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Associations between triglyceride-glucose body mass index and all-cause mortality in ICU patients with sepsis and acute heart failure

Heping Xu^{1*†}, Jinyuan Xie^{1†}, Huan Niu¹, Xiongwei Cai¹ and Ping He¹

Abstract

Background The triglyceride–glucose body mass index (TyG-BMI) has been recognized as a significant predictor of cardiovascular disease risk and plays a crucial role in assessing insulin resistance. However, the correlation between the TyG-BMI and clinical outcomes in patients with sepsis and acute heart failure (AHF) has not been sufficiently explored. This study aimed to investigate the associations between TyG-BMI and clinical outcomes in patients with sepsis and AHF.

Methods We conducted a retrospective analysis of ICU-admitted patients via data from the MIMIC-IV database. Multivariable logistic regression, sensitivity analysis, and restricted cubic spline (RCS) models were used to assess the relationship between TyG-BMI and all-cause mortality. K–M survival analysis and Boruta analysis were employed to evaluate the predictive value of the TyG-BMI. Subgroup analyses considered the effects of age, sex, ethnicity, and comorbidities.

Results Among the 1,729 patients, a higher TyG-BMI was associated with lower all-cause mortality at 90 and 180 days. Each standard deviation increase in the TyG-BMI was linked to 0.2% and 0.3% reductions in 90-day and 180-day all-cause mortality, respectively. Kaplan–Meier analysis revealed significantly lower all-cause mortality in patients with higher TyG-BMIs ($P < 0.0001$). The RCS model revealed a nonlinear relationship between the TyG-BMI and mortality. Boruta analysis identified the TyG-BMI as an important clinical feature. Sensitivity analyses revealed that the association remained significant after patients with myocardial infarction, malignancies, or missing data were excluded. The subgroup analysis revealed that for the 90-day and 180-day mortality rates, significant interactions were found only in the subgroup of patients with kidney diseases ($P < 0.05$).

Conclusion The TyG-BMI may have potential value in predicting mortality in ICU patients with sepsis and AHF, supporting early risk assessment and clinical intervention. This study provides critical insights into patient prognosis.

Keywords Triglyceride glucose-body mass index, Acute heart failure, Sepsis, All-cause mortality, MIMIC-IV

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Introduction

Acute heart failure (AHF) presents a major clinical challenge and is frequently encountered by physicians across diverse medical settings. AHF often results from the decompensation of chronic heart failure, which can be triggered by various factors, with sepsis being a major contributor. The impact of sepsis-induced AHF on patient outcomes has drawn significant attention because of its association with adverse prognoses. A comprehensive population-based study by Manyoo Agarwal [1] et al. (2018), utilizing data from the U.S. Census Bureau, demonstrated that among 26,696,440 patients hospitalized for sepsis, 21.2% had concurrent heart failure. This comorbidity is strongly associated with increased mortality rates, exceeding 70% in cases where sepsis is accompanied by cardiomyopathy [2–4].

Sepsis-induced cardiac dysfunction increases mortality risk, extends hospital stays, and significantly increases healthcare costs [5]. These observations highlight the need for early identification and intervention in patients with sepsis and heart failure. Early treatment is crucial for improving outcomes and reducing complications. Given the substantial burden of sepsis-associated AHF, identifying early prognostic biomarkers is essential for guiding clinical management and enhancing survival rates.

Insulin resistance (IR), which is characterized by decreased sensitivity of peripheral tissues to insulin, is common in sepsis patients. This condition impairs insulin sensitivity and disrupts glucose and fatty acid metabolism through insulin signaling pathways in the heart, affecting heart failure [6]. Currently, several methods are widely used in clinical practice to assess IR. Among these, the homeostasis model assessment of insulin resistance (HOMA-IR) is simple and economical, but its accuracy may be limited in individuals with severe obesity. On the other hand, insulin release tests, such as the oral glucose tolerance test (OGTT), are considered the gold standard for assessing insulin resistance, although they are time-consuming and costly. In addition, the triglyceride-glucose (TyG) index has emerged as a promising biomarker for assessing insulin resistance [7]. Given the strong link between IR and obesity [8], recent studies suggest that the TyG-body mass index (BMI) may be a valuable tool for assessing IR [9–11].

Despite these advancements, the relationships between TyG-BMI and clinical outcomes in patients with sepsis and acute heart failure remain underexplored. This study aims to address this gap by investigating the associations between the TyG-BMI and patient outcomes in this high-risk population. These findings could offer new insights for improving clinical management and patient prognosis.

Methods

Data source

The data used in this study were obtained from the MIMIC-IV database (version 2.2) [12], which was developed and publicly released by the Complex Systems Monitoring Group at Beth Israel Deaconess Medical Center (BIDMC), Boston, Massachusetts. The database includes comprehensive data from over 50,000 patients admitted between 2008 and 2019, covering demographics, laboratory results, vital signs, disease diagnoses, and follow-up survival information. As the database is anonymized and does not contain protected health information, the BIDMC Institutional Review Board granted a waiver of informed consent for research use. Data extraction was performed by the corresponding author, He Ping Xu, who completed the CITI Program online training (record ID: 59568270) and used PostgreSQL for data management.

Definitions

The TyG index was calculated as $\ln[\text{fasting glucose (mg/dL)} \times \text{fasting TG (mg/dL)} / 2]$ [13]. BMI was defined as $\text{body weight (kg)} / \text{height}^2 \text{ (m)}$, and the TyG-BMI index was defined as the TyG index $\times$ BMI [14, 15]. The TyG-BMI index was categorized into tertiles: T1 (< 227.8), T2 ($227.8\text{--}287.4$), and T3 (> 287.4). Sepsis was diagnosed per the Sepsis-3 criteria (SOFA score ≥ 2), and septic shock was defined as sepsis with lactate > 2.0 mmol/L requiring vasopressors [16]. In this study, we included patients admitted to the ICU with a diagnosis of acute heart failure (AHF). AHF patients were identified on the basis of the diagnosis codes from the International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10).

Inclusion and exclusion criteria

Inclusion criteria

1. Patients aged 18 years or older.
2. Patients were diagnosed with sepsis and acute heart failure upon initial ICU admission.

Exclusion criteria

1. Patients with prior ICU admissions were excluded to avoid data duplication.
2. Patients with a survival time of less than 24 h were excluded to ensure adequate evaluation of clinical status and outcomes.
3. Patients missing essential data (serum fasting glucose, triglyceride, weight, height) or with incomplete records were excluded, as these data are necessary for accurate TyG-BMI calculations.

