The triglyceride-glucose index played an important role in prognosis in critically ill patients with heart disease

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Research

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Abstract

Background

As an alternative method to evaluate insulin resistance (IR), triglyceride-glucose index (TyG) was shown to be related to the severity and prognosis of cardiovascular diseases. The main objective of this study was to explore the association between TyG and in-hospital mortality in critically ill patients with heart disease

Method:

TyG was calculated as previously reported: $\ln [\text{fasting TGs (mg/dL)} * \text{FBG (mg/dL)} / 2]$. All patients were divided into four different categories based on TyG quartiles. Primary outcome was in-hospital mortality. Binary logistic regression analysis was performed to determine the independent effect of TyG.

Result

4839 critically ill patients with heart disease were included. In-hospital mortality increased as TyG quartiles increased (Quartile 4 vs Quartile 1: 12.1 vs 5.3, $P < 0.001$). Even after adjusting for confounding variables, TyG was still independently associated with the increased risk of in-hospital mortality in critically ill patients with heart disease (Quartile 4 vs Quartile 1: OR, 95% CI: 2.43, 1.79–3.31, $P < 0.001$, P for trend < 0.001). However, we did not observe the association between increased TyG and the risk of mortality in patients with diabetes. Furthermore, as TyG quartiles increased, the length of intensive care unit (ICU) stay was prolonged (Quartile 4 vs Quartile 1: 2.3, 1.3–4.9 vs 2.1, 1.3–3.8, $P = 0.007$). And the significant interactions were not found in most subgroups.

Conclusion

TyG was independently correlated with in-hospital mortality in critically ill patients with heart disease.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide in contemporary society. Especially, in patients with severe CVD, the mortality was greatly increased [1–2]. In order to reduce the mortality of serious CVD patients, coronary artery care unit (CCU) and cardiac intensive care unit (CICU) came into being. After decades of development, they eventually focused on the management of patients with severe CVD which needed meticulous care and targeted treatment [3–4]. Nowadays, the status of CCU and CICU are increasingly important, besides, a variety of studies target on how to predict and improve prognosis of patients. As for clinicians, easily accessible and reliable prognostic indicators for critically ill patients with heart disease are always welcomed.

Type 2 diabetes mellitus (T2DM) has been widely proven to be one of the most significant risk factors for CVD [5]. The key mechanism of T2DM is insulin resistance (IR), which has been shown to be closely associated with the development of CVD and atherosclerosis [6–9]. However, as the gold standard test for IR, the hyperinsulinaemic-euglycaemic clamp is time-consuming, expensive and complex [10]. In this sense, the triglyceride-glucose index (TyG index) has emerged as an alternative method, which evaluate IR by using the levels of glycemia (mg/dl) and fasting triglycerides (TG) (mg/dl) [11]. Studies have indicated that TyG index was associated positively with T2DM risk [12–15]. Notably, previous studies have manifested that TyG index was related to the increased risk of worse outcomes in patients with CVD. Zhao et.al recently demonstrated that TyG index had a prognostic role in patients with T2DM and non-ST-segment elevation acute coronary syndrome (NSTEMI) undergoing percutaneous coronary intervention (PCI) [16]. In addition, high TyG index was also proved to be associated with increased incidence of CVD events in healthy Caucasian and China participants [17–19]. Nevertheless, to the best of our knowledge, no research has demonstrated the effect of TyG index in patients with severe cardiovascular disease. Thus, our main objective in this study was to investigate the relationship between TyG index and in-hospital mortality of critically ill patients with heart disease.

2. Method

2.1. Population selection criteria. CCU and CICU patients were potentially eligible. Adult patients (≥ 18 years) hospitalized for more than 2 days at their first admission were available. Patients meeting the following criteria were excluded: (1) hospital admission for non-heart disease; (2) triglyceride and glucose data missing; (3) APS and APACHE IV data missing. A total of 4839 patients were included (Fig. 1).

2.2. Data extraction. The data used in this study was from eICU Collaborative Research Database [20], which collected information on 20,859 admissions from 208 hospitals in the United States between 2014 and 2015. This database is available at: <https://doi.org/10.13026/C2WM1R>. And the author was approved to access to the database through Protecting Human Research Participants exam (certificate number: 9728458).

Following data were collected: demographics (age, gender and race), vital signs (blood pressure, heart rate, respiration rate, oxygen saturation), body mass index, diagnoses and comorbidities (congestive heart failure, coronary artery disease, acute coronary syndrome, ST-elevation myocardial infarction(STEMI), non-ST-elevation myocardial infarction(NSTEMI), arrhythmias, cardiac arrest, bradycardia, atrial fibrillation, ventricular arrhythmias, atrioventricular block, cardiomyopathy, valve disease, shock, pulmonary embolism, pulmonary hypertension, hypertension, diabetes, hypercholesterolemia, chronic obstructive pulmonary disease(COPD), respiratory failure, chronic kidney disease, acute kidney injury, malignancy, stroke, sepsis), laboratory parameters(white blood cell, lymphocyte, monocyte and neutrophil percentage, red blood cell platelet, hemoglobin, hematocrit, glucose, triglyceride, creatinine, blood nitrogen urea, sodium, potassium), medication use(antiplatelet, oral anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor

blocker(ACEI/ARB), statin), acute physiology score(APS) and Acute Physiology and Chronic Health Evaluation IV (APACHE IV)[21].

TyG index was obtained by the formula $\text{Ln} [\text{fasting triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]$.

2.3. Grouping and outcomes. All enrolled patients were divided into four different categories based on the TyG quartiles. The primary outcome was in-hospital mortality. Secondary outcomes were length of intensive care unit (ICU) stay and length of hospital stay.

2.4. Statistical analysis. Normally distributed continuous variables were expressed as mean $\pm$ standard deviation (SD) and compared between groups using analysis of variance. Skewed data were expressed as median and interquartile range (IQR) and compared using Kruskal–Wallis test. Categorical variables were expressed as number (percentage) and identified significant heterogeneity in the frequencies using Chi-square test.

The relationship between TyG and in-hospital mortality was identified by binary logistic regression analysis and the results were expressed as odds ratio (OR) and 95% confidence interval (CI). P for trend was calculated. Covariates were selected by statistical analysis and clinical doubt to modulate the outcome. The curves that conformed to the general trend were plotted through local weighted regression (Lowess). Subgroup analysis was used to determine the relationship between TyG and in-hospital mortality in different subgroups, P for interaction was calculated. A two-tailed P value < 0.05 was considered statistically significant. All data analysis were performed by Stata V.15.1.

