ORIGINAL ARTICLE

The Triglyceride-Glucose Index is associated with hospital and Intensive Care Unit Mortality in critically ill patients with Acute Coronary Syndrome

Zihuai Huang[1], Qianqian Zou[2], Ya Lin[3]

[1]Orthopedics Department, Wenzhou Peoples' Hospital, Wenzhou, Zhejiang, China, [2]Department of Ultrasound, Wenzhou Peoples' Hospital, Wenzhou, Zhejiang, China, [3]Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China

Background: Acute coronary syndrome (ACS) is one of the leading causes of death, but there is no attention paid to the risk stratification of patients with ACS. **Aims:** We evaluated the utility of the triglyceride-glucose (TyG) index in predicting the hospital and intensive care unit (ICU) mortality of critically ill patients with ACS. **Materials and Methods:** The study patients were collected from the eICU Collaborative Research Database. TyG index was calculated as the ln (fasting glucose level [mg/dL] × triglyceride level [mg/dL]/2). The endpoints were hospital and ICU mortality. The univariate and multivariate logistic regressions and subgroup analysis were used to determine the relationship between the TyG index and two endpoints. The scatter plots, bar graphs and smoothing curves further proved it. **Results:** 5237 critically ill patients with ACS were enrolled. The TyG index was obviously higher in nonsurvivors groups than survivors groups. TyG index was significantly associated with hospital mortality in univariate analysis (odds ratio [OR] 1.33, 95% confidence interval [CI] 1.15–1.53, $P < 0.001$), adjusted model I (OR 1.59, 95% CI 1.36–1.85, $P < 0.001$) and adjusted model II (OR 2.23, 95% CI 1.50–3.31, $P < 0.001$). The ICU mortality showed the same trends (OR 1.50, 95% CI 1.26–1.78, OR 1.73, 95% CI 1.45–2.06, OR 2.53, 95% CI 1.59–4.03, $P < 0.001$). The same trends were observed after stratified by tertiles and quartiles. There were continuous linear relations between the TyG index and hospital and ICU mortality. **Conclusion:** TyG index is an independent predictor of ICU and hospital mortality in critically ill patients with ACS.

Key words: Acute coronary syndrome, glucose, mortality, prognosis, triglycerides

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INTRODUCTION

Acute coronary syndrome (ACS) is among the leading causes of accidental death in the world.[1] Although advances in diagnostic and therapeutic developments have greatly reduced the incidence rate of this disease, it remains to be one of the major health problems concerned with people.[2-4] Thus, early risk stratification has an important effect on the prevention and management of patients with ACS, especially the critically ill patients.

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Previous human and animal studies have confirmed that hyperglycemia[5,6] and dyslipidemia[7,8] have a direct pro-atherogenic role on vascular cells and promote the appearance of atherosclerosis and coronary artery disease (CAD). Based on this, some scholars have put forward the concept of the triglyceride-glucose (TyG) index. As it has been shown, the TyG index was significantly associated with insulin resistance (IR).[9-11] And IR is related to a cluster of cardiometabolic risk factors that contribute to the increased risk of cardiovascular disease (CVD),[12-15] such as stroke,[16]

Address for correspondence: Dr. Ya Lin, Department of Cardiology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang 325000, China.
E-mail: linny233@163.com

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coronary heart disease,[17] hypertension,[18] and congestive heart failure (CHF).[19] Thus, the TyG index has been taken as a convenient and economical test method and a reliable surrogate variable for IR,[20,21] and the instructive role of the TyG index in CVD should be appreciated.

Unfortunately, no relevant study has focused on the impact of the TyG index on mortality in critically ill patients with ACS. Therefore, this study aimed to further investigate the association between the TyG index and hospital and intensive care unit (ICU) mortality in critically ill patients with ACS. Additionally, patient diagnoses in this study were based on the International Classification of Diseases, Ninth Revision (ICD-9), a system used by healthcare providers, researchers, and health insurance companies to code and classify all diagnoses, symptoms, and procedures recorded in conjunction with hospital care.[22]

METHODS

Source of data

We conducted a retrospective cohort study in which data were collected from a large, multi-center ICU database called the eICU Collaborative Research Database (eICU-CRD) v2.0.[23] The database covers comprehensive clinical data of 200,859 patients admitted to the ICU between 2014 and 2015 at 208 hospitals located throughout the United States. After successfully completing the National Institutes of Health Web-based training course and the Protecting Human Research Participants examination (no. 40683764), we were given permission to extract data from eICU-CRD.