Outcome

The primary endpoints were 90-day and 180-day all-cause mortality. The secondary endpoints included in-hospital mortality and 28-day all-cause mortality.

Data extraction

This study collected baseline data within 24 h of ICU admission, including demographic characteristics (age, sex, ethnicity, etc.), medical history (myocardial infarction, congestive heart failure, cerebrovascular disease, etc.), initial SOFA score, SAPSII, and Charlson comorbidity index. Vital signs included blood pressure, heart rate, respiratory rate, temperature, and pulse oximetry. The laboratory parameters included white blood cell count, hemoglobin, platelet count, anion gap, bicarbonate, chloride, glucose, triglycerides, sodium, potassium, creatinine, blood urea nitrogen, calcium, and prothrombin time. The clinical outcomes monitored included septic shock; in-hospital mortality; and 28-day, 90-day, and 180-day all-cause mortality. Additionally, the ICU length of stay and total hospital length of stay were recorded.

Statistical analysis

This study presents continuous variables as the means (standard deviations) or medians (interquartile ranges) and categorical variables as percentages. Baseline characteristics across TyG-BMI categories were compared via chi-square tests for categorical data, one-way ANOVA for normally distributed continuous data, and the Kruskal-Wallis H test for nonnormally distributed continuous data. The relationships between the TyG-BMI and 90-day and 180-day all-cause mortality were assessed via multivariable logistic regression. Multicollinearity was evaluated with variance inflation factor (VIF) values, with a $VIF > 5$ indicating significant multicollinearity. Four progressively adjusted models were developed: Model 1: unadjusted; Model 2: adjusted for age, sex, ethnicity, medical history (cerebrovascular disease, renal disease), Charlson comorbidity index, SOFA and SAPSII scores, and shock-related variables; Model 3: further adjusted for blood pressure, heart rate, respiratory rate, temperature, and SpO₂; Model 4: additionally adjusted for laboratory parameters and therapeutic drugs (e.g., white blood cell count, glucose, sodium, creatinine, β -blockers, and diuretics).

Subgroup analyses were performed on the basis of factors such as age (<65 years, ≥ 65 years), sex, medical history, and septic shock. Sensitivity analyses, including logistic regression excluding patients with myocardial infarction and/or cerebrovascular disease, were conducted to validate the findings. Analyses were also performed on datasets with no missing values for robustness.

Nonlinear relationships between TyG-BMI and mortality were visualized via restricted cubic spline curves.

Kaplan–Meier survival analysis was used to compare the survival rates of ICU patients with sepsis and acute heart failure stratified by the TyG-BMI. The Boruta algorithm was used to assess the importance of TyG-BMI as a predictor variable, marking features as “important” or “unimportant” on the basis of Z values compared with shadow features. The default Boruta parameters included a significance level of $P = 0.01$ and a maximum of 100 iterations [17]. All analyses were performed via R version 4.2.1 and Stata version 18.0, with two-sided tests and a significance threshold of $P < 0.05$.

Results

Baseline characteristics of the participants

In the MIMIC-IV database, a total of 1,729 patients met the inclusion criteria, as depicted in Fig. 1. Table 1 provides a detailed summary of the baseline characteristics of patients stratified by TyG-BMI. The mean age of these patients was 70.7 years ($SD = 13.7$), with approximately 58.6% being male. TyG-BMI was divided into three tertiles: T1 (<227.8), T2 (227.8–287.4), and T3 (>287.4).

No significant differences were detected between the tertiles in terms of ethnicity, myocardial infarction, congestive heart failure, cerebrovascular disease, renal disease, Charlson Comorbidity Index, SAPS II score, systolic blood pressure, heart rate, anion gap, sodium, calcium, BUN, antiplatelet agents, β -blockers, diuretics, lipid-lowering drugs, ACEIs or digoxin ($P > 0.05$). However, patients in the highest tertile (T3) demonstrated a significantly greater prevalence of chronic pulmonary disease and diabetes than did controls. Additionally, T3 patients presented significantly higher SOFA scores, diastolic blood pressure, and mean blood pressure. These patients also had higher heart rates; respiratory rates; temperatures; white blood cell counts; and hemoglobin, platelet, bicarbonate, blood glucose, and potassium levels. Furthermore, the ICU length of stay and hospital length of stay were longer than those at T1. Conversely, patients in T3 were younger, had a lower proportion of males, and experienced lower mortality rates at 28, 90, and 180 days.

Associations of the TyG-BMI with the clinical outcomes of sepsis patients with AHF

The relationships between the TyG-BMI and clinical outcomes are detailed in Table 2. Patients were stratified into three groups on the basis of their TyG-BMI. We employed four distinct logistic regression models to evaluate the independent impact of the TyG-BMI on mortality in ICU patients with sepsis combined with acute heart failure. Logistic regression analysis revealed a negative association between TyG-BMI and the risk of 90-day and 180-day mortality. After all the clinical covariates were adjusted, each one-unit increase in TyG-BMI corresponded to a 0.2% and 0.3% reduction in 90-day and