3. Result

3.1. Subjects and baseline characteristics. 4839 patients were analyzed (Fig. 1). According to TyG quartiles, all patients were divided into four groups: $\text{TyG} < 8.51$ ($n = 1201$), $8.51 \leq \text{TyG} < 8.92$ ($n = 1221$), $8.92 \leq \text{TyG} < 9.37$ ($n = 1214$), $\text{TyG} \geq 9.37$ ($n = 1203$). The characteristics of different TyG groups were summarized in Table 1, patients with high TyG levels had the following characteristics: elder, Caucasian, higher blood pressure and higher body mass index. Moreover, patients in higher PLR quartiles also tended to present more diagnoses and comorbidities of coronary artery disease, acute coronary syndrome, STEMI, NSTEMI, cardiac arrest, shock, diabetes, respiratory failure, chronic kidney disease, acute kidney injury, sepsis whereas less congestive heart failure, arrhythmias, bradycardia, atrial fibrillation, cardiomyopathy, valve disease, COPD. Besides, Table 1 indicated that as TyG quartiles increased, white blood cell, lymphocyte percentage, red blood cell, hemoglobin, hematocrit, platelet, glucose, triglyceride, creatinine, blood nitrogen urea, potassium values tended to increase, while monocyte and neutrophil percentage, sodium values tended to decrease. Of note, there was no statistically significant difference in administration of medication among the TyG categories. Furthermore, patients with higher TyG index had significantly higher APS score which was used to evaluate the severity of ICU patients and predict their prognosis (Table 1).

3.2. Association between PLR and outcomes. Overall, in-hospital mortality rate was 8.5%. As TyG quartiles increased, in-hospital mortality increased significantly (Quartile 4 vs Quartile 1: 12.1 vs 5.3, $P < 0.001$) (Table 2). In unadjusted logistic regression analysis, there was a positive association between TyG and in-hospital mortality (Quartile 4 vs Quartile 1: OR, 95% CI: 2.43, 1.79–3.31, $P < 0.001$, P for trend < 0.001). In model 2, after adjusting for age, gender and ethnicity, higher TyG quartiles were markedly related to the increased risk of in-hospital mortality (Quartile 4 vs Quartile 1: OR, 95% CI: 2.90, 2.12–3.96, $P < 0.001$, P for trend < 0.001). In model 3, adjusted for more confounding variables, the TyG index was still independently associated with the increased risk of in-hospital mortality (Quartile 4 vs Quartile 1: OR, 95% CI: 1.83, 1.27–2.64, $P < 0.001$, P for trend < 0.001). Furthermore, when TyG was considered as a continuous variable in the model for analysis, we observed that for each unit increase in the TyG index, the risk of in-hospital mortality increased approximately 0.35-fold in Model 1 ($p < 0.001$), 0.43-fold in Model 2 ($p < 0.001$), 0.23-fold in Model 3 ($p < 0.001$) respectively (Table 3). Interestingly, of the 4069 patients who didn't suffer from diabetes, we found that TyG had a significant effect on in-hospital mortality either in logistics regression with or without adjusting for confounding variables, which was consistent with the conclusion drawn in Table 3. Conversely, as we screened patients with diabetes ($N = 770$) for logistics regression analysis, no significant correlation has been shown between TyG and in-hospital mortality with or without adjusting for confounding risk factors (Table 4). Besides, from Lowess curve in Fig. 2, we found that the relationship between TyG and mortality was linear. Specifically, as TyG increased, in-hospital mortality increased.

Table 1
Characteristics of patients stratified by TyG quartiles.

Characteristics	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
Age(years)	65.2 ± 13.8	67.8 ± 14.4	67.0 ± 13.4	64.5 ± 13.6	61.5 ± 12.8	< 0.001
Gender, n(%)						0.626
Male	2993(61.9)	756(63.0)	743(60.9)	741(61.0)	753(62.6)	
Female	1846(38.1)	445(37.0)	478(39.1)	473(39.0)	450(37.4)	
Ethnicity, n(%)						0.001
Caucasian	3668(75.8)	887(73.9)	929(76.1)	934(76.9)	918(76.3)	
African American	663(13.7)	198(16.5)	176(14.4)	155(12.8)	134(11.1)	
Other	508(10.5)	116(9.7)	116(9.5)	125(10.3)	151(12.6)	
Vital signs						
Systolic blood pressure(mmHg)	122.3 ± 18.0	120.7 ± 19.0	121.6 ± 17.2	122.7 ± 17.8	124.5 ± 18.0	< 0.001
Diastolic blood pressure(mmHg)	66.5 ± 10.9	65.8 ± 11.3	66.4 ± 10.8	66.8 ± 10.4	67.2 ± 11.1	0.011
Mean blood pressure(mmHg)	82.4 ± 12.0	81.2 ± 12.5	82.0 ± 11.8	82.7 ± 11.7	83.5 ± 11.9	< 0.001
Heart rate(beats/min)	85.0 ± 20.6	83.0 ± 20.3	85.0 ± 20.8	85.3 ± 20.4	86.9 ± 20.8	< 0.001
Respiration rate(beats/min)	20.0 ± 5.8	20.0 ± 5.5	20.1 ± 5.7	19.9 ± 6.0	20.1 ± 6.1	0.694
Oxygen saturation(%)	98(95, 100)	98(95, 99)	98(95, 100)	98(95, 100)	98(95, 99)	0.535

Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were presented as number (percentage). P values were calculated using analysis of variance, Kruskal–Wallis test or Chi-square test to compare differences in variables between different TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; TyG: triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Characteristics	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
Body mass index(kg/m ²)	29.5 ± 6.7	27.3 ± 6.5	28.9 ± 6.5	30.0 ± 6.7	31.8 ± 6.4	< 0.001
Diagnoses and comorbidities, n(%)						
Congestive heart failure	793(16.4)	242(20.2)	210(17.2)	180(14.8)	161(13.4)	< 0.001
Coronary artery disease	3043(62.9)	691(57.5)	776(63.6)	802(66.1)	774(64.3)	< 0.001
Acute coronary syndrome	2295(47.4)	511(42.6)	608(49.8)	601(49.5)	575(47.8)	0.001
STEMI	1035(21.4)	223(18.6)	267(21.9)	275(22.7)	270(22.4)	0.050
NSTEMI	563(11.6)	122(10.2)	168(13.8)	131(10.8)	142(11.8)	0.032
Arrhythmias	1234(25.5)	358(29.8)	354(29.0)	280(23.1)	242(20.1)	< 0.001
Cardiac arrest	430(8.9)	75(6.2)	98(8.0)	126(10.4)	131(10.9)	< 0.001
Bradycardia	178(3.7)	59(4.9)	47(3.9)	38(3.1)	34(2.8)	0.033
Atrial fibrillation	675(14.0)	194(16.2)	199(16.3)	154(12.7)	128(10.6)	< 0.001
Ventricular arrhythmias	344(7.1)	87(7.2)	99(8.1)	82(6.8)	76(6.3)	0.355
Atrioventricular block	127(2.6)	35(2.9)	36(3.0)	30(2.5)	26(2.2)	0.569
Cardiomyopathy	297(6.1)	85(7.1)	103(8.4)	54(4.5)	55(4.6)	< 0.001
Valve disease	182(3.8)	53(4.4)	54(4.4)	48(4.0)	27(2.2)	0.014

Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were presented as number (percentage). P values were calculated using analysis of variance, Kruskal–Wallis test or Chi-square test to compare differences in variables between different TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; TyG: triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Characteristics	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
Shock	975(20.2)	220(18.3)	225(18.4)	251(20.7)	279(23.2)	0.008
Pulmonary embolism	58(1.2)	15(1.3)	16(1.3)	14(1.2)	13(1.1)	0.957
Pulmonary hypertension	49(1.0)	18(1.5)	13(1.1)	11(0.9)	7(0.6)	0.156
Hypertension	1133(23.4)	291(24.2)	284(23.3)	264(21.8)	294(24.4)	0.384
Diabetes	770(15.9)	97(8.1)	162(13.3)	197(16.2)	314(26.1)	< 0.001
Hypercholesterolemia	452(9.3)	94(7.8)	117(9.6)	110(9.1)	131(10.9)	0.077
COPD	352(7.3)	105(8.7)	98(8.3)	75(6.2)	74(6.2)	0.026
Respiratory failure	1038(21.5)	202(16.8)	248(20.3)	287(23.6)	301(25.0)	< 0.001
Chronic kidney disease	546(11.3)	149(12.4)	106(8.7)	144(11.9)	147(12.2)	0.011
Acute kidney injury	659(13.6)	128(10.7)	128(10.5)	184(15.2)	219(18.2)	< 0.001
Malignancy	121(2.5)	22(1.8)	35(2.9)	38(3.1)	26(2.2)	0.144
Stroke	233(4.8)	65(5.4)	62(5.1)	49(4.0)	57(4.7)	0.433
Sepsis	519(10.7)	105(8.7)	103(8.4)	140(11.5)	171(14.2)	< 0.001
Laboratory parameters						
White blood cell (10 ⁹ /L)	11.3 ± 5.3	10.3 ± 4.8	11.1 ± 5.1	11.9 ± 5.4	12.1 ± 5.8	< 0.001
Lymphocyte percentage (%)	17.8 ± 10.5	17.1 ± 9.8	17.6 ± 10.5	17.5 ± 10.6	18.8 ± 10.9	< 0.001

Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were presented as number (percentage). P values were calculated using analysis of variance, Kruskal–Wallis test or Chi-square test to compare differences in variables between different TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; TyG: triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Characteristics	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
Monocyte percentage (%)	7.6 ± 2.9	8.0 ± 3.1	7.7 ± 2.8	7.4 ± 2.8	7.3 ± 2.9	< 0.001
Neutrophil percentage (%)	71.9 ± 11.6	72.4 ± 11.4	72.1 ± 11.6	72.3 ± 11.6	70.9 ± 11.8	0.003
Red blood cell (10 ⁹ /L)	4.3 ± 0.8	4.2 ± 0.7	4.2 ± 0.8	4.3 ± 0.8	4.4 ± 0.8	< 0.001
Platelet (10 ⁹ /L)	227 ± 83	219 ± 79	227 ± 84	231 ± 81	233 ± 86	< 0.001
Hemoglobin (g/dL)	12.8 ± 2.4	12.6 ± 2.2	12.6 ± 2.5	12.8 ± 2.5	13.2 ± 2.3	< 0.001
Hematocrit (%)	38.5 ± 6.6	38.0 ± 6.1	38.0 ± 6.8	38.5 ± 6.9	39.4 ± 6.5	< 0.001
Glucose (mg/dL)	139.6 ± 39.3	116.6 ± 21.4	129.8 ± 28.1	142.1 ± 34.3	170.1 ± 47.1	< 0.001
Triglyceride (mg/dL)	140.6 ± 109.6	65.3 ± 16.9	98.9 ± 21.4	136.9 ± 33.4	261.7 ± 156.1	< 0.001
Creatinine (mg/dL)	1.44 ± 1.25	1.34 ± 1.12	1.38 ± 1.19	1.49 ± 1.32	1.54 ± 1.37	< 0.001
Blood nitrogen urea (mg/dL)	24.6 ± 17.0	23.3 ± 15.5	24.5 ± 16.7	24.4 ± 16.5	25.9 ± 18.9	0.002
Sodium (mmol/L)	137.3 ± 4.4	137.3 ± 4.5	137.5 ± 4.3	137.6 ± 4.3	136.9 ± 4.6	< 0.001
Potassium (mmol/L)	4.2 ± 0.7	4.1 ± 0.6	4.1 ± 0.6	4.2 ± 0.7	4.2 ± 0.7	< 0.001
TyG	8.9(8.5, 9.4)	8.3(8.1, 8.4)	8.7(8.6, 8.8)	9.1(9.0, 9.2)	9.7(9.5, 10.1)	< 0.001
Medication use, n(%)						

Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were presented as number (percentage). P values were calculated using analysis of variance, Kruskal–Wallis test or Chi-square test to compare differences in variables between different TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; TyG: triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Characteristics	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
Antiplatelet	2611(54.0)	629(52.4)	662(54.2)	661(54.5)	659(54.8)	0.639
Oral anticoagulants	375(7.8)	107(8.9)	96(7.9)	94(7.7)	78(6.5)	0.173
Beta-blockers	1877(38.8)	430(35.8)	476(39.0)	481(39.6)	490(40.7)	0.079
ACEI/ARB	1054(21.8)	270(22.5)	266(21.8)	247(20.4)	271(22.5)	0.531
Statin	1680(34.7)	386(32.1)	443(36.3)	421(34.7)	430(35.7)	0.145
APS	35(25, 50)	33(24, 46)	35(25, 48)	36(25, 53)	38(26, 56)	< 0.001
APACHE IV	49(36, 64)	48(36, 61)	49(36, 64)	49(35, 67)	49(35, 68)	0.146
Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were presented as number (percentage). P values were calculated using analysis of variance, Kruskal–Wallis test or Chi-square test to compare differences in variables between different TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; TyG: triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.						

