for assessing insulin resistance (IR) and has been shown to be significantly correlated with stroke. However, only a few studies have been conducted in this field, with conflicting conclusions.

Methods This study based on the eICU database, investigated the association between TyG-BMI and 28-day mortality in critically ill ischemic stroke (IS) patients. Multivariate Cox regression models were employed to analyze the impacts of the TyG-BMI on 28-day hospital and ICU mortality. Restricted cubic splines (RCS) were applied to explore the nonlinear relationship between the TyG-BMI and 28-day mortality. K–M curves were utilized for outcome comparisons among different TyG-BMI groups. Additionally, interaction and subgroup analyses were performed to validate the robustness of the results.

Results A total of 1,362 critically ill patients with IS were enrolled, with a mean age of 68.41 ± 14.16 years; 47.50% were male. Multivariate Cox regression analysis revealed that, the high TyG-BMI group had significantly higher 28-day hospital mortality(HR = 1.734, $P = 0.032$) and ICU mortality (HR = 2.337, $p = 0.048$). RCS analysis showed a nonlinear positive correlation between the TyG-BMI and 28-day hospital mortality. Below the inflection point of the TyG-BMI = 380.37, each increase of 1 standard deviation (SD) (approximately 25.5 units) in the TyG-BMI was associated with a 37.3% increase in 28-day hospital mortality (HR = 1.373, $P = 0.015$), and above 380.376, each 1-SD increase in the TyG-BMI resulted in an 87.9% decrease in 28-day hospital mortality (HR = 0.121, $P = 0.057$). The log-likelihood ratio test P value = 0.004. For 28-day ICU mortality, the TyG-BMI exhibited a significant positive linear correlation in RCS.

Conclusions Elevated TyG-BMI is significantly associated with an increased risk of short-term all-cause mortality in patients with critically ill IS in the United States. This result provides compelling evidence to address the existing discrepancies in this research domain, indicating that the TyG-BMI could serve as a straightforward and efficient biomarker for identifying critically ill IS patients at high risk of mortality.

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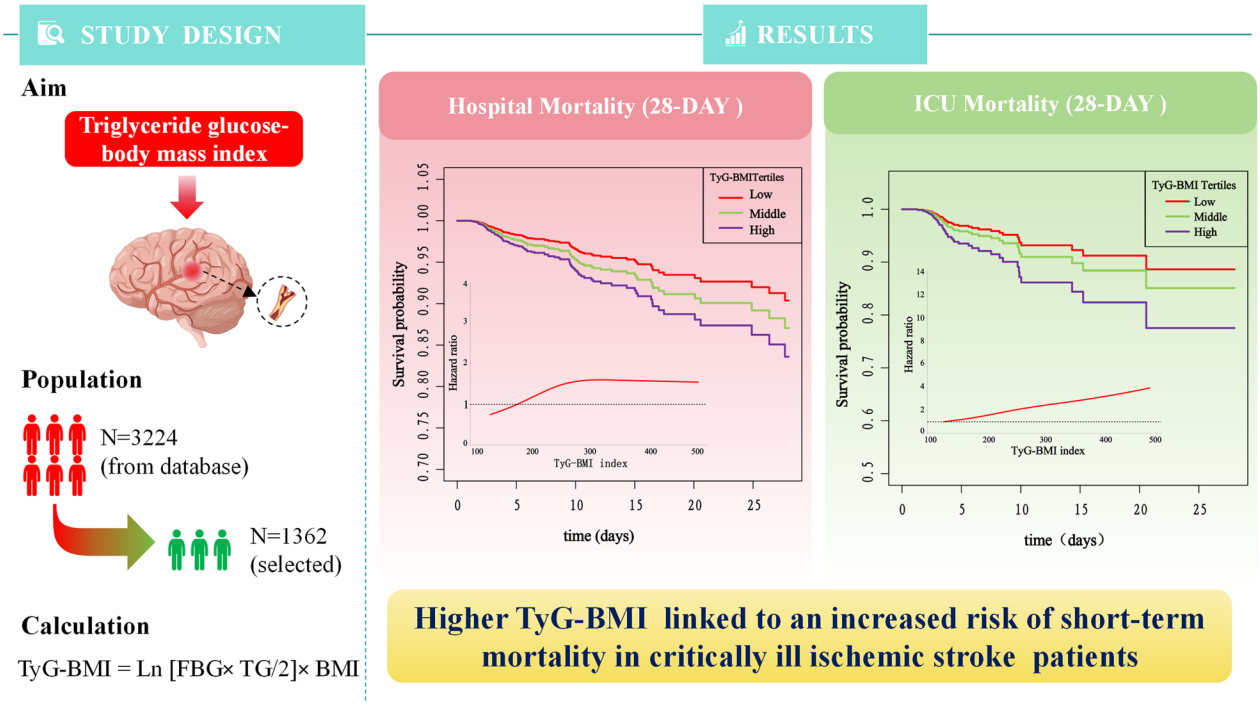
Graphic abstract



Keywords Ischemic stroke, Triglyceride glucose–body mass index (TyG–BMI), Prognosis, Mortality, Insulin resistance, Critically ill ischemic stroke patients

Introduction

Ischemic stroke (IS) is characterized by focal neurological dysfunction and cerebral tissue necrosis, typically resulting from insitu thrombotic processes or the embolization of atherothrombos from proximal arterial sources [1]. According to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification [2], large artery atherosclerotic stroke, small vessel occlusion stroke, and cardioembolic stroke are common causes of acute ischemic stroke. Furthermore, hematological disorders, including essential thrombocythemia, polycythemia vera, and thrombotic thrombocytopenic purpura, may also manifest as acute ischemic stroke and account for the most common causes of ischemic stroke attributed to other cause [3]. Accurate identification of the etiology of ischemic stroke is critical for guiding treatment, as the necessary treatment methods, recurrence risk, and prognosis vary according to the underlying causes. Epidemiological data indicate a trend toward increasing incidence and mortality of IS globally, particularly in low- and middle-income countries, with a significant increase in stroke incidence among younger populations under 70 years of age [4]. Globally, stroke ranks as the second leading cause of mortality and the third leading contributor to disability-adjusted life-years (DALYs) lost [4, 5]. In China, it has emerged as the primary driver of death and disability among the adult population [5]. The global aging population has significantly increased the burden of IS, leading to more elderly individuals being admitted to the ICU and facing higher mortality and disability rates. Previous studies have showed that fluctuations in blood pressure [6, 7], hyperglycemia [8], dyslipidemia [9] (including total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), and white blood cell count [10] and C-reactive protein [11] are associated with poor outcomes in acute IS. However, reliance solely on these traditional indicators is limited. Therefore, it remains crucial to identify risk factors that are both effective and direct predictors of mortality risk while being clinically feasible and amenable to intervention. This is essential for developing effective treatment strategies targeted at high-risk patients.