Selection criteria of patients

All critically ill inpatients with ACS diagnosed by ICD-9 diagnosis code were enrolled in this study. Exclusion criteria were as follows: (1) repeat or multiple ICU admissions; (2) aged <18 years old or right-censored age; (3) lack of information of glucose and triglyceride (TG) during ICU stay; (4) lack of the status of discharge hospital or ICU.

Data extraction

Extracting data from eICU-CRD was completed using Structured Query Language with the PostgreSQL tool (version 9.6). The data was recorded in the baseline table, including demographics, vital signs, comorbidities and medical history, laboratory parameters, medication use, scoring system and hospital or ICU length of stay (LOS). Age, gender and race were included in demographics, and vital signs covered temperature, heart rate, respiratory rate, and mean blood pressure (MBP). Previous myocardial infarction (MI), atrial fibrillation (AF), CHF, diabetes, hepatic failure, chronic kidney disease, chronic obstructive pulmonary disease (COPD), hypertension, malignancy, and stroke were incorporated into comorbidities and medical history. These laboratory parameters were obtained, including white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb), red cell distribution width (RDW), platelet, blood urea nitrogen (BUN), creatinine, glucose, total cholesterol (TC), TG, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), potassium, sodium, chloride, and B-type natriuretic peptide (BNP). All the above laboratory variables were recorded at the first time after admission. We also showed the usage of aspirin, clopidogrel, metoprolol, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and statins. In addition, the acute physiology and chronic health evaluation (APACHE) IV score was also calculated. The APACHE IV score can provide clinically useful in-hospital LOS predictions for critically ill patients[24,25] and has better discrimination compared to other prediction models.[26] Other involved admission height and weight.

The TyG index was calculated as the ln (fasting glucose level [mg/dL] × TG level [mg/dL]/2).

The major endpoints of this study were hospital and ICU mortality.

Statistical analysis

Continuous variables were first assessed for normality using the Shapiro–Wilk test. Normal data were expressed in mean with standard deviation and compared by Student's *t*-test. Non-normal data were expressed in median with interquartile range (Q1-Q3) and were compared by the Kruskal–Wallis rank-sum test. Categorical variables were expressed in absolute numbers with percentages and analyzed by the Chi-square or Fisher's exact test. Group comparisons were performed with Student's *t*-tests or Kruskal–Wallis rank-sum test for continuous variables and with Chi-square or Fisher's exact test for categorical variables. The effect size was calculated as the standardized mean difference. In order to evaluate the relationship between TyG index and hospital and ICU mortality, univariate and multivariate logistic regression models were developed that sequentially adjusted for demographic characteristics only and then additionally for temperature, respiratory rate, heart rate, MBP, admission height, admission weight, WBC, RBC, Hb, RDW, platelet, BUN, creatinine, glucose, TC, LDL-C, HDL-C, potassium, sodium, chloride, prior MI, AF, CHF, diabetes, hepatic failure, CKD, COPD, hypertension, malignancy, and stroke. The first tertile and quartile groups of the TyG index were regarded as the reference group, and the results were summarized as Odds Ratio (OR) with 95% confidence interval (CI). Then the *P* value for the trend was calculated. And the association between the TyG index and mortality was also assessed using Cox proportional hazards models,

with results presented as hazard ratio and 95% CI. The smoothing curves were used to observe the trends of the death rate as the TyG index increased. Subgroup analysis was conducted to estimate the interaction between the TyG index and hospital and ICU mortality. Statistical analyses were performed by EmpowerStats version 4.2 (http://www.empowerstats.com/cn/, XandY solutions, Inc., Boston, MA, USA) and R software version 4.3.3 (R Core Team 2024); $P < 0.05$ was considered to be statistically significant.