Table 2
Outcomes of patients stratified by TyG quartiles

Outcomes	Total (n = 4839)	Quartiles of TyG				P Value
		Quartile 1(n = 1201)	Quartile 2(n = 1221)	Quartile 3(n = 1214)	Quartile 4(n = 1203)	
		TyG < 8.51	8.51 ≤ TyG < 8.92	8.92 ≤ TyG < 9.37	TyG ≥ 9.37	
In-hospital mortality, n(%)	413(8.5)	64(5.3)	87(7.1)	117(9.6)	145(12.1)	< 0.001
Length of ICU stay (days)	2.2(1.3, 4.3)	2.1(1.3, 3.8)	2.2(1.3, 4.2)	2.4(1.3, 4.7)	2.3(1.3, 4.9)	0.007
Length of hospital stay (days)	5.9(3.3, 11.1)	5.7(3.2, 9.8)	6.0(3.5, 11.5)	6.2(3.3, 11.7)	5.9(3.1, 11.5)	0.100
Continuous variables were presented as median (IQR). Categorical variables were presented as number (percentage). P values were calculated using Kruskal–Wallis test or Chi-square test to compare differences in outcomes between different TyG quartiles. Abbreviation: TyG: triglyceride-glucose index; ICU: intensive care unit.						

Table 3
The association between TyG and in-hospital mortality

	OR (95% CI)	P Value	P for trend
Model 1			< 0.001
Quartile 1: TyG < 8.51	Reference		
Quartile 2: $8.51 \leq \text{TyG} < 8.92$	1.36(0.98–1.90)	0.068	
Quartile 3: $8.92 \leq \text{TyG} < 9.37$	1.89(1.38–2.60)	< 0.001	
Quartile 4: TyG ≥ 9.37	2.43(1.79–3.31)	< 0.001	
Continuous	1.35(1.23–1.48)	< 0.001	
Model 2			< 0.001
Quartile 1: TyG < 8.51	Reference		
Quartile 2: $8.51 \leq \text{TyG} < 8.92$	1.40(1.00-1.95)	0.051	
Quartile 3: $8.92 \leq \text{TyG} < 9.37$	2.07(1.50–2.85)	< 0.001	
Quartile 4: TyG ≥ 9.37	2.90(2.12–3.96)	< 0.001	
Continuous	1.43(1.30–1.58)	< 0.001	
Model 3			< 0.001
Quartile 1: TyG < 8.51	Reference		
Quartile 2: $8.51 \leq \text{TyG} < 8.92$	1.15(0.80–1.68)	0.448	
Quartile 3: $8.92 \leq \text{TyG} < 9.37$	1.47(1.03–2.11)	0.035	
Quartile 4: TyG ≥ 9.37	1.83(1.27–2.64)	0.001	
Continuous	1.23(1.10–1.38)	< 0.001	

Models were derived from binary logistic regression analysis. P for trend was calculated using binary logistic analysis to determine whether there was a trend when TyG was included as a grouping variable in the model (Quartile 1–4). When TyG was included as a grouping variable in the model, P values were calculated using binary logistic analysis to determine whether there was a relationship between TyG quartiles and in-hospital mortality with Quartile1 serving as the reference group. When TyG was included as a continuous variable in the model, P values were calculated using binary logistic analysis to determine whether there was a relationship between TyG and in-hospital mortality. Model 1: unadjusted. Model 2: adjusted for age, gender, ethnicity. Model 3: adjusted for age, gender, ethnicity, systolic blood pressure, diastolic blood pressure, respiration, congestive heart failure, STEMI, cardiac arrest, acute kidney injury, respiratory failure, stroke, malignancy, white blood cell, neutrophil percentage, oral anticoagulants, ACEI/ARB, APACHE IV, length of ICU stay and length of hospital stay. Abbreviation: TyG: triglyceride-glucose index; STEMI: ST-elevation myocardial infarction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APACHE IV: Acute Physiology and Chronic Health Evaluation IV; ICU: intensive care unit; OR: odds ratio; CI: confidence interval.

Table 4
The association between TyG and in-hospital mortality in patients with DM or no-DM

DM	OR (95% CI)	P Value	P for trend	No-DM	OR (95% CI)	P Value	P for trend
Model 1			0.291	Model 1			< 0.001
Quartile 1: TyG < 8.51	Reference			Quartile 1: TyG < 8.51	Reference		
Quartile 2: 8.51 ≤ TyG < 8.92	1.14(0.46–2.79)	0.782		Quartile 2: 8.51 ≤ TyG < 8.92	1.37(0.95–1.96)	0.090	
Quartile 3: 8.92 ≤ TyG < 9.37	1.33(0.57–3.12)	0.515		Quartile 3: 8.92 ≤ TyG < 9.37	1.95(1.39–2.74)	< 0.001	
Quartile 4: TyG ≥ 9.37	1.44(0.65–3.21)	0.373		Quartile 4: TyG ≥ 9.37	2.62(1.87–3.66)	< 0.001	
Continuous	1.13(0.90–1.41)	0.297		Continuous	1.38(1.25–1.53)	< 0.001	
Model 2			0.009	Model 2			< 0.001
Quartile 1: TyG < 8.51	Reference			Quartile 1: TyG < 8.51	Reference		
Quartile 2: 8.51 ≤ TyG < 8.92	1.14(0.46–2.81)	0.781		Quartile 2: 8.51 ≤ TyG < 8.92	1.41(0.98–2.02)	0.062	
Quartile 3: 8.92 ≤ TyG < 9.37	1.37(0.58–3.24)	0.477		Quartile 3: 8.92 ≤ TyG < 9.37	2.15(1.52–3.03)	< 0.001	
Quartile 4: TyG ≥ 9.37	1.58(0.69–3.60)	0.280		Quartile 4: TyG ≥ 9.37	3.16(2.24–4.46)	< 0.001	
Continuous	1.17(0.92–1.48)	0.196		Continuous	1.48(1.33–1.64)	< 0.001	
Model 3			< 0.001	Model 3			< 0.001
Quartile 1: TyG < 8.51	Reference			Quartile 1: TyG < 8.51	Reference		
Quartile 2: 8.51 ≤ TyG < 8.92	1.38(0.47–4.04)	0.554		Quartile 2: 8.51 ≤ TyG < 8.92	1.25(0.83–1.89)	0.283	
Quartile 3: 8.92 ≤ TyG < 9.37	1.79(0.63–5.04)	0.273		Quartile 3: 8.92 ≤ TyG < 9.37	1.57(1.05–2.36)	0.028	
Quartile 4: TyG ≥ 9.37	2.37(0.87–6.46)	0.091		Quartile 4: TyG ≥ 9.37	2.08(1.38–3.16)	0.001	