The triglyceride-glucose (TyG) index serves as a straightforward and reliable surrogate marker for assessing insulin resistance(IR) [12, 13], calculated by multiplying fasting triglyceride and fasting glucose levels. Substantial research has demonstrated that the TyG index has significant clinical utility across various metabolic and cardiovascular diseases [14–16]. Regarding IS, TyG index has exhibited significant clinical utility

[17–24]. Specifically, an elevated TyG index is associated with an increased risk of IS, providing value for optimizing disease risk assessment [21, 25]. A higher TyG index also independently predicts poor prognosis, such as stroke recurrence, increased overall mortality, and early neurological deterioration, in IS patients [18, 26, 27]. Additionally, an elevated TyG index corresponds with worsening carotid atherosclerosis in patients with IS [28]. Furthermore, an elevated TyG index also demonstrates predictive value for adverse functional outcomes and neurological deterioration in IS patients following thrombolytic therapy [29]. In summary, the TyG index, serving as a simple and easily measurable biomarker, holding significant promise for clinical utilization in the field of IS.

Recent studies have indicated that combining the TyG index with measures of obesity, including body mass index (BMI), waist circumference (WC), and the waist-to-height ratio (WtHR), markedly enhances the precision of IR assessment. Compared with the use of the TyG index or other obesity indicators in isolation, a combined evaluation strategy is a more effective approach for accurately identifying IR [30]. Among them, the TyG-BMI has shown significant applicability in predicting the risk of developing type 2 diabetes [31], all-cause mortality and cardiovascular mortality in patients with chronic kidney disease [32], as well as the risk of developing various metabolic disorders, such as sleep apnea and frail [33, 34]. Nevertheless, research on the TyG-BMI in acute IS remains scarce. A recent study based on the MIMIC-IV database found that a lower TyG-BMI is significantly associated with increased long-term all-cause mortality risk in stroke patients. Conversely, no significant association was observed between TyG-BMI and short-term all-cause mortality [35]. This conflicting conclusion challenges prior research findings [36, 37]. Currently, there is a lack of research on TyG-BMI in the critically ill IS population. This study, which is based on the eICU database, aims to investigate the relationship between the TyG-BMI and 28-day mortality in critically ill IS patients, this will help address existing research gaps and offer more precise biomarker references for clinical applications.

Methods

Source of data

This study utilizes the eICU Collaborative Research Database (eICU-CRD v2.0), a comprehensive centralized repository of intensive care unit (ICU) patients from 208 U.S. hospitals spanning 2014 to 2015, capturing clinical data from over 200,000 ICU admissions [38]. Managed by Philips Healthcare, the database employs automated data gathering and electronic storage, containing detailed patient demographics, diagnoses, physiological metrics, laboratory findings, medication details, and outcomes. All research procedures strictly adhered to the Helsinki Declaration guidelines. Access to the database was granted to the lead author, Qingrong Ouyang, post successful completion of the Collaborative Institutional Training Initiative (CITI) program for "Research with only data or specimens," certified with ID: 65,871,703.

Study population

Initial screening of the eICU-CRD database via the search term "neurologic| disorders of vasculature|stroke|ischemic stroke" identified 3,244 cases of acute IS. To ensure data accuracy and relevance, specific exclusion criteria were applied as follows: (1) hospital stays less than 24 h. (2) Missing discharge status. (3) Repeated admission to ICU. (4) Data on blood glucose, triglycerides, and body mass index were either missing or classified as extreme outliers. In this study, extreme outliers refer to TyG-BMI values significantly exceeding 550 (with a sample size of 3). After these criteria were applied, a total of 1,362 patients were selected for further analysis. The flowchart illustrating the population selection process is depicted in Fig. 1.

Data extraction

The variables extracted from eICU-CRD v2.0 include the following: (1) The general clinical characteristics included age, sex, ethnicity, body mass index (BMI), length of hospital stay, vital signs (respiratory rate, heart rate, and mean arterial pressure (MAP)), and the Sequential Organ Failure Assessment (SOFA) score. (2) The laboratory parameters include blood urea nitrogen, blood glucose, creatinine, potassium, triglycerides, total cholesterol, sodium, and HDL-C, among others, all blood indicators were measured for the first time within 24 h after admission to the ICU. (3) The following comorbidities were considered: sepsis, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), acute myocardial infarction (AMI), diabetes, pneumonia, and the use of mechanical ventilation. (4) Outcome measure: In-hospital death or intensive care unit (ICU) death occurred within 28 days.

TyG-BMI index calculation

We calculated the TyG-BMI for each patient via the following formula: TyG-BMI = Ln [FBG (mg/dL) × TG (mg/dL)/2] × BMI (kg/m2).

Statistical analysis

Student's t test and one-way ANOVA were used for normally distributed continuous variables, and the results are presented as the means ± standard deviations (SD). Skewed or nonnormally distributed continuous variables were compared via the Kruskal–Wallis rank sum test and are expressed as median interquartile ranges (IQR). Categorical variables were analyzed using either Fisher's exact test or the chi-square test and are reported