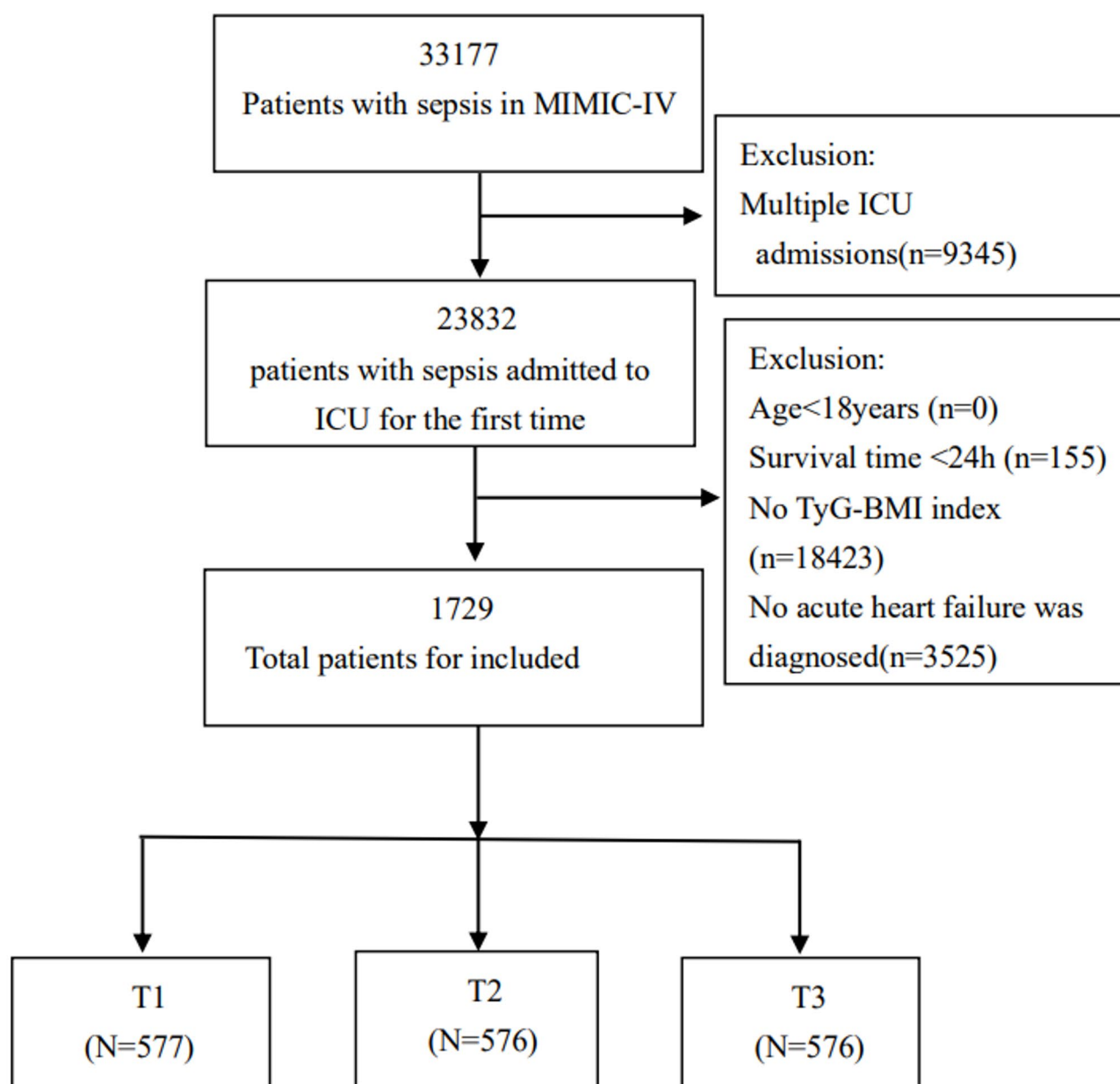


Fig. 1 Flow chart of patient selection for analysis

180-day mortality rates, respectively ($p < 0.01$). When TyG-BMI was analyzed as a categorical variable (divided into tertiles) with the lowest TyG-BMI group used as the reference, mortality rates at 90 days and 180 days decreased with increasing TyG-BMI ($P < 0.05$).

In addition, we conducted further logistic regression analysis to assess the impact of including BMI and TyG as covariates in four different models (Table S1). When TyG and BMI were included as covariates, the odds ratios (ORs) for 90-day mortality and 180-day mortality were as follows: 1.017 (95% CI: 0.817–1.266, $p = 0.879$) and 0.975 (95% CI: 0.959–0.991, $p = 0.003$) for 90-day mortality and 0.927 (95% CI: 0.749–1.147, $p = 0.484$) and 0.974 (95%

CI: 0.959–0.990, $p = 0.002$) for 180-day mortality. These results suggest that the effect of the TyG-BMI on mortality in ICU sepsis patients may be driven primarily by BMI.

Restricted cubic spline

The threshold for the TyG-BMI was established via restricted cubic splines (RCSs) to illustrate the nonlinear relationship between the TyG-BMI at ICU admission and 90-day and 180-day mortality rates. As depicted in Fig. 2, there was a nonlinear negative correlation between the ICU admission TyG-BMI and mortality rates at 90 days and 180 days in patients with sepsis combined with acute

Table 1 Baseline characteristics and outcomes of patients with sepsis combined with acute heart failure stratified by TyG-BMI