DM	OR (95% CI)	P Value	P for trend	No-DM	OR (95% CI)	P Value	P for trend
Continuous	1.32(0.99–1.77)	0.057		Continuous	1.28(1.12–1.46)	< 0.001	
<p>Models were derived from binary logistic regression analysis. P for trend was calculated using binary logistic analysis to determine whether there was a trend when TyG was included as a grouping variable in the model (Quartile 1–4). When TyG was included as a grouping variable in the model, P values were calculated using binary logistic analysis to determine whether there was a relationship between TyG quartiles and in-hospital mortality with Quartile1 serving as the reference group. When TyG was included as a continuous variable in the model, P values were calculated using binary logistic analysis to determine whether there was a relationship between TyG and in-hospital mortality. In DM group: Model 1: unadjusted. Model 2: adjusted for age, gender, ethnicity. Model 3: adjusted for age, gender, ethnicity, systolic blood pressure, respiratory failure, stroke, pulmonary embolism, hemoglobin, hematocrit, APACHE IV. In No-DM group: Model 1: unadjusted. Model 2: adjusted for age, gender, ethnicity. Model 3: adjusted for age, gender, ethnicity, systolic blood pressure, diastolic blood pressure, congestive heart failure, STEMI, cardiac arrest, malignancy, respiratory failure, shock, stroke, acute kidney injury, white blood cell, neutrophil percentage, sodium, oral anticoagulants, ACEI/ARB, APS, APACHE IV, length of ICU stay and length of hospital stay. Abbreviation: TyG: triglyceride-glucose index; DM: diabetes; STEMI: ST-elevation myocardial infarction; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV; ICU: intensive care unit; OR: odds ratio; CI: confidence interval.</p>							

Besides, increased TyG quartiles were associated with prolonged length of ICU stay (Quartile 4 vs Quartile 1: 2.3, 1.3–4.9 vs 2.1, 1.3–3.8, $P = 0.007$), while with the growth of the TyG index, the length of hospital stay failed to increase significantly (Quartile 4 vs Quartile 1: 5.9, 3.1–11.5 vs 5.7, 3.2–9.8, $P = 0.100$) (Table 2). Moreover, we drew the box plot to reflect the relationship between TyG and length of ICU and hospital stay more intuitively. The obvious association between TyG and length of ICU stay was indicated (Fig. 3).

3.3. Subgroup analysis. Patients complicated by arrhythmias or atrial fibrillation had higher risk of in-hospital mortality for TyG while patients with sepsis had lower risk of in-hospital mortality (Table 5).

Table 5
Subgroup analysis of associations between in-hospital mortality and TyG.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Age (years)						0.259
<66	2376	Reference	1.44(0.80–2.60)	1.70(0.97–2.98)	2.40(1.42–4.05)	
≥66	2463	Reference	1.35(0.90–2.02)	2.20(1.50–3.24)	3.12(2.12–4.60)	
Gender						0.659
Male	2993	Reference	1.52(0.99–2.34)	1.84(1.21–2.79)	2.44(1.63–3.64)	
Female	1846	Reference	1.15(0.68–1.94)	1.95(1.21–3.17)	2.43(1.51–3.90)	
Ethnicity						0.722
Caucasian	3668	Reference	1.45(0.99–2.11)	1.89(1.31–2.71)	2.38(1.67–3.39)	
African American	663	Reference	1.58(0.62–4.03)	3.52(1.51–8.22)	5.45(2.37–12.50)	
Other	508	Reference	0.61(0.19–1.92)	0.68(0.23–2.02)	0.96(0.37–2.51)	
Body mass index (kg/m ²)						0.707
<29.5	2679	Reference	1.56(1.03–2.35)	2.47(1.67–3.65)	2.62(1.74–3.96)	
≥29.5	2160	Reference	1.07(0.60–1.89)	1.27(0.74–2.18)	2.15(1.31–3.52)	
Systolic blood pressure (mmHg)						0.239
<122	2592	Reference	1.49(1.00–2.23)	1.85(1.25–2.73)	2.66(1.82–3.90)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
≥122	2247	Reference	1.17(0.64–2.13)	2.09(1.21–3.59)	2.46(1.46–4.14)	0.159
Diastolic blood pressure (mmHg)						
<67	2647	Reference	1.37(0.93–2.00)	1.72(1.19–2.49)	2.62(1.84–3.72)	
≥67	2790	Reference	1.52(0.75–3.07)	2.72(1.42–5.18)	2.48(1.30–4.76)	0.078
Mean blood pressure (mmHg)						
<82	2552	Reference	1.36(0.91–2.04)	1.92(1.31–2.83)	2.86(1.97–4.15)	
≥82	2287	Reference	1.44(0.80–2.60)	1.99(1.34–3.48)	2.17(1.25–3.74)	0.449
Heart rate (beats/min)						
<97	1781	Reference	1.35(0.81–2.25)	1.85(1.14–3.00)	2.43(1.52–3.88)	
≥85	2226	Reference	1.51(0.98–2.35)	1.88(1.23–2.87)	2.37(1.57–3.57)	0.063
Respiration rate (beats/min)						
<20	2444	Reference	1.27(0.75–2.15)	1.54(0.93–2.55)	1.94(1.18–3.17)	
≥20	2395	Reference	1.43(0.93–2.20)	2.21(1.47–3.33)	2.81(1.90–4.17)	0.695
Oxygen saturation (%)						
<97	2814	Reference	1.21(0.80–1.81)	1.71(1.18–2.48)	2.41(1.69–3.44)	
≥97	3058	Reference	1.39(0.89–2.15)	1.94(1.28–2.94)	2.45(1.64–3.68)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Congestive heart failure						0.150
Yes	793	Reference	2.05(1.05–3.99)	2.91(1.51–5.60)	4.05(2.13–7.72)	
No	4046	Reference	1.21(0.83–1.78)	1.73(1.20–2.48)	2.21(1.56–3.14)	
Coronary artery disease						0.095
Yes	3043	Reference	1.10(0.67–1.83)	1.42(0.88–2.28)	1.92(1.22–3.03)	
No	1796	Reference	1.76(1.12–2.76)	2.78(1.81–4.27)	3.35(2.21–5.09)	
Acute coronary syndrome						0.940
Yes	2295	Reference	1.02(0.55–1.89)	1.55(0.87–2.76)	2.31(1.33–3.98)	
No	2544	Reference	1.67(1.12–2.49)	2.24(1.53–3.28)	2.65(1.83–3.84)	
STEMI						0.223
Yes	1035	Reference	1.17(0.37–3.75)	1.65(0.55–4.89)	3.68(1.36–9.92)	
No	3804	Reference	1.43(1.01–2.02)	2.00(1.44–2.79)	2.39(1.73–3.30)	
NSTEMI						0.755
Yes	563	Reference	1.80(0.62–5.25)	1.52(0.48–4.79)	2.56(0.89–7.32)	
No	4276	Reference	1.33(0.93–1.89)	1.93(1.39–2.69)	2.44(1.77–3.35)	
Arrhythmias						0.006