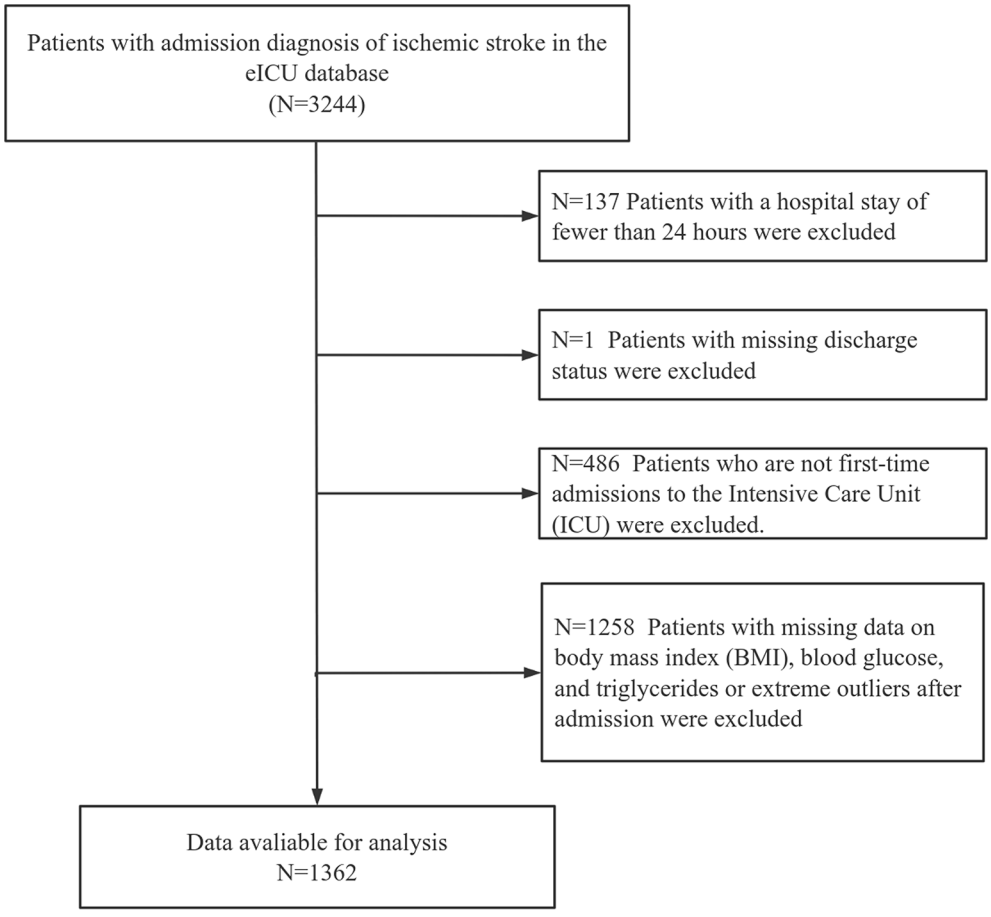


Fig. 1 Flowchart of the selection of patients

as numbers and percentages. Three multivariate Cox proportional hazard regression models were employed to investigate the impact of the TyG-BMI on 28-day mortality, and hazard ratios (HR) were calculated. Model 1 was unadjusted for covariates; Model 2 considered age, sex, and ethnicity; Model 3 was further adjusted for sex, age, ethnicity, respiratory rate, heart rate, MAP, ventilation status, SOFA score, diabetes, sepsis, COPD, CHF, AMI, cardiac rhythm, pneumonia, serum creatinine, total cholesterol, blood urea nitrogen, serum potassium, and sodium levels. The study utilized the Cox model with restricted cubic splines (RCS) to examine the dose–effect relationship between the TyG-BMI and 28-day mortality. Moreover, a two-piecewise linear regression model was employed to identify thresholds in the nonlinear association between the TyG-BMI and 28-day hospital mortality. Stratified analyses were carried out to assess the robustness of the results, which were visually depicted via forest plots. Statistical analyses were conducted using Empower-Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) and the statistical software package R. A two-tailed P value less than 0.05 indicated statistical significance.

Results

Baseline characteristics of the study participants

This study enrolled 1362 participants, with an average age of 68.41 ± 14.16 years and 47.50% male. The participants were divided into low ($n = 448$), medium ($n = 461$), and high ($n = 453$) TyG-BMI groups. The comparisons among the three groups regarding age, BMI, heart rate, mean MAP, and mechanical ventilation revealed significant differences. Notably, the high TyG-BMI group exhibited a lower mean age ($P < 0.001$), a higher BMI ($P < 0.001$), an increased heart rate ($P = 0.006$), a higher MAP ($P = 0.016$), and a greater utilization of mechanical ventilation ($P = 0.024$). Furthermore, the high TyG-BMI group presented elevated levels of blood urea nitrogen, glucose, triglycerides, and total cholesterol but lower HDL cholesterol (all $P < 0.05$). Regarding clinical outcomes, the high TyG-BMI group exhibited a higher 28-day hospital mortality ($P = 0.022$) and 28-day ICU mortality ($P = 0.014$). No significant differences were observed in the incidence of COPD, CHF, or AMI (Table 1).

Table 1 Baseline characteristics of participants classified by the triglyceride glucose-body mass index (TyG-BMI)