Characteristics	TyG-BMI				P
	Total (N= 1729)	T1 (N= 577)	T2 (N= 576)	T3 (N= 576)	
TyG-BMI	271.9(87.1)	195.8(24.4)	255.1(16.7)	364.9(84.7)	< 0.0001
Demographic					
Age, years	70.7(13.7)	74.5(13.5)	71.1(13.9)	66.4(12.4)	0.014
Sex (male, n)	1013(58.6)	336(58.2)	360(62.5)	317(55.0)	0.036
Ethnicity (white, n)	1193(69.0)	403(69.8)	403(70.0)	387(67.2)	0.515
Comorbidities					
Myocardial infarction	484(28.0)	170(29.5)	164(28.5)	150(26.0)	0.412
Congestive heart failure	1225(70.9)	406(70.4)	400(69.4)	419(72.7)	0.446
Chronic pulmonary disease	569(32.9)	190(32.9)	166(28.8)	213(37.0)	0.013
Diabetes without control	512(29.6)	123(21.3)	153(26.6)	236(41.0)	< 0.0001
Cerebrovascular disease	238(13.8)	95(16.5)	71(12.3)	72(12.5)	0.070
Renal disease	633(36.6)	203(35.2)	214(37.2)	216(37.5)	0.678
Severity scores					
Charlson comorbidity index	7(4–8)	7(5–9)	6(5–8)	6(5–8)	0.108
First day of SOFA	7(5–10)	7(5–9)	7(5–10.5)	7(5–11)	0.0002
SAPSII	42(34–51)	42(35–51)	43(34–52)	42(33–51)	0.573
Vital signs					
SBP, mmHg	112.4(105.0–122.6)	111.9(104.4–122.3)	111.9(104.7–122.2)	113.6(105.5–123.1)	0.120
DBP, mmHg	59.2(52.8–65.9)	58.5(52.1–65)	58.9(52.3–65.7)	60.3(54.4–67.1)	0.0002
MBP, mmHg	74.6(69.0–80.7)	74.0(68.0–79.5)	74.4(68.9–80.4)	75.7(70.3–81.9)	0.0008
Heart rate, beats/min	83.6(75.7–94.4)	83.5(75.8–94.5)	83.0(74.8–94.0)	84.4(76.6–95.0)	0.332
Respiratory rate, beats/min	19.4(17.1–22.5)	19.3(16.8–22.8)	18.7(16.8–21.9)	19.8(17.6–22.7)	0.001
Temperature, °C	36.8(36.6–37.1)	36.8(36.5–37.0)	36.8(36.5–37.1)	36.9(36.7–37.2)	< 0.0001
SpO ₂ , %	97.3(95.8–98.6)	97.5(96.0–98.8)	97.4(95.8–98.7)	96.9(95.4–98.2)	< 0.0001
Laboratory parameters					
WBC, cell/mm ³	12.2(8.95–16.1)	11.7(8.8–15.5)	12.1(8.8–15.9)	12.7(9.2–16.95)	0.039
Hemoglobin, mg/dL	10.1(8.9–11.8)	9.9(8.9–11.7)	10.1(8.9–11.8)	10.4(9.1–12.0)	0.043
Platelet, cell/mm ³	185(138.5–254)	183(136–260.5)	176(132–246)	197(146.8–257.0)	0.013
Anion gap, mEq/L	14.5(12.5–17.5)	14.5(12.5–17.0)	15(12.5–18.0)	15.0(12.5–17.5)	0.087
Bicarbonate, mEq/L	23.0(20.0–25.5)	23.0(20–25.5)	22.5(20.0–25.0)	23.0(20.5–26.0)	0.0006
Glucose, mg/dL	136.4(117.5–171.8)	127.4(109–148)	135.6(117–170.3)	149.5(127.1–192.1)	< 0.0001
Sodium, mEq/L	138.0(135.5–140.5)	138.0(135.5–140.5)	138(135–140.5)	138.5(136.0–140.5)	0.477
Potassium, mEq/L	4.35(3.95–4.8)	4.3(3.9–4.7)	4.3(3.9–4.8)	4.4(4.0–4.85)	0.027
Calcium, mg/dL	8.25(7.9–8.7)	8.25(7.9–8.7)	8.3(7.9–8.8)	8.25(8.0–8.7)	0.438
BUN, mg/dL	27.0(18.0–44.5)	26.5(17.5–44.0)	27(18–45.8)	27.0(18.0–44.3)	0.567
PT, sec	14.6(13.3–17.8)	14.8(13.4–18.0)	15.0(13.4–18.3)	14.3(13.1–17.1)	0.002
Medications					
Antiplatelet agents	1507(87.2)	512(88.7)	508(88.2)	487(84.5)	0.069
lipid-lowering drugs	1377(79.6)	444(76.9)	471(81.8)	462(80.2)	0.116
ACEI	990(57.2)	331(57.4)	330(57.3)	329(57.1)	0.996
β-blocker	1566(90.6)	528(91.5)	529(91.8)	509(88.4)	0.084
Diuretics	1651(95.5)	550(95.3)	546(94.8)	555(96.3)	0.430
Digoxin	253(14.6)	99(17.1)	78(13.5)	76(13.2)	0.108
Outcome					
Septic shock	1069(61.8)	327(56.7)	375(65.1)	367(63.7)	0.007
LOS ICU	4.5 (2.2–9.3)	4.3(2.2–8.5)	4.5(2.3–9.3)	5.0(2.3–10.7)	0.020
LOS hospital	10.5(6.4–17.0)	9.9(6.2–15.9)	10.6(6.4–16.7)	11.2(6.8–18.6)	0.028
In-hospital mortality	333(19.3)	120(20.8)	117(20.3)	96(16.7)	0.151
28-day mortality	369(21.3)	146(25.3)	127(22.0)	96(16.7)	0.001

Table 1 (continued)

Characteristics	TyG-BMI				P
	Total (N= 1729)	T1 (N=577)	T2 (N=576)	T3 (N=576)	
90-day mortality	508(29.4)	206(35.7)	165(28.6)	137(23.8)	<0.0001
180-day mortality	570(33.0)	237(41.1)	186(32.3)	147(25.5)	<0.0001

Continuous variables are presented as the means (SDs) or medians (quartiles), whereas categorical variables are presented as absolute numbers (percentages). SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO₂, pulse oxygen saturation; TyG, triglyceride–glucose; SOFA, Sequential Organ Failure Assessment; SAPS II, simplified acute physiology score II; WBC, white blood cell; BUN, blood urea nitrogen; PT, prothrombin time; ACEI, angiotensin converting enzyme inhibitor; LOS, length of stay

Table 2 Relationships between the TyG-BMI and all-cause mortality according to different models

TyG-BMI	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
90-day mortality	0.997 (0.996,0.999)	<0.0001	0.998 (0.997,1.000)	0.026	0.998 (0.997,1.000)	0.037	0.998 (0.996,0.999)	0.004
Tertile1	Ref		Ref		Ref		Ref	
Tertile2	0.723(0.564,0.927)	0.010	0.706(0.538,0.926)	0.012	0.745(0.565,0.983)	0.038	0.708(0.527,0.952)	0.022
Tertile3	0.562(0.435,0.726)	<0.0001	0.630(0.472,0.840)	0.002	0.650(0.483,0.875)	0.004	0.600(0.434,0.830)	0.002
P for trend	<0.0001		<0.0001		<0.0001		<0.0001	
180-day mortality	0.997 (0.996,0.998)	<0.0001	0.998 (0.996,0.999)	0.006	0.998 (0.997,1.000)	0.012	0.997 (0.996,0.999)	0.001
Tertile1	Ref		Ref		Ref		Ref	
Tertile2	0.684(0.538,0.871)	0.002	0.676(0.519,0.880)	0.004	0.709(0.541,0.928)	0.012	0.679(0.510,0.903)	0.008
Tertile3	0.492(0.383,0.631)	<0.0001	0.542(0.409,0.718)	<0.0001	0.560(0.419,0.748)	<0.0001	0.513(0.374,0.703)	<0.0001
P for trend	<0.0001		<0.0001		<0.0001		<0.0001	

OR, odds ratio; CI, confidence interval

Model 1: Unadjusted model

Model 2: Adjusted for age, sex, ethnicity, cerebrovascular disease, renal disease, the Charlson comorbidity index, the SOFA score, the SAPSII score and septic shock

Model 3: Adjusted for variables included in Model 2 + SBP, heart rate, respiratory rate, temperature and SpO₂

Model 4: Adjusted for variables included in Model 3 + white blood cell count, hemoglobin, platelet count, anion gap, bicarbonate, calcium, blood urea nitrogen, sodium, potassium, prothrombin time, glucose, β -blockers, diuretics, lipid-lowering drugs and ACEIs