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Yes	1234	Reference	1.37(0.73–2.58)	3.33(1.87–5.93)	4.20(2.36–7.46)	
No	3605	Reference	1.36(0.92–2.01)	1.51(1.04–2.21)	2.03(1.42–2.92)	
Cardiac arrest						0.694
Yes	430	Reference	0.90(0.45–1.82)	1.32(0.69–2.51)	2.13(1.14–3.99)	
No	4409	Reference	1.45(0.98–2.15)	1.86(1.27–2.70)	2.20(1.52–3.18)	
Bradycardia						0.444
Yes	178	Reference	0.94(0.20–4.41)	1.18(0.25–5.58)	1.33(0.28–6.33)	
No	4661	Reference	1.39(0.99–1.96)	1.94(1.40–2.68)	2.49(1.82–3.41)	
Atrial fibrillation						0.018
Yes	675	Reference	1.76(0.81–3.79)	3.54(1.69–7.39)	5.09(2.45–10.60)	
No	4164	Reference	1.28(0.89–1.86)	1.67(1.18–2.37)	2.16(1.54–3.02)	
Ventricular arrhythmias						0.111
Yes	237	Reference	0.69(0.26–1.82)	1.22(0.50–2.96)	2.06(0.86–4.92)	
No	4495	Reference	1.35(0.96–1.92)	1.83(1.31–2.54)	2.29(1.66–3.16)	
Atrioventricular block						0.821
Yes	127	Reference	0.47(0.04–5.45)	1.83(0.29–11.78)	2.15(0.33–13.92)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
No	4712	Reference	1.39(0.99–1.95)	1.90(1.38–2.61)	2.44(1.79–3.33)	0.554
Cardiomyopathy						
Yes	297	Reference	1.48(0.42–5.22)	2.07(0.53–8.07)	3.45(0.98–12.07)	0.952
No	4542	Reference	1.36(0.96–1.92)	1.88(1.36–2.60)	2.38(1.74–3.27)	
Valve disease						0.067
Yes	182	Reference	3.33(0.85–13.08)	1.94(0.44–8.58)	3.79(0.83–17.26)	
No	4657	Reference	1.28(0.90–1.80)	1.89(1.37–2.62)	2.41(1.76–3.29)	0.006
Shock						
Yes	975	Reference	1.08(0.65–1.79)	1.36(0.84–2.20)	1.63(1.03–2.58)	0.249
No	3864	Reference	1.68(1.06–2.66)	2.37(1.53–3.68)	3.05(1.98–4.68)	
Pulmonary embolism						0.814
Yes	43	-	0.89(0.01–0.57)	0.47(0.10–2.18)	-	
No	4781	Reference	1.33(0.95–1.86)	1.79(1.30–2.46)	2.28(1.68–3.10)	0.814
Pulmonary hypertension						
Yes	49	Reference	0.91(0.13–6.40)	0.50(0.05–5.51)	0.83(0.07–9.69)	0.814
No	4790	Reference	1.39(0.99–1.95)	1.96(1.42–2.71)	2.52(1.84–3.44)	
Hypertension						
Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.						

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Yes	1133	Reference	1.28(0.60–2.70)	1.75(0.85–3.60)	2.25(1.14–4.44)	
No	3706	Reference	1.38(0.95–2.00)	1.92(1.35–2.72)	2.49(1.77–3.51)	
Diabetes						0.109
Yes	770	Reference	1.14(0.46–2.79)	1.33(0.57–3.12)	1.44(0.65–3.21)	
No	4069	Reference	1.37(0.95–1.96)	1.95(1.39–2.74)	2.62(1.87–3.66)	
Hypercholesterolemia						0.199
Yes	452	Reference	1.65(0.48–5.66)	1.53(0.43–5.39)	1.46(0.43–5.01)	
No	4387	Reference	1.34(0.95–1.90)	1.93(1.39–2.68)	2.56(1.86–3.51)	
COPD						0.833
Yes	352	Reference	1.35(0.53–3.41)	1.83(0.72–4.67)	2.71(1.12–6.59)	
No	4487	Reference	1.37(0.96–1.96)	1.94(1.39–2.72)	2.46(1.78–3.42)	
Respiratory failure						0.419
Yes	1038	Reference	1.27(0.77–2.11)	1.58(0.98–2.55)	2.41(1.52–3.81)	
No	3801	Reference	1.28(0.81–2.03)	1.79(1.16–2.77)	1.88(1.21–2.91)	
Chronic kidney disease						0.388
Yes	546	Reference	0.54(0.20–1.43)	1.79(0.90–3.56)	2.49(1.28–4.82)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
No	4293	Reference	1.60(1.11–2.31)	1.95(1.36–2.78)	2.45(1.73–3.47)	
Acute kidney injury						0.574
Yes	659	Reference	1.29(0.69–2.41)	1.80(1.02–3.16)	1.86(1.08–3.21)	
No	4180	Reference	1.43(0.95–2.13)	1.71(1.15–2.54)	2.29(1.57–3.35)	
Malignancy						0.426
Yes	121	Reference	0.70(0.19–2.66)	1.06(0.30–3.67)	1.25(0.33–4.69)	
No	4718	Reference	1.39(0.98–1.97)	1.92(1.38–2.67)	2.52(1.84–3.46)	
Sepsis						< 0.001
Yes	519	Reference	1.27(0.67–2.43)	1.07(0.58–1.99)	0.94(0.51–1.71)	
No	4320	Reference	1.45(0.97–2.17)	2.18(1.50–3.19)	3.02(2.10–4.36)	
Stroke						0.754
Yes	233	Reference	1.25(0.40–3.96)	2.52(0.85–7.50)	2.62(0.91–7.52)	
No	4606	Reference	1.38(0.97–1.95)	1.88(1.35–2.62)	2.44(1.77–3.36)	
Antiplatelet						0.793
Yes	2611	Reference	2.01(1.18–3.43)	2.32(1.37–3.91)	2.79(1.67–4.66)	
No	2228	Reference	1.05(0.68–1.63)	1.72(1.15–2.58)	2.34(1.59–3.45)	
Oral anticoagulants						0.765