N	Total	Low TyG-BMI (< 218.2)	Middle TyG-BMI (218.3-272.6)	High TyG-BMI (>272.7)	P-value
	1362	448	461	453	
Age, mean(SD), year	68.41 ± 14.16	71.97 ± 14.96	68.45 ± 13.19	64.85 ± 13.43	< 0.001
Gender(male), n(%)	647(47.50%)	235(52.46%)	189(41.00%)	223(49.23%)	0.002
Ethnicity, n(%)					0.938
Caucasian	1024(75.18%)	332(74.11%)	343(74.40%)	349(77.04%)	
African American	169(12.41%)	56(12.50%)	58(12.58%)	55(12.14%)	
Hispanic	81(5.95%)	29(6.47%)	29(6.29%)	23(5.08%)	
Other or unknown	88(6.46%)	31(6.92%)	31(6.72%)	26(5.74%)	
Body mass index, mean(SD), kg/m2	28.59 ± 6.75	22.40 ± 2.72	27.55 ± 2.19	35.76 ± 5.87	< 0.001
Respiratory rate, median(IQR), bpm	26.0(11.0–34.0)	24.0(11.0–34.0)	25.0(11.0–34.0)	27.0(11.0–34.0)	0.162
Heart rate, mean(SD), /min,	90.32(30.62)	87.67(30.93)	89.32(30.94)	93.99(29.70)	0.006
MAP, mean(SD), mmHg	109.60(40.88)	105.70(39.97)	109.48(40.67)	113.59(41.69)	0.016
Mechanical ventilation use, n(%)	230(17.01%)	61(13.68%)	77(16.81%)	92(20.54%)	0.024
SOFA score	2.00(1.00–3.00)	2.00(1.00–3.00)	2.00(0.00–3.00)	2.00(1.00–4.00)	0.091
SEPSIS, n(%)	10(0.73%)	2(0.45%)	1(0.22%)	7(1.55%)	0.043
COPD, n(%)	49(3.60%)	18(4.02%)	11(2.39%)	20(4.42%)	0.217
CHF, n(%)	45(3.30%)	18(4.02%)	13(2.82%)	14(3.09%)	0.572
AMI, n(%)	22(1.62%)	7(1.56%)	10(2.17%)	5(1.10%)	0.44
Diabetes mellitus, n(%)	171(12.56%)	32(7.14%)	62(13.45%)	77(17.00%)	< 0.001
Pneumonia, n(%)	68(4.99%)	21(4.69%)	25(5.42%)	22(4.86%)	0.867
Triglycerides, median(IQR), mg/dL	105.0(76.25–149.0)	82.0(62.0-108.0)	110.0(82.0-153.0)	136.0(98.0-202.0)	< 0.001
Glucose, mean(SD), mg/dL	133.0(57.03)	111.91(31.89)	134.82(50.40)	151.99(73.47)	< 0.001
Blood urea nitrogen, median(IQR), mg/dL	16.0(12.0–21.0)	16.0(11.0–20.0)	16.0(12.0–21.0)	16.0(12.0-23.50)	0.046
Serum creatinine, median(IQR), mg/dl	0.89(0.72–1.16)	0.82(0.67–1.04)	0.89(0.74–1.18)	0.93(0.77–1.21)	< 0.001
Total cholesterol, median(IQR), mg/dL	154.0(129.0-184.25)	151.59(39.74)	162.22(44.70)	164.96(53.20)	< 0.001
Serum, potassium, mean(SD), mmol/L	3.95 ± 0.53	3.93 ± 0.53	3.92 ± 0.51	4.00 ± 0.56	0.051
Sodium, mean(SD), mmol/L	139.14 ± 3.61	139.05 ± 3.86	139.05 ± 3.55	139.31 ± 3.40	0.602
HDLc, mean(SD), mg/dL	43.98 ± 14.89	48.84 ± 16.35	43.31 ± 13.97	39.83 ± 12.76	< 0.001
TYG-BMI, mean(SD)	253.43 ± 66.70	187.78 ± 22.87	243.96 ± 16.12	328.00 ± 51.77	< 0.001
Hospital 28 day mortality, n(%)	124(9.10%)	33(7.37%)	36(7.81%)	55(12.14%)	0.022
ICU 28 day mortality, n(%)	52(3.82%)	12(2.68%)	13(2.82%)	27(5.96%)	0.014

MAP, mean arterial pressure; SOFA score, sequential organ failure assessment score; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; AMI, acute myocardial infarction; HDLc, high-density lipoprotein-cholesterol; TYG-BMI, triglyceride glucose-body mass index

The impact of the TyG-BMI on 28-day mortality

Univariate analysis was performed to explore the associations between various factors and 28-day hospital and ICU mortality outcomes. (Supplementary Tables 1 and Table 2). The results indicated that the use of mechanical ventilation and higher SOFA score were significantly associated with increased 28-day hospital and ICU mortality. However, demographic factors, comorbidities, and most laboratory parameters did not show significant associations. Notably, the high TyG-BMI group exhibited a significantly higher risk of 28-day in-hospital mortality compared to the low TyG-BMI group (HR = 1.563, $P = 0.043$).

Multivariate Cox regression analysis was employed to examine the independent impact of the TyG-BMI on 28-day hospital and ICU mortality, as presented in Table 2. Regarding hospital mortality, in the fully adjusted Model III, TyG-BMI was not significantly associated with 28-day mortality (HR = 1.002, $P = 0.118$). However, among the three TyG-BMI groups, the high TyG-BMI group displayed a significantly increased 28-day mortality risk compared to the low TyG-BMI group in the fully adjusted models (HR = 1.734, $P = 0.032$). Additionally, there was a significant association between the TyG-BMI trend across the three groups and an elevated 28-day mortality risk in the fully adjusted models (HR = 1.324, $P = 0.027$). For ICU mortality, a continuous TyG-BMI was significantly associated with a higher risk according to all three models. In fully adjusted Model 3, the highest TyG-BMI tertile exhibited a significantly elevated risk of ICU mortality compared to the lowest tertile (HR = 2.337, $p = 0.048$). Kaplan-Meier curves were employed to compare outcomes among various TyG-BMI subgroups and 28-day mortality. The analysis revealed that patients in the highest TyG-BMI group exhibited the lowest survival

Table 2 Relationship between TyG-BMI and 28-day mortality in different logistic regression models

Categories	Model1		Model2		Model3	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Hospital mortality						
TyG-BMI Continuous variable	1.002(1.000, 1.004)	0.063	1.003(1.001, 1.005)	0.017	1.002(0.999, 1.005)	0.118
TyG-BMI Tertiles						
Tertile1(≤ 218.2)	1		1		1	
Tertile2(218.3-272.6)	1.035(0.645, 1.661)	0.885	1.110(0.688, 1.788)	0.669	1.253(0.744, 2.110)	0.395
Tertile3(≥ 272.7)	1.578(1.026, 2.427)	0.038	1.749(1.123, 2.725)	0.013	1.734(1.049, 2.865)	0.032
P for trend	1.277(1.025, 1.591)	0.029	1.343(1.072, 1.682)	0.01	1.324(1.033, 1.698)	0.027
ICU mortality						
TyG-BMI Continuous variable	1.003(1.000, 1.007)	0.042	1.003(1.000, 1.007)	0.049	1.004(1.001, 1.008)	0.018
TyG-BMI Tertiles						
Tertile1(≤ 218.2)	1		1		1	
Tertile2(218.3-272.6)	0.959(0.437, 2.103)	0.917	0.977(0.444, 2.152)	0.954	1.296(0.518, 3.243)	0.58
Tertile3(≥ 272.7)	1.74(0.885, 3.430)	0.108	1.727(0.864, 3.451)	0.122	2.337(1.009, 5.414)	0.048
P for trend	1.375(0.972, 1.947)	0.072	1.364(0.957, 1.942)	0.086	1.571(1.039, 2.375)	0.032

Model 1 unadjusted for covariates

Model 2 considered age, gender, and ethnicity

Model 3 adjusted for gender, age, ethnicity, respiratory rate, heart rate, mean arterial pressure (MAP), ventilation status, SOFA score, diabetes, sepsis, COPD, CHF, AMI, cardiac rhythm, pneumonia, serum creatinine, total cholesterol, blood urea nitrogen, serum potassium, and sodium levels