RESULTS

Baseline characteristics of the participants

A total of 5237 critically ill patients with ACS were enrolled in this study, and the specific criteria of inclusion and exclusion are shown in Figure 1. According to hospital and ICU mortality, the patients in this study were categorized into survivors and nonsurvivors groups, respectively. Table 1 summarizes the baseline characteristics between the two groups. There were some similarities between the hospital nonsurvivors' group and the ICU non-survivors' group. They were older than the survivors, and most of them were men. In addition, nonsurvivors' groups had higher values of respiratory rate, heart rate, hospital LOS, ICU LOS, WBC, BUN, creatinine, glucose, LDL-C, potassium, TyG index, and APACHE IV score, whereas temperature, MBP, admission height, admission weight, RBC, Hb, TC, HDL-C, and BNP were lower than survivors' groups. Furthermore, nonsurvivors' groups reported more medical history of AF, CHF, CKD and stroke. However, patients in the hospital nonsurvivors' group had more frequent malignancy, and the ICU nonsurvivors' group had less frequent hypertension. Survivors in both groups were more likely to use ACEIs and ARBs. Moreover, there was no significant difference on race, MBP, platelets, TG, sodium, and chloride. The use of certain drugs and the occurrence of some comorbidities in nonsurvivors' groups were consistent with those survivors' groups.

Triglyceride-glucose index and mortality

As depicted in Figure 2a, we discovered that the TyG index was obviously higher in the hospital non-survivors' group than the hospital survivors' group (9.02 ± 0.72 vs. 9.17 ± 0.79, $P < 0.001$). For ICU mortality [Figure 2b], the comparison between the survivors' group and the nonsurvivors' group was consistent with those in hospital mortality (9.02 ± 0.72 vs. 9.25 ± 0.84, $P < 0.001$).

The association between the TyG index and the death risk of hospital and ICU status in critically ill patients with ACS was identified by univariate and multivariate logistic regression [Table 2]. First, the TyG index was taken as a continuous variable. In univariate analysis, we observed that as the 1-unit TyG index increased, the rate of hospital death raised by 33% ($P < 0.001$). In model I, after adjustments for age, race and gender, the TyG index was associated with hospital mortality (OR 1.59, 95% CI 1.36–1.85, $P < 0.001$). In model II, after adjustment for a comprehensive set of covariates incorporating demographic characteristics, physical examinations, laboratory tests, and comorbid conditions, the TyG index remained to be associated with hospital mortality (OR 2.23, 95% CI 1.50–3.31, $P < 0.001$). In addition, the TyG index was also related to ICU mortality in univariate analysis (OR 1.50, 95% CI 1.26–1.78, $P < 0.001$),

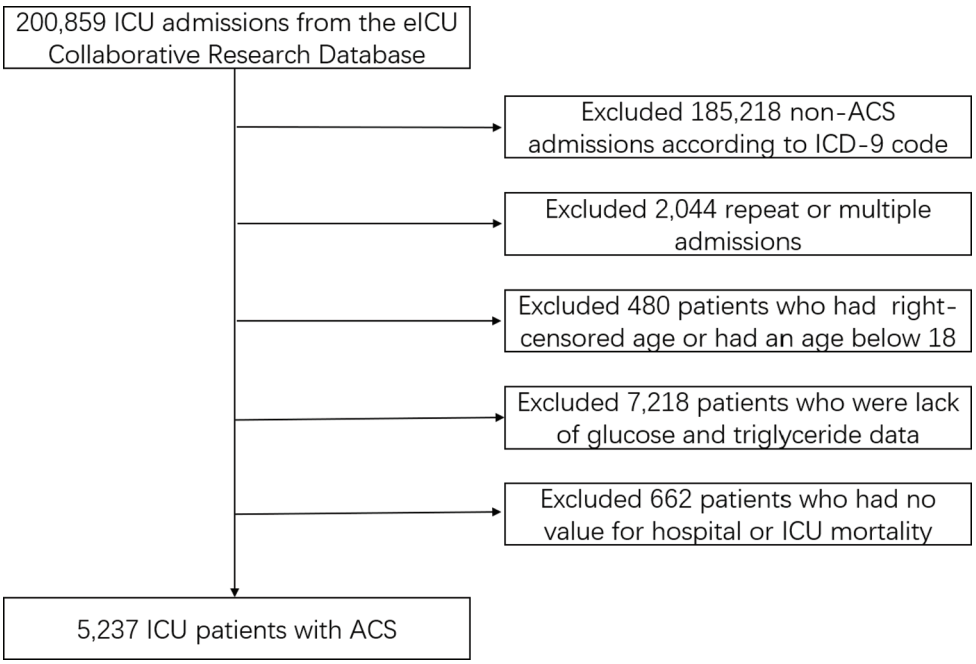

Figure 1: Flow chart of study selection. ICU = Intensive care unit; ACS = Acute coronary syndrome; ICD-9 = International Classification of Diseases, Ninth Revision