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Yes	375	Reference	2.88(0.55– 15.23)	4.22(0.86– 20.86)	2.10(0.34– 12.88)	
No	4464	Reference	1.31(0.93– 1.84)	1.81(1.31– 2.50)	2.40(1.76– 3.28)	
Beta-blockers						0.242
Yes	1877	Reference	2.51(1.28– 4.94)	2.23(1.13– 4.44)	4.22(2.23– 8.02)	
No	2962	Reference	1.10(0.74– 1.63)	1.89(1.32– 2.70)	2.05(1.43– 2.93)	
ACEI/ARB						0.221
Yes	1054	Reference	3.42(1.10– 10.62)	1.94(0.56– 6.71)	2.28(0.69– 7.51)	
No	3785	Reference	1.22(0.86– 1.74)	1.86(1.34– 2.59)	2.48(1.80– 3.41)	
Statin						0.348
Yes	1680	Reference	2.23(0.97– 5.13)	3.37(1.52– 7.48)	3.93(1.79– 8.61)	
No	3159	Reference	1.28(0.88– 1.85)	1.71(1.21– 2.43)	2.30(1.64– 3.22)	
White blood cell (10 ⁹ /L)						0.763
<11.3	2849	Reference	1.63(1.00– 2.66)	1.60(0.97– 2.65)	2.21(1.37– 3.57)	
≥11.3	1990	Reference	1.06(0.67– 1.67)	1.72(1.13– 2.60)	2.13(1.42– 3.21)	
Lymphocyte percentage (%)						0.428
<17.8	3159	Reference	1.60(1.09– 2.33)	2.18(1.52– 3.13)	2.68(1.87– 3.84)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
≥17.8	1680	Reference	0.80(0.38–1.66)	1.30(0.68–2.50)	2.15(1.18–3.89)	
Monocyte percentage (%)						0.542
<7.6	2972	Reference	1.20(0.79–1.83)	1.74(1.17–2.58)	2.43(1.67–3.53)	
≥7.6	1876	Reference	1.65(0.96–2.84)	2.12(1.25–3.61)	2.22(1.30–3.79)	
Neutrophil percentage (%)						0.122
<71.9	1548	Reference	0.74(0.33–1.64)	0.91(0.42–1.96)	2.06(1.08–3.93)	
≥71.9	3291	Reference	1.57(1.09–2.28)	2.22(1.56–3.15)	2.66(1.87–3.76)	
Red blood cell (10 ⁹ /L)						0.320
<4.3	2270	Reference	1.38(0.90–2.12)	2.20(1.47–3.28)	3.17(2.14–4.69)	
≥4.3	2569	Reference	1.40(0.82–2.41)	1.69(1.01–2.83)	2.06(1.25–3.38)	
Platelet (10 ⁹ /L)						0.683
<227	2688	Reference	1.39(0.91–2.12)	1.84(1.22–2.78)	2.42(1.63–3.60)	
≥227	2151	Reference	1.34(0.79–2.29)	1.99(1.21–3.27)	2.49(1.54–4.04)	
Hemoglobin (g/dL)						0.691
<12.8	2175	Reference	1.41(0.94–2.13)	1.82(1.22–2.71)	2.83(1.91–4.18)	
≥12.8	2664	Reference	1.33(0.75–2.36)	2.20(1.30–3.71)	2.55(1.53–4.23)	

Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
Hematocrit (%)						0.810
<38.5	2201	Reference	1.37(0.89–2.11)	1.94(1.28–2.94)	2.82(1.88–4.24)	
≥38.5	2638	Reference	1.39(0.82–2.34)	1.93(1.18–3.16)	2.36(1.47–3.78)	
Creatinine (mg/dL)						0.670
<1.44	3525	Reference	1.22(0.78–1.89)	1.68(1.10–2.56)	2.15(1.43–3.23)	
≥1.44	1314	Reference	1.57(0.93–2.64)	1.96(1.20–3.20)	2.44(1.51–3.92)	
Blood nitrogen urea (mg/dL)						0.356
<24.6	3236	Reference	1.45(0.91–2.33)	1.93(1.23–3.02)	2.46(1.59–3.80)	
≥24.6	1603	Reference	1.24(0.77–2.01)	1.84(1.17–2.89)	2.29(1.49–3.54)	
Sodium (mmol/L)						0.722
<137	1802	Reference	1.72(1.02–2.90)	2.26(1.37–3.75)	2.12(1.30–3.48)	
≥137	3037	Reference	1.15(0.74–1.78)	1.68(1.12–2.52)	2.66(1.80–3.92)	
Potassium (mmol/L)						0.255
<4.2	2638	Reference	0.99(0.63–1.58)	1.25(0.81–1.95)	1.94(1.28–2.95)	
≥4.2	2201	Reference	1.93(1.18–3.17)	2.91(1.82–4.65)	3.09(1.95–4.88)	
APS						0.086
<41	2937	Reference	1.77(0.86–3.65)	2.03(0.99–4.16)	1.95(0.94–4.05)	
<p>Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.</p>						

Subgroups	N	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for interaction
≥41	1902	Reference	1.14(0.77– 1.69)	1.53(1.06– 2.21)	2.01(1.41– 2.86)	
APACHE IV						0.155
<53	2799	Reference	1.92(0.91– 4.03)	1.65(0.77– 3.56)	2.08(0.99– 4.34)	
≥53	2040	Reference	1.17(0.80– 1.72)	1.86(1.30– 2.66)	2.46(1.74– 3.49)	
Binary logistic regression analysis was used and results were presented as OR (odds ratio) and 95% CI (confidence interval). P for interaction was calculated using binary logistic analysis to determine whether there is interaction between different subgroups and TyG quartiles. Abbreviation: STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COPD: chronic obstructive pulmonary disease; triglyceride-glucose index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; APS: acute physiology score; APACHE IV: Acute Physiology and Chronic Health Evaluation IV.						