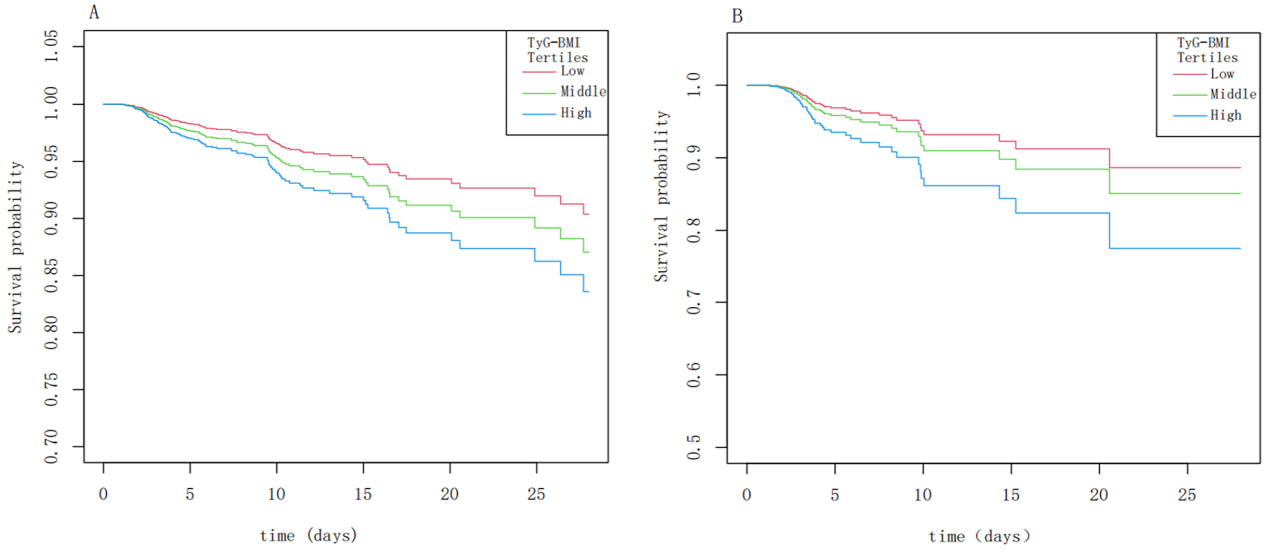


Fig. 2 Kaplan–Meier survival analysis curves for 28-day all-cause mortality, hospital mortality (**A**) and ICU mortality (**B**)

rate, while those in the lowest TyG-BMI group demonstrated the highest survival rate (Fig. 2A and B).

Relationship between the TyG-BMI and 28-day mortality

The Cox model with RCS revealed a nonlinear relationship between the TyG-BMI and the hazard ratio for 28-day hospital mortality (Fig. 3A). When the TyG-BMI is low, an increase in the index corresponds to a linear increase in the risk of mortality. However, once the TyG-BMI index exceeds a certain threshold (approximately 300 visual), the increase in mortality risk becomes less pronounced, indicating a "plateau effect". Notably, a distinct linear positive correlation was observed for ICU mortality, as the risk of death steadily increased with increasing TyG-BMI, as shown in Fig. 3B.

Two-piece linear regression analysis was employed to determine the inflection point for the nonlinear relationship of hospital mortality. The model revealed a threshold at a TyG-BMI value of 380.376. Below this threshold, each increase of 1 standard deviation (SD) (approximately 25.5 units) in the TyG-BMI was associated with a 37.3% increase in 28-day hospital mortality (HR = 1.373, $P = 0.015$); beyond the inflection point, each 1-SD increase in the TyG-BMI resulted in an 87.9% decrease in 28-day hospital mortality (HR = 0.121, $P = 0.057$), means that the TyG-BMI surpassed a specific threshold,