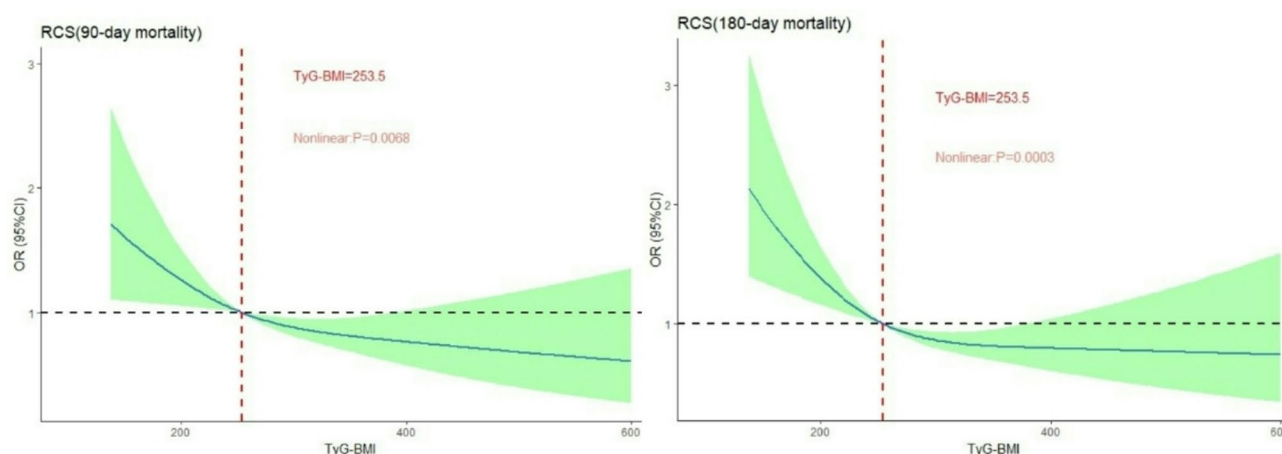


Fig. 2 Nonlinear relationships between the TyG-BMI and 90-day and 180-day mortality rates. The model was adjusted for age, sex, ethnicity, cerebrovascular disease, renal disease, Charlson comorbidity index, SOFA score, SAPSII score, septic shock, SBP, heart rate, respiratory rate, temperature, SpO₂, white blood cell count, hemoglobin, platelet count, anion gap, bicarbonate, glucose, sodium, potassium, blood urea nitrogen, calcium, prothrombin time, β -blockers, diuretics, lipid-lowering drugs and ACEIs

heart failure ($P < 0.01$), characterized by an L-shaped curve. Specifically, when the TyG-BMI at admission was less than 253.5, the risk of 90-day and 180-day mortality increased sharply as the TyG-BMI decreased. In contrast, when the TyG-BMI exceeded 253.5, the mortality risk decreased progressively with increasing TyG-BMI

(nonlinear $P < 0.01$). However, as the TyG-BMI continued to rise, the odds ratio (OR) decreased. Overall, elevated TyG-BMI values at ICU admission were associated with a lower risk of short-term mortality.

Kaplan–Meier analysis

The study population was divided into three groups based on TyG-BMI tertiles: T1, T2, and T3. Kaplan–Meier survival analysis was performed to assess 90-day and 180-day mortality rates among these groups of patients with sepsis combined with acute heart failure. As illustrated in Fig. 3, the survival curve for the T1 group was significantly lower than that for the T2 and T3 groups (log-rank test, $P < 0.0001$). The differences between groups were statistically significant ($P < 0.05$), indicating that a lower TyG-BMI at ICU admission is associated with higher mortality rates at 90 days and 180 days.

Subgroup analysis

To explore potential clinical heterogeneity, we conducted interaction and stratification analyses (Fig. 4). We assessed the relationship between the TyG-BMI and 90-day and 180-day mortality across various subgroups. Stratification was based on age (< 65 years and ≥ 65 years), sex, ethnicity, myocardial infarction, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, diabetes, renal disease, and septic shock. For 90-day and 180-day mortality, significant interactions were found only in the subgroup of patients with renal disease ($P < 0.05$). These findings suggest that the impact of the TyG-BMI on mortality may depend on specific clinical characteristics.

Sensitivity analysis

The results of the sensitivity analysis are presented in Table 3. When patients with myocardial infarction were excluded, the odds ratios (ORs) for 90-day and 180-day mortality were 0.997 (95% CI: 0.995–0.999) and 0.997

(95% CI: 0.995–0.999), respectively. When both cerebrovascular disease patients and myocardial infarction patients were excluded, the ORs were 0.997 (95% CI: 0.994–0.999) and 0.997 (95% CI: 0.995–0.999), respectively. After all individuals with missing values were removed, the ORs were 0.998 (95% CI: 0.996–0.999) and 0.997 (95% CI: 0.996–0.999), respectively. Trend tests across the T1, T2, and T3 strata remained statistically significant ($P < 0.01$).

Boruta algorithm

Figure 5 shows the results of feature selection via the Boruta algorithm. In the Boruta analysis, variables in the green area were identified as important features, whereas those in the red area were classified as nonessential. The results indicate that the TyG-BMI was consistently identified as a significant predictor for both 90-day and 180-day mortality risk prediction via the Boruta algorithm.

Discussion

This study, which is based on the MIMIC-IV database, analyzed the relationship between triglyceride–glucose (TyG) body mass index (BMI) and mortality in ICU patients with sepsis complicated by acute heart failure (AHF). The results revealed a significant reverse J-shaped relationship between the TyG-BMI and all-cause mortality at 90 and 180 days. Specifically, patients with a lower TyG-BMI presented a greater risk of mortality, with a critical threshold identified at 253.5. Even after adjusting for multiple confounding factors, this relationship remained significant, and sensitivity analyses further confirmed its stability across different subgroups, suggesting that the TyG-BMI is an independent predictor of