4. Discussion

This study affirmed the relationship between TyG and in-hospital mortality in critically ill patients with heart disease. (1) TyG index was a strong indicator of in-hospital mortality in critically ill patients with heart disease, even after adjusting for possible confounding variables. Whereas, we failed to reveal a significant association between the TyG index and in-hospital mortality in patients with diabetes. (2) The Lowess curve presented a positive relationship between TyG and in-hospital mortality. (3) Significant interactions were not observed in most subgroups. (4) Length of ICU was prolonged as TyG increased.

Previous studies have indicated that IR was strongly associated with the development and prognosis of cardiovascular disease [22–24]. The underlying biological mechanism might be close association between IR and endothelial dysfunction which was able to cause cardiovascular disease [25–27]. Moreover, IR might disrupt the metabolic stability of energy substrates used by the heart, resulting in fatty toxicity during cardiac metabolism and eventually led to major adverse cardiac events [28]. As we know, the euglycemic-hyperinsulinemic clamp is the gold standard method for the diagnosis of IR [29]. However, due to the high cost and complex operation of this method, it is relatively difficult to carry out in practical clinical application. The homeostasis model assessment of insulin resistance (HOMA-IR) is a substitutive method for IR evaluation [30]. While it requires insulin concentration which is not routine clinical examination item. In this respect, TyG index which is calculated by fasting TGs and glucose is more readily available in clinical practice. And it has been proven to have a good predictive ability on IR compared with the above-mentioned two methods [31–32]. Therefore, as a good substitute indicator for IR, TyG index may be a risk factor which associated with prognosis of cardiovascular disease.

TyG has been extensively demonstrated to be significantly related to the development of a variety of diseases in former studies. A recent meta-analysis which included 13 cohort studies confirmed that TyG index was strongly related to the incidence of diabetes [33]. Furthermore, higher TyG index has been indicated to be associated with the increased risk of ischemic stroke [34]. Similarly, a large number of studies have also confirmed the relationship between TyG and CVD. A previous prospective cohort study proved that higher TyG index was related to the increased complexity of coronary lesions and the risk of worse outcomes in patients with NSTEMI-ACS [35]. Zhao et al. [16] enrolled 798 patients with T2DM and NSTEMI-ACS who underwent PCI and revealed that the level of TyG index was strongly associated with the incidence of adverse cardiovascular event during a 36-month follow-up. Luo et al. [35] reached the same conclusion in STEMI patients who were treated with PCI. Besides, TyG index was also proved to be an independent predictor of major cardiovascular events in patients with T2DM complicated by ACS undergoing PCI [36]. Even among patients with stable CAD, higher TyG index was still associated with the increased risk of mortality [37–38]. Thus, paying attention to TyG in clinical practice and improving the level of nursing, monitoring may improve the prognosis and reduce mortality.

This study drawn a similar conclusion that increased TyG was independently related to the in-hospital mortality in critically ill patients with heart disease, providing evidence for the use of TyG in patients with severe cardiovascular disease. While, when conducting multiple logistic regression analysis, there was no significant association between TyG and in-hospital mortality among patients with diabetes in model 1–3. The discrepancy might be explained by the fact that the small number of patients with diabetes in the cohort.

Interestingly, gender differences appeared to have an impact on the prediction of adverse outcomes of TyG. The previous study has shown that the ability of TyG to predict adverse cardiovascular events was better in women than men when $TyG > 9.53$ [19]. The plausible explanation might be that female patients with diabetes had a higher incidence of cardiovascular disease [39]. However, in the gender subgroup in our study, we failed to find the obvious interaction ($P = 0.659$). The explain might be that patients enrolled in this study have clearly been diagnosed with cardiovascular disease and mortality of those was extremely high. Therefore, sex differences were attenuated.

Through the Lowess curve, we found that in-hospital mortality increased as the increase of TyG value. This was consistent with the conclusion that TyG was an independent predictor when considered as a continuous variable in multivariate logistic regression, which reconfirmed the reliability of TyG application in critically ill patients with heart disease.

In addition, higher TyG quartiles were associated with the increased length of ICU stay, which brought the psychological, physical, and financial burden on patients. Most of critically ill patients with heart disease have limited mobility so that complex clinical examination cannot be performed. In this circumstance, some of complex predictive scores can't be calculated. Therefore, easily accessible indicators like TyG are more cost-effective and important for ICU patients.

5. Limitation

This study is a single-center retrospective cohort study. Due to the limitations of the retrospective study, selection bias and recall bias cannot be avoided, and the causal relationship cannot be determined. Furthermore, in patients with diabetes, the accuracy of the model is reduced because of the small sample size. And we are not able to demonstrate whether the appropriate treatment which aimed to reduce the TyG value related to the lower incidence of adverse clinical outcomes.

6. Conclusion

To summarize, the results indicated that TyG was an independent predictor of in-hospital mortality in critically ill patients with heart disease. And through multivariate logistic regression, the in-hospital mortality increased significantly as TyG quartiles increased. When considered as a continuous variable, TyG has been proven to significantly related to adverse events. Furthermore, high TyG was associated with prolonged ICU stay length.

Declarations

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Competing Interests

Authors declare no competing interests

Ethical Approval

This study was exempted from institutional review Board approval for the following reasons: (1) retrospective design, which was lack of direct patient intervention; (2) Privacert certification of reidentification risk conforming to safe harbor standards for security protocols (Cambridge, MA) (HIPAA Certification no. 1031219-2).

Supplementary material

The original data from the study is in the supplementary file.

Method statement

All methods were carried out in accordance with relevant guidelines and regulations.

Data Availability

The data used in this study was from eICU Collaborative Research Database [24], which is available at: <https://doi.org/10.13026/C2WM1R>. The author was approved to access to the database through Protecting Human Research Participants exam (certificate number: 9728458).

Authors' Contributions

Guangyao Zhai and Biyang Zhang contributed equally to this study.

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Supplementary

Supplementary Materials is not available with this version.

Figures

Figure 1

Flow chart of study population. Abbreviation: CCU: coronary artery care unit; CICU: cardiac intensive care unit.

Figure 2

Association between the triglyceride-glucose index and in-hospital mortality presented through Lowess smoothing.

Figure 3

Association between the triglyceride-glucose index and the length of ICU and hospital stay through box plot. Abbreviation: ICU: intensive care unit.