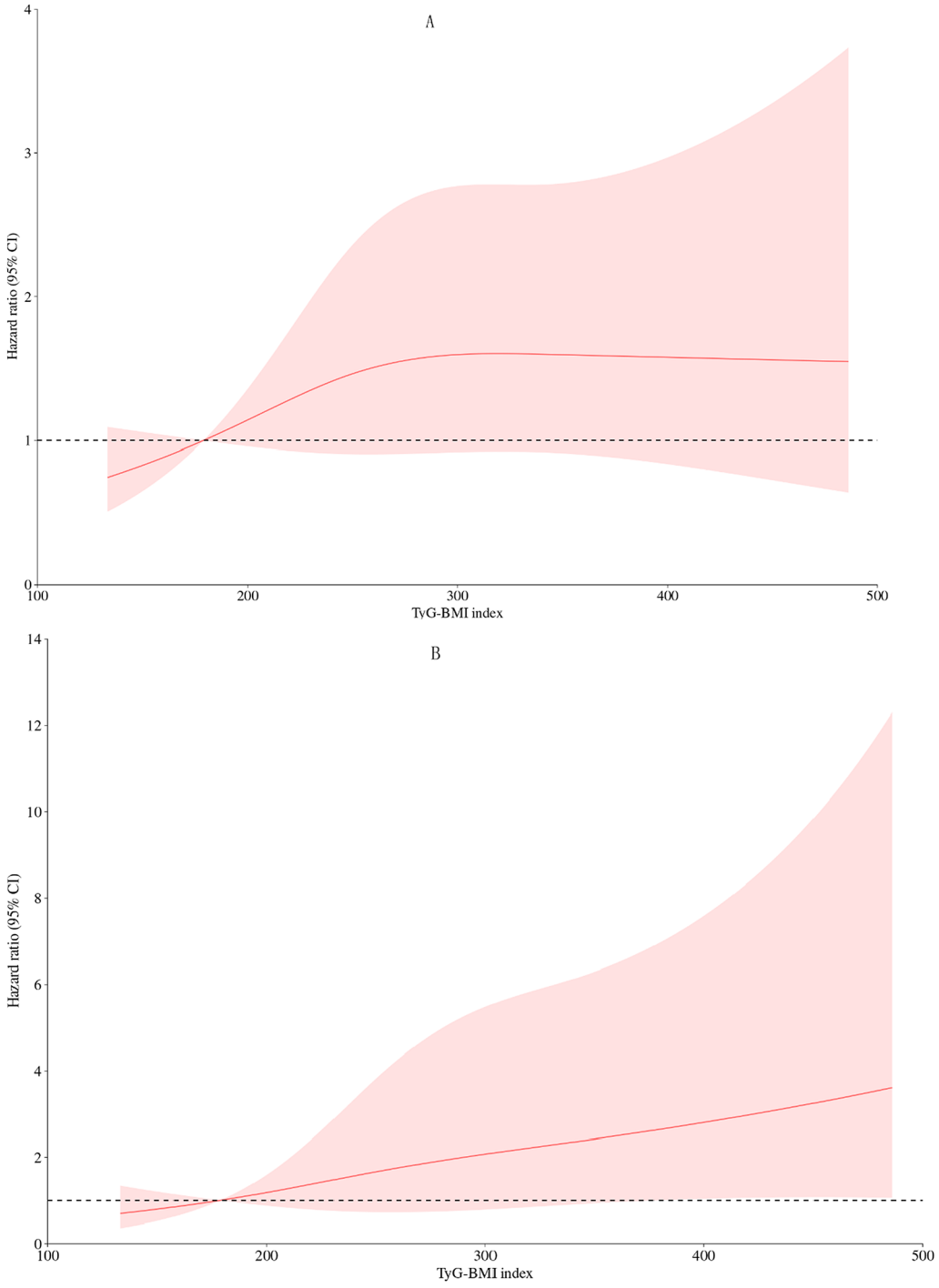


Fig. 3 Restricted cubic spline analysis illustrating the relationship between TyG-BMI and 28-day hospital mortality (**A**) and 28-day ICU mortality (**B**)

its association with mortality underwent a transformation, where the increase in mortality risk tended to plateau and even decline. Additionally, the disparity in effect sizes between the two segments of the TyG-BMI demonstrated statistical significance (P for log likelihood ratio test = 0.004), indicating a notable nonlinear relationship(Table 3).

Subgroup analysis

The association between the TyG-BMI and 28-day hospital mortality remained consistent across various patient subgroups, although some variations were observed. As shown in Fig. 4A, the TyG-BMI was significantly associated with increased mortality risk in patients aged above 60 years (HR = 1.066, $P = 0.024$) and in males (HR = 1.076, $P = 0.029$). Additionally, the TyG-BMI was

Table 3 Threshold effect analysis of TyG-BMI on hospital mortality

	TyG-BMI		TyG-BMI per SD	
	HR (95% CI)	P value	HR (95% CI)	P value
Inflection point (K)	380.376		1.823	
< K	1.005 (1.001, 1.008)	0.015	1.373 (1.064, 1.772)	0.015
> K	0.970 (0.940, 1.001)	0.057	0.121 (0.014, 1.061)	0.057
P for log likelihood ratio test	0.004		0.004	

The adjustments are same to Model 3.

significantly associated with 28-day hospital mortality in subgroups with increased total cholesterol (HR = 1.082, $P = 0.031$) and decreased blood urea nitrogen (HR = 1.094, $P = 0.032$). A further interaction test indicated no significant interaction effect between TyG-BMI and the 28-day mortality outcome across different subgroups ($p \geq 0.05$). The TyG-BMI also showed consistent trends across various subgroups, with a significant association with higher 28-day ICU mortality in subgroups aged ≥ 60 years (OR = 1.104, $P = 0.033$), those with total cholesterol levels ≥ 154 mg/dL (OR = 1.139, $P = 0.018$), and patients with serum potassium levels < 3.9 mmol/L (OR = 1.139, $P = 0.033$). Notably, patients with pneumonia experienced significantly elevated ICU mortality. (OR = 1.286, $P = 0.015$). The interaction test revealed significant interaction effects in the pneumonia and CHF subgroups, with p-value<0.05. (Fig. 4B).

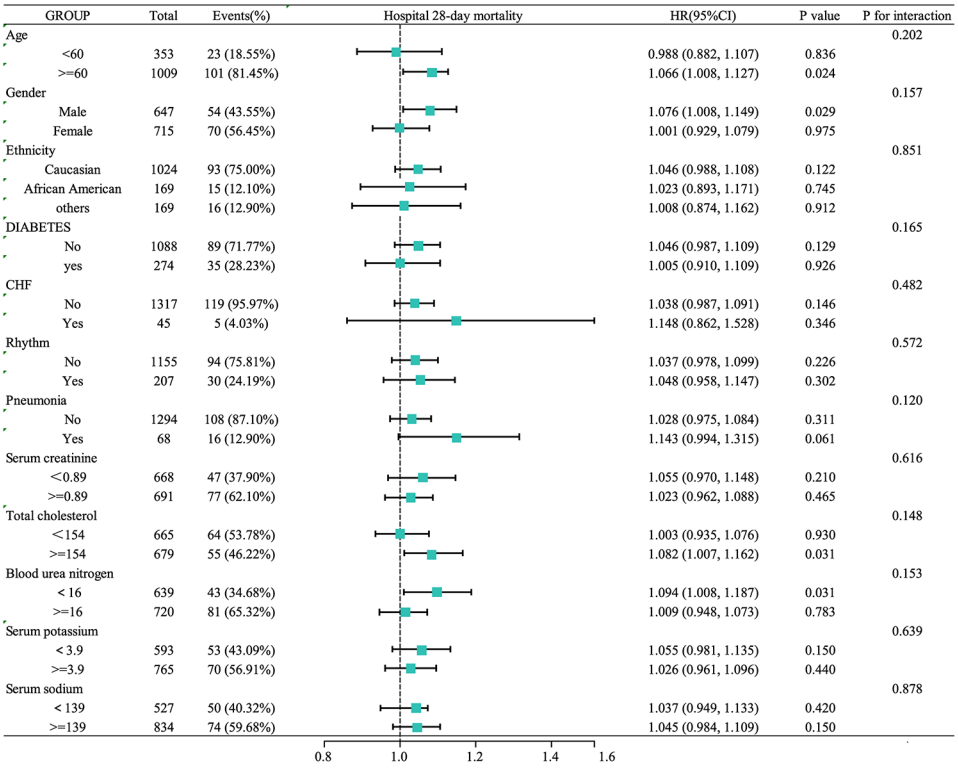
Discussion

This study is the first to investigate the association between the TyG-BMI and 28-day mortality in critically ill IS patients in the eICU database. It reveals a nonlinear positive correlation with hospital mortality and a positive linear correlation with ICU mortality. This key finding presents initial evidence for the potential of the TyG-BMI as a prognostic tool in critical IS populations. Importantly, our research challenges the conclusions of several recent studies based on the MIMIC-IV database. These studies revealed a negative relationship, indicating that a lower TyG-BMI is associated with higher all-cause mortality in stroke patients [35], as well as in individuals with severe atrial fibrillation [39]and heart failure [40]. The findings of our study offer robust evidence that helps address the existing discrepancies and ambiguities within this research domain. Additionally, our findings align with earlier studies involving the TyG index across various subgroups of IS patients [20, 37, 41], enhancing the reliability of the TyG-BMI in predicting mortality risk in critical IS patients.