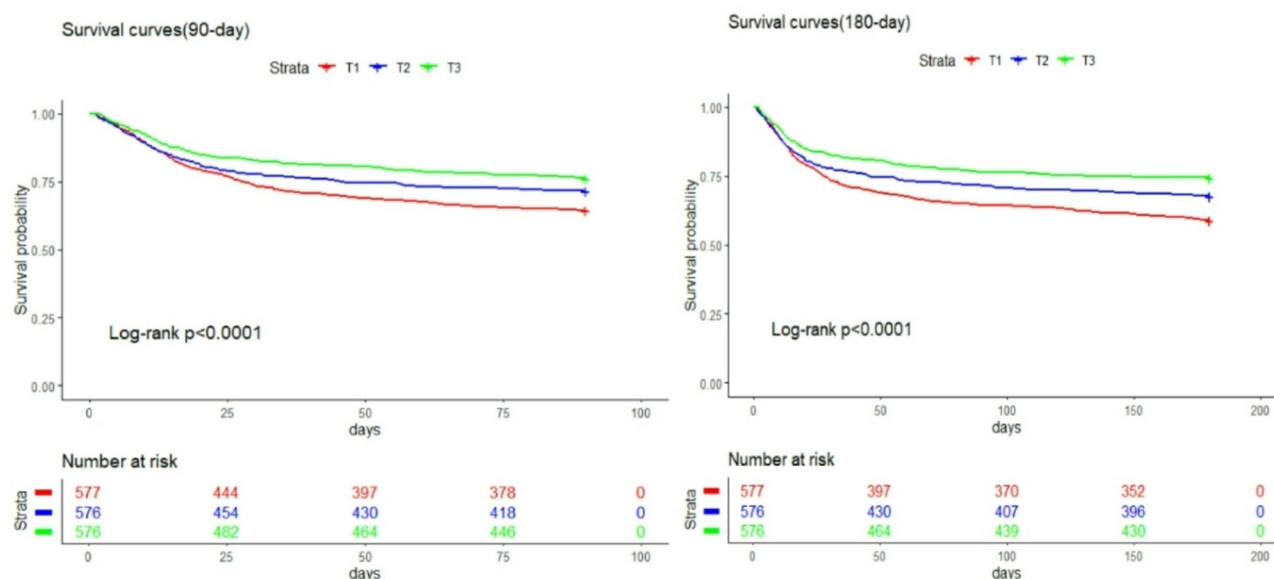


Fig. 3 Kaplan–Meier plots for 90-day and 180-day mortality by ICU admission TyG-BMI strata

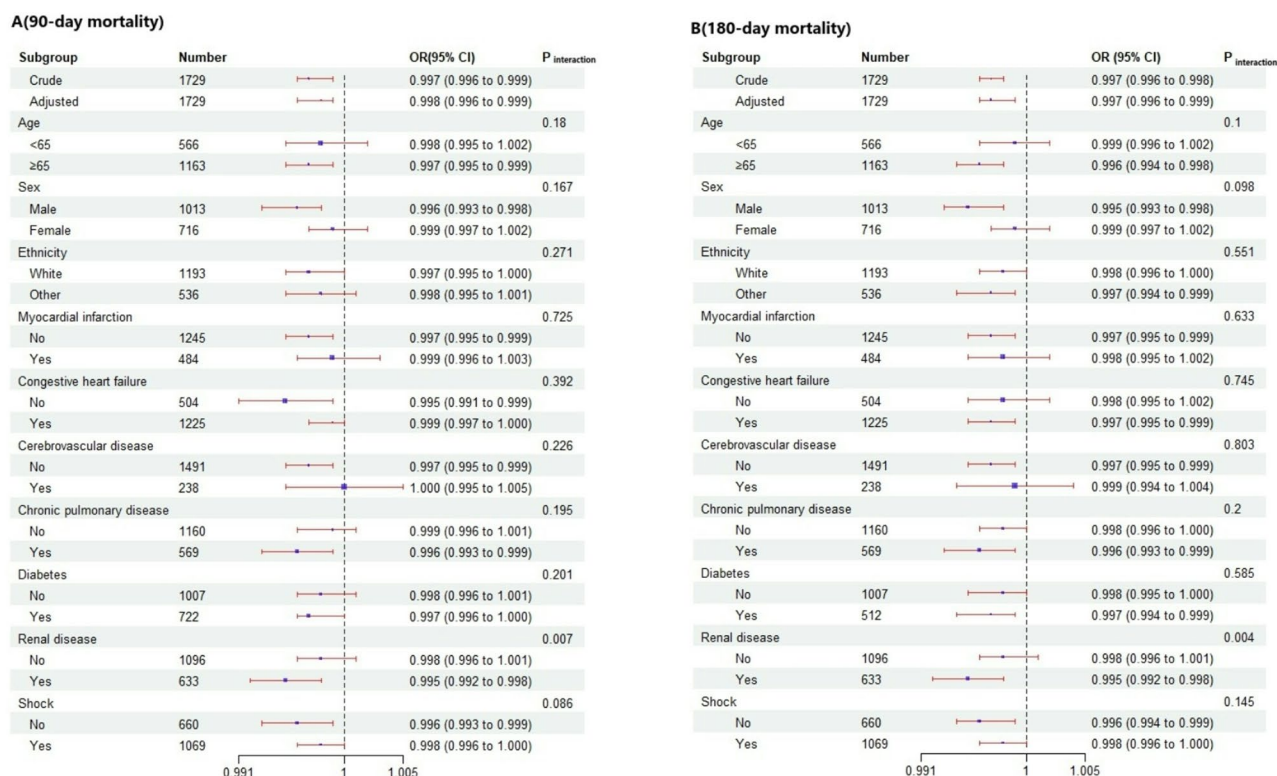


Fig. 4 Effect size of the TyG-BMI on 90-day and 180-day mortality in prespecified and exploratory subgroups. The effect size was adjusted for age, sex, ethnicity, cerebrovascular disease, renal disease, Charlson comorbidity index, SOFA score, SAPSII score, septic shock, SBP, heart rate, respiratory rate, temperature, SpO₂, white blood cell count, hemoglobin, platelet count, anion gap, bicarbonate, glucose, sodium, potassium, blood urea nitrogen, calcium, prothrombin time, β-blockers, diuretics, lipid-lowering drugs and ACEIs, with the exception of the subgroup variable

Table 3 Sensitivity analyses

TyG-BMI	90-day mortality			180-day mortality		
	OR(95%CI)	P	P for trend	OR(95%CI)	P	P for trend
Excluding participants with myocardial infarction						
Model	0.997(0.995,0.999)	0.002		0.997(0.995,0.999)	0.001	
Tertile1	Ref			Ref		
Tertile2	0.692(0.490,0.976)	0.036		0.698(0.501,0.972)	0.033	
Tertile3	0.502(0.341,0.740)	< 0.0001	< 0.0001	0.449(0.309,0.653)	< 0.0001	< 0.0001
Excluding participants with myocardial infarction and cerebrovascular disease						
Model	0.997(0.994,0.999)	0.001		0.997(0.995,0.999)	0.002	
Tertile1	Ref			Ref		
Tertile2	0.729(0.499,1.065)	0.102		0.781(0.542,1.124)	0.184	
Tertile3	0.503(0.330,0.766)	0.001	< 0.0001	0.463(0.308,0.697)	< 0.0001	< 0.0001
Exclude all individuals with missing values						
Model	0.998(0.996,0.999)	0.005		0.997(0.996,0.999)	0.003	
Tertile1	Ref			Ref		
Tertile2	0.682(0.503,0.927)	0.014		0.657(0.488,0.884)	0.006	
Tertile3	0.587(0.420,0.820)	0.002	< 0.0001	0.510(0.368,0.706)	< 0.0001	< 0.0001