TyG has gained widespread recognition as a surrogate marker for IR because of its strong correlation with traditional measures of insulin sensitivity, such as the hyperinsulinemic-euglycemic clamp, which is considered the gold standard for assessing IR [42]. Multiple studies have shown that TyG correlates significantly with IR across different populations. Initially, in 2008, Simental-Mendía and colleagues [13] introduced a significant correlation between TyG and the homeostasis model assessment of insulin resistance (HOMA-IR), a widely utilized surrogate for IR, suggesting that TyG presents a simpler and more cost-effective alternative, particularly advantageous in expansive epidemiological investigations. A subsequent study conducted within a Brazilian population unveiled a strong association between the TyG index and diverse indicators of adiposity, metabolic profiles, and subclinical atherosclerosis markers linked to IR, highlighting the superior performance of the TyG index over the HOMA2-IR index in specific aspects [43]. Similarly, among Asian hypertensive patients [44], the TyG index is positively correlated with IR, highlighting its relevance in Asian populations. Nevertheless, some studies have raised concerns regarding the diagnostic accuracy of the TyG index, noting inconsistencies in its sensitivity and specificity across different investigations, likely due to the lack of standardized definitions of IR and study heterogeneity [45]. Despite these limitations, TyG is widely accepted as an alternative marker for IR due to its strong correlation with traditional methods, offering a practical and cost-effective solution in healthcare settings without advanced testing capabilities.

In recent years, multiple studies have shown that the integration of the TyG index with indicators of obesity, such as BMI, WC and the WtHR, improves the accuracy, sensitivity and specificity of the prediction of IR [46–48]. The TyG-BMI, which is closely associated with chronic inflammation, endothelial dysfunction and metabolic syndrome [49, 50], all contribute to an elevated risk of stroke and has demonstrated utility in evaluating the risk of adverse cardiovascular events [51–53]. Specifically, a prospective study on patients with AMI revealed that the TyG-BMI independently predicts the occurrence of major adverse cardiovascular and cerebrovascular events (MACCEs) [53]. Higher TyG-BMI values were also associated with an increased incidence of heart failure and corresponding hospitalization rates within the coronary heart disease population [54]. Furthermore, examination of long-term outcomes in heart failure patients with concomitant coronary heart disease revealed a nonlinear relationship between TyG-BMI and all-cause mortality and heart failure rehospitalization rates, and a TyG-BMI exceeding a certain threshold was associated with an elevated risk of heart failure-related rehospitalization [55]. Moreover, research has indicated that the TyG-BMI is positively correlated with the risk of developing type 2 diabetes [56], diabetic complications

(A)



(B)

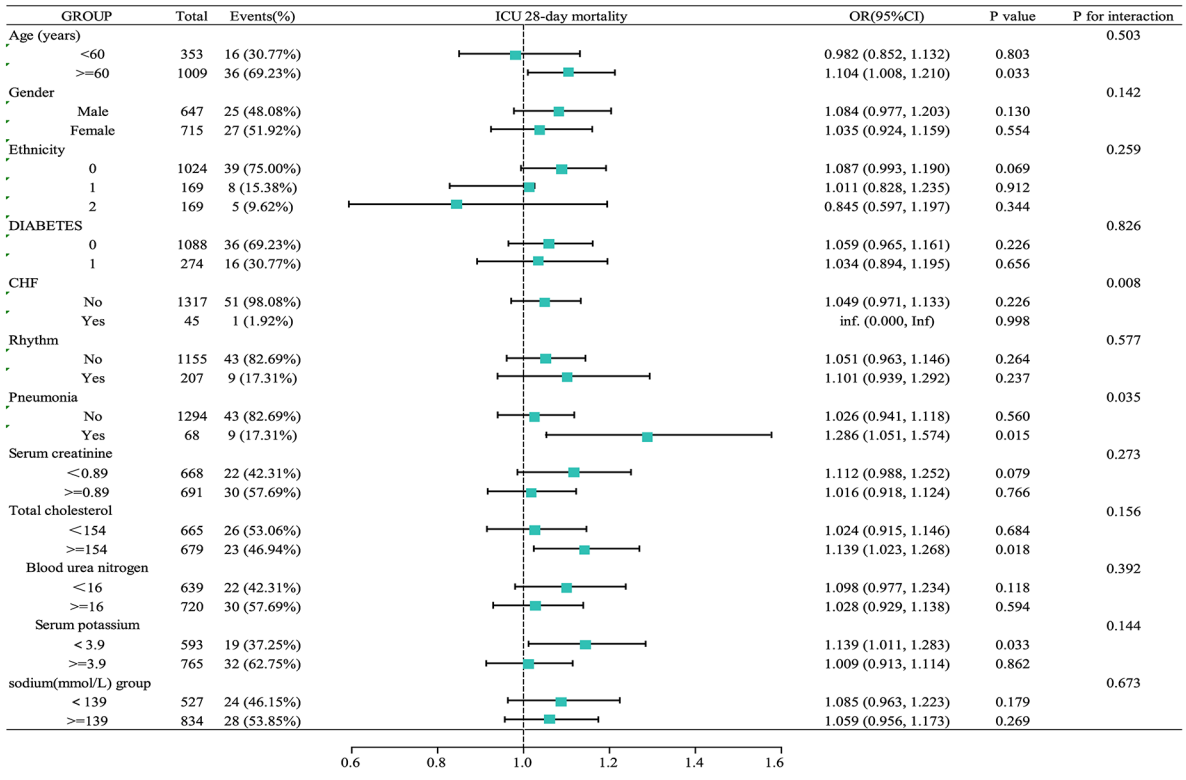


Fig. 4 **A**. Forest plots of hazard ratios for the hospital mortality across different subgroups. CHF, congestive heart failure. **B** Forest plots of hazard ratios for the ICU mortality across different subgroups. CHF, congestive heart failure

[57], and nonalcoholic fatty liver disease [58, 59]. Currently, only a few studies have delved into the connection between the TyG-BMI and stroke. Three large-sample studies from Chinese populations have shown a strong positive correlation between TyG-BMI and the risk of IS in the general population [36], as well as in middle-aged and elderly populations [37], and changes in TyG-BMI (increase or decrease) have a significant impact on stroke risk in middle-aged and elderly population, specifically, individuals with a consistently high TyG-BMI face a markedly elevated risk of stroke [60]. Interestingly, a recent study sourced from the MIMIC-IV database revealed that lower TyG-BMI values are linked to an increased risk of long-term all-cause mortality in patients with critically ill stroke [35]. In other words, elevated TyG-BMI levels might act as a protective factor against adverse outcomes in critically ill stroke patients. The authors offered a somewhat speculative explanation for this phenomenon, suggesting that lower TyG-BMI levels in stroke survivors could indicate severe malnutrition or metabolic decompensation. These conditions are intimately associated with disease severity and heightened mortality risk. However, this interpretation appears to be significantly insufficient. In this context, our study based on the eICU database, explores the association between the TyG-BMI and 28-day mortality in patients with critically ill IS. A positive nonlinear relationship between the TyG-BMI and 28-day hospital mortality, and a positive linear association with ICU mortality, were discovered in this population. Specifically, when the TyG-BMI is < 380, an increase in the TyG-BMI is associated with increased 28-day hospital mortality. However, when TyG-BMI was > 380, the relationship between TyG-BMI and 28-day hospital mortality reached a plateau. We believe that this is due to the significant decrease in sample size when the TyG-BMI was > 380 (69 cases, 5% of the total population). The results of this study support that the TyG-BMI is a risk factor in diseases, consistent with the conclusions of TyG-BMI in most studies. This finding adds robust evidence to the existing literature on the correlation between TyG-BMI and stroke.

The precise mechanisms underlying the associations between the TyG-BMI and the incidence and mortality of ischemic stroke have not been fully elucidated. As a reliable biomarker for IR, the TyG-BMI may impact adverse outcomes through the following pathways. Firstly, the elevated TyG-BMI, which is indicative of dysregulated glucose and lipid metabolism, may promote the accumulation of fat within the vasculature and the formation of atherosclerotic plaques [28, 61]. The presence of these intravascular atherosclerotic lesions can precipitate vessel narrowing or obstruction, ultimately culminating in the occurrence of ischemic stroke. Secondly, sustained elevations in TyG-BMI can trigger the continuous release of inflammatory mediators, such as CRP and various cytokines [62, 63]. These inflammatory factors are closely associated with the pathogenesis of IR and can adversely impact the structural integrity and functional capacity of the vascular endothelium [64]. This detrimental interplay exacerbates the progression of atherosclerosis and thrombus formation, consequently intensifying both the incidence and mortality risk of IS [65]. Lastly, TyG-BMI has also been strongly associated with other cardiovascular risk factors, such as hypertension [66], heart failure [54], and coronary artery disease [53]. These shared risk factors are known to play a pivotal role in diverse cerebrovascular events, significantly contributing to increased mortality among critical IS patients.

This study is the first to reveal a significant positive correlation between the TyG-BMI and the short-term mortality risk of critically ill IS patients, reinforcing the clinical utility of the TyG-BMI in predicting adverse outcomes associated with IS. The dose–response correlation between the TyG-BMI and 28-day mortality provides quantitative numerical references for the clinical prediction of short-term mortality risk in critical IS patients. In addition, stratified analysis confirmed that this association remained stable across different age, sex, and comorbidity subgroups, enhancing the reliability of the results. However, this study has several limitations that warrant consideration. First, as a retrospective cohort study, a causal relationship between the TyG-BMI and prognosis could not be established. Second, owing to the absence of stroke subtype information in the database, analysis and comparison of the predictive value for various types of IS were not feasible. Third, while the study accounted for multiple confounders, it did not include key prognostic indicators such as the National Institutes of Health Stroke Scale (NIHSS) score, cause of death and anatomical localization of the responsible Vessels, which may have affected the comprehensiveness of the results. Fourth, the database included only 28-day mortality data, and the impact of the TyG-BMI on long-term prognosis was not further evaluated. Finally, the eICU-CRD v2.0 database covered only the period from 2014 to 2015, which may affect the applicability of the findings in the current medical era. Further prospective research is crucial to validate the predictive value of the TyG-BMI in multicenter patient cohorts, different populations, and various subtypes of IS, as well as long-term outcomes. Additionally, biomarkers related to lipid metabolism disorders, inflammatory response, and endothelial dysfunction could be included to explore the relationship between TyG-BMI and the mechanisms of IS more deeply in animal models. Furthermore, the application value of the TyG-BMI in the recurrence and prognosis of IS should be investigated, which will assist in providing a basis for clinical risk assessment and personalized management.

Conclusion

This study revealed that an elevated TyG-BMI is significantly linked to an increased risk of short-term all-cause mortality in critically ill patients with IS in the United States. These findings provide strong evidence to help resolve the existing uncertainties within this research domain, indicating the potential of the TyG-BMI as a simple and effective biomarker for identifying patients at high risk of mortality. Monitoring and managing triglycerides, blood glucose, and weight on a daily basis may help reduce the risk of short-term mortality in patients with acute IS or those at risk of an IS.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Author contributions

Qingrong OuYang contributed to conceptualization, data extraction, statistical analysis, and drafting of the original manuscript. Lei Xu, Ming Yu, contributed to study design and manuscript review. All authors critically reviewed significant intellectual content and approved the final version submitted for publication.

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None.

Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

This study was conducted in strict accordance with the principles of the Helsinki Declaration. The establishment of this database was approved by the Massachusetts Institute of Technology (Cambridge, MA), and informed consent was obtained for the original data collection. Therefore, ethical approval and informed consent were not required for this manuscript.

Conflict of interest

The authors declare that the research was conducted without any commercial or financial relationships that could be perceived as potential conflicts of interest.

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