OR, odds ratio; CI, confidence interval; Ref, reference; Adjusted for age, sex, ethnicity, cerebrovascular disease, renal disease, Charlson comorbidity index, SOFA score, SAPSII score, septic shock, SBP, heart rate, respiratory rate, temperature, SpO₂, white blood cell count, hemoglobin, platelet count, anion gap, bicarbonate, glucose, sodium, potassium, blood urea nitrogen, calcium, prothrombin time, β-blockers, diuretics, lipid-lowering drugs and ACEIs

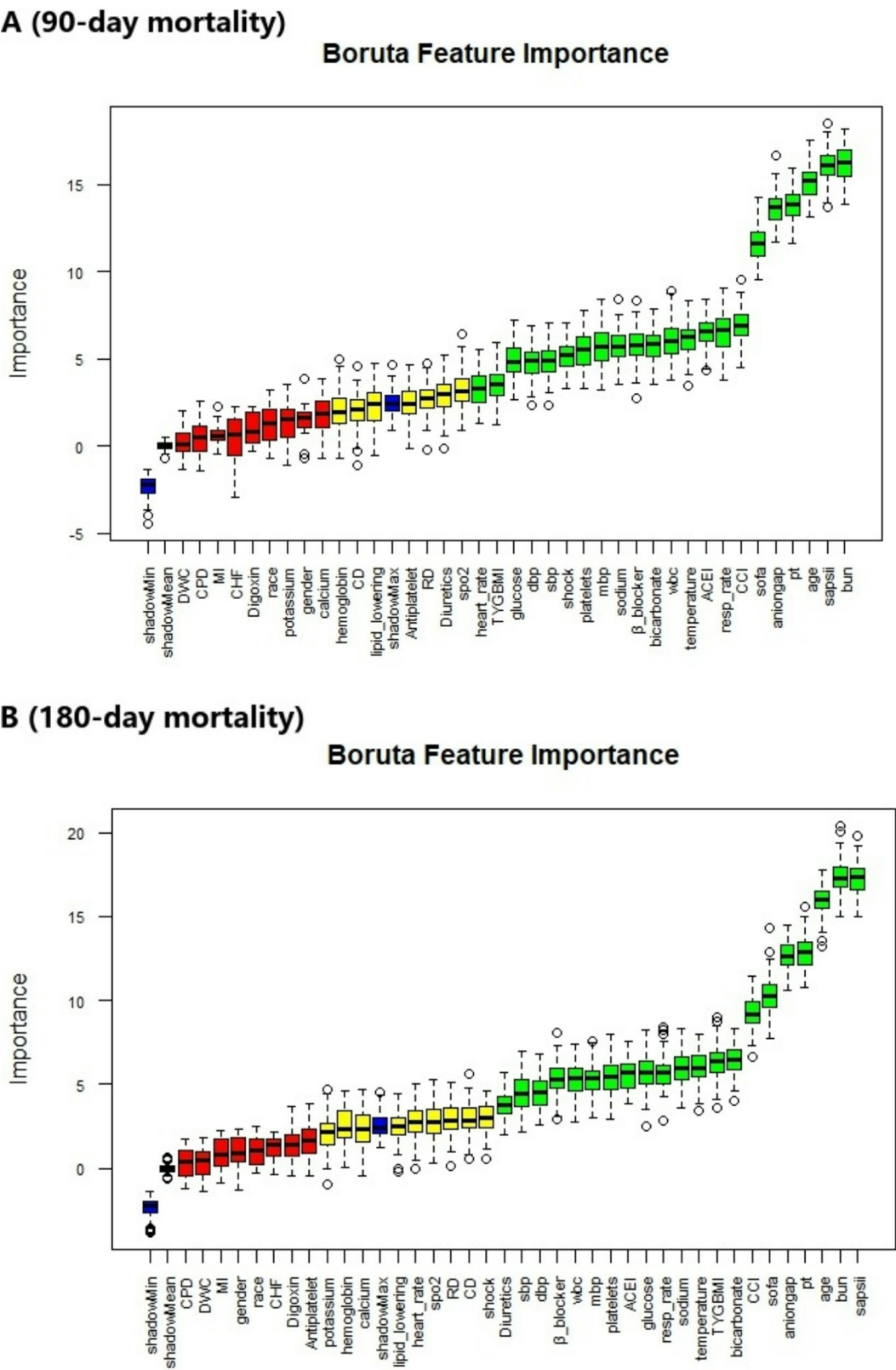


Fig. 5 (See legend on next page.)

(See figure on previous page.)

Fig. 5 Feature selection for predicting 90-day and 180-day mortality risk via the Boruta algorithm. The horizontal axis represents the name of each variable, and the vertical axis represents the Z value of each variable. The box plot shows the Z value of each variable during model calculation. The green boxes represent important variables, and the red boxes represent unimportant variables. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO₂, pulse oxygen saturation; MI, myocardial infarction; CHF, congestive heart failure; CD, cerebrovascular disease; CPD, chronic pulmonary disease; DWC, diabetes without control; RD, renal disease; CCI, Charlson comorbidity index. TyG, triglyceride–glucose; TyG-BMI, TyG × BMI; SOFA, Sequential Organ Failure Assessment score; SAPS II, simplified acute physiology score II; WBC, white blood cell; BUN, blood urea nitrogen; PT, prothrombin time; ACEI, angiotensin converting enzyme inhibitor

mortality. This association may be attributed to the “obesity paradox.” This finding offers a new perspective for risk assessment and prevention strategies in patients with sepsis and AHF.

Previous research by Dou J et al. established a significant association between the TyG-BMI and all-cause mortality in heart failure patients. Their study revealed that higher TyG-BMI indices were associated with lower mortality risk over a 360-day period [18]. Our study further corroborates this finding, particularly with the observed reverse J-shaped relationship, which aligns with previous heart failure research [18, 19], underscoring the need for further investigation in the context of sepsis and AHF.

This study specifically focused on the relationship between TyG-BMI and mortality in patients with sepsis complicated by AHF. The results indicated that patients with higher TyG-BMIs (T3 group) had lower 90-day and 180-day mortality rates despite having more health issues. Kaplan–Meier survival analysis further confirmed that patients with lower TyG-BMIs (T1 group) had significantly higher mortality rates. Additionally, there was a nonlinear relationship between TyG-BMI and mortality: when the TyG-BMI was below 253.5, the mortality risk sharply increased; above this threshold, the risk gradually decreased. Boruta analysis identified the TyG-BMI as an important predictor of 90-day and 180-day mortality.

In subgroup analyses, significant interactions were observed in specific populations ($P < 0.05$). Notably, the impact of the TyG-BMI on mortality was more pronounced in patients with kidney disease. These findings suggest that the statistical significance of the effect of the TyG-BMI in these groups may be due to the increased complexity of health conditions in renal-compromised patients. These findings suggest that the TyG-BMI may have a protective effect on these subgroups, highlighting its potential as a prognostic indicator and tool for individualized treatment. Future studies should further explore the potential applications and mechanisms of the TyG-BMI in high-risk populations to provide more targeted guidance for clinical treatment decisions.

The association between the TyG index and heart failure has been well documented, with higher TyG index levels linked to increased risks of heart failure, mortality, and hospital readmission [20–22]. Additionally, in ICU patients with sepsis, a U-shaped relationship has been observed between the TyG index and all-cause mortality

[23–25]. The relationship between BMI and heart failure has also been confirmed in several large-scale randomized controlled trials, with individuals with lower BMIs facing higher risks of HF hospitalization and all-cause mortality, whereas those who are overweight present lower risks [26–28]. In patients with sepsis complicated by AHF, the inverse relationship between the TyG-BMI index and all-cause mortality may be influenced by both BMI and insulin resistance (IR). Studies have shown that more than 70% of the obese population exhibits IR, and IR is closely associated with obesity [29–31]. Obesity has been found to have a protective effect in patients already diagnosed with HF, a phenomenon known as the “obesity paradox” [32]. This paradox can be explained by several mechanisms: patients with sepsis and AHF are often in a catabolic state, and higher BMI or obesity may indicate greater physiological reserves, potentially leading to better outcomes [33]. Obesity is associated with a hypermetabolic state of elevated glucose and fatty acids, which can activate immune responses and influence inflammation, factors that may help modulate inflammatory responses and improve disease outcomes [34, 35]. Moreover, obese individuals tend to have lower levels of B-type natriuretic peptide (BNP), indicating better hemodynamic profiles, allowing for better tolerance of beneficial medications [36, 37]. Finally, anti-inflammatory adipokines may play a protective role in obese patients. For example, while tumor necrosis factor- α (TNF- α) is associated with cardiac injury, soluble TNF- α receptors produced by adipose tissue can neutralize TNF- α , suggesting a cardioprotective effect [38, 39].

The findings of this study have important implications for clinical practice and patient self-management. First, the TyG-BMI could serve as an effective predictor in the management of patients with sepsis complicated by AHF, especially as patients with lower TyG-BMI indices face significantly greater mortality risks, indicating the need for enhanced monitoring and early intervention in this group. Second, close attention to the nutritional status of HF patients and timely nutritional support are crucial for improving patient prognosis. However, several limitations exist in this study. First, the retrospective nature of the investigation limits the ability to establish definitive causal relationships. Although we employed multivariate adjustments and subgroup analyses to mitigate the influence of confounding factors, these potential factors may still affect clinical outcomes. Second, the retrospective

design could introduce selection bias and residual confounding, affecting the external validity of the results. Furthermore, our study primarily assessed baseline TyG-BMI indices, failing to capture the dynamic changes in insulin resistance during the disease course. Finally, this study was based on single-center data, necessitating validation through multicenter studies to ensure the generalizability of the findings. Future research should aim to address these limitations with broader samples and more rigorous designs to provide stronger evidence supporting the use of the TyG-BMI index as a predictive marker.

Conclusion

In conclusion, this cohort study revealed that a higher TyG-BMI was strongly associated with reduced all-cause mortality in ICU patients suffering from sepsis combined with acute heart failure (AHF). These findings suggest that the TyG-BMI could serve as a valuable prognostic tool, aiding clinicians in early risk assessment and timely intervention to enhance patient outcomes.

Abbreviations

AHF	Acute heart failure
ANOVA	Analysis of variance
AUC	Area under the curve
BIDMC	Beth Israel deaconess medical center
BMI	Body mass index
BUN	Blood urea nitrogen
CCI	Charlson comorbidity index
CD	Cerebrovascular disease
CHF	Congestive heart failure
CI	Confidence interval
CPD	Chronic pulmonary disease
DBP	Diastolic blood pressure
DWC	Diabetes without control
FBG	Fasting blood glucose
ICD-10	International classification of diseases 10
ICU	Intensive care unit
IQR	Interquartile range
IR	Insulin resistance
LOS	Length of stay
MBP	Mean blood pressure
MI	Myocardial infarction
MIMIC	Medical information mart for intensive care
MIT	Massachusetts institute of technology
OR	Odds ratio
PT	Prothrombin time
RCS	Restricted cubic spline
RD	Renal disease
ROC	Receiver operating characteristic
SAPS II	Simplified acute physiology score II
SBP	Systolic blood pressure
SD	Standard deviation
SOFA	Sequential organ failure assessment score
SpO ₂	Pulse oxygen saturation
SQL	Structured query language
TG	Triglyceride
TyG index	Triglyceride-glucose index
TyG-BMI	Triglyceride glucose-body mass index
VIF	Variance inflation factor
WBC	White blood cell

Supplementary Information

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Supplementary Material 1

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Author contributions

Conceptualization, Methodology, Formal Analysis HPX and JYX; Visualization, Investigation, HN and XWC; Writing - Original Draft, HPX and JYX; Writing - Review & Editing, PH and HN; Funding acquisition HPX.

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Data availability

All datasets used during the present study are publicly available in the MIMIC-IV v2.2 database (<https://mimic.physionet.org/>).

Declarations

Ethics approval and consent to participate

MIMIC-IV is an anonymized public database approved by the institutional review boards of the Massachusetts Institute of Technology (MIT) and Beth Israel Deaconess Medical Center (BIDMC). The requirement for informed consent was waived because of the thorough anonymization and deidentification of all patient information in the database.

Consent for publication

The submitted manuscript has been read and approved by all the authors.

Competing interests

The authors declare no competing interests.

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