Table 1: Baseline characteristics of study population

Variables	Hospital mortality				ICU mortality			
	Survivors (*n*=4899)	Nonsurvivors (*n*=338)	*P*	Effect size	Survivors (*n*=5008)	Nonsurvivors (*n*=229)	*P*	Effect size
Age (years)	63.00 (54.00-73.00)	72.00 (64.00-80.00)	<0.001	0.585	63.00 (54.00-73.00)	71.00 (62.00-79.00)	<0.001	0.447
Male	3205 (65.42)	188 (55.62)	<0.001	0.202	3265 (65.20)	128 (55.90)	0.004	0.191
Race								
White	3837 (78.32)	277 (81.95)	0.127	0.123	3927 (78.41)	187 (81.66)	0.395	0.097
Black	444 (9.06)	20 (5.92)			449 (8.97)	15 (6.55)		
Other	618 (12.61)	41 (12.13)			632 (12.62)	27 (11.79)		
Temperature (°C)	36.44±0.71	35.71±1.80	<0.001	0.539	36.43±0.75	35.60±1.85	<0.001	0.592
Respiratory rate (beats/min)	24.29±15.31	29.41±14.12	<0.001	0.347	24.40±15.34	29.55±13.35	<0.001	0.358
Heart rate (beats/min)	87.09±30.32	107.43±34.94	<0.001	0.622	87.44±30.50	109.36±35.13	<0.001	0.666
MBP (mmHg)	88.77±38.12	86.57±48.82	0.316	0.05	88.85±38.41	83.79±48.31	0.055	0.116
Admission height (cm)	171.27±10.35	168.47±10.05	<0.001	0.275	171.18±10.37	169.00±9.78	0.002	0.217
Admission weight (kg)	87.22±21.53	82.13±22.51	<0.001	0.231	87.06±21.50	83.23±23.87	0.009	0.169
Hospital LOS (days)	3.20 (2.11-6.33)	5.60 (2.98-11.33)	<0.001	0.383	3.26 (2.13-6.61)	4.77 (2.22-8.26)	0.009	0.142
ICU LOS (days)	1.59 (0.98-2.69)	4.61 (2.26-8.14)	<0.001	0.718	1.62 (0.99-2.79)	4.35 (1.99-7.74)	<0.001	0.628
Comorbidities and medical history								
Prior MI	19 (0.39)	3 (0.89)	0.169	0.063	22 (0.44)	0	0.315	0.094
AF	285 (5.82)	60 (17.75)	<0.001	0.377	311 (6.21)	34 (14.85)	<0.001	0.284
CHF	392 (8.00)	63 (18.64)	<0.001	0.317	412 (8.23)	43 (18.78)	<0.001	0.312
Diabetes	1053 (21.49)	86 (25.44)	0.089	0.093	1083 (21.63)	56 (24.45)	0.31	0.067
Hepatic failure	21 (0.43)	2 (0.59)	0.661	0.023	21 (0.42)	2 (0.87)	0.31	0.057
CKD	271 (5.53)	52 (15.38)	<0.001	0.326	289 (5.77)	34 (14.85)	<0.001	0.302
COPD	234 (4.78)	23 (6.80)	0.095	0.087	243 (4.85)	14 (6.11)	0.388	0.055
Hypertension	764 (15.60)	44 (13.02)	0.205	0.074	784 (15.65)	24 (10.48)	0.034	0.154
Malignancy	13 (0.27)	3 (0.89)	0.045	0.082	14 (0.28)	2 (0.87)	0.111	0.078
Stroke	134 (2.74)	35 (10.36)	<0.001	0.312	146 (2.92)	23 (10.04)	<0.001	0.293
Laboratory parameters								
WBC (10^9/L)	11.39±5.40	16.90±29.43	<0.001	0.26	11.47±5.48	17.87±35.29	<0.001	0.254
RBC (10^{12}/L)	4.23±0.66	3.98±0.77	<0.001	0.354	4.22±0.66	4.00±0.76	<0.001	0.311
Hb (g/dL)	12.73±2.07	11.97±2.46	<0.001	0.331	12.71±2.09	12.02±2.42	<0.001	0.304
RDW (%)	14.13±1.59	15.12±2.13	<0.001	0.526	14.15±1.61	15.07±2.16	<0.001	0.481
Platelet (10^9/L)	215.70±73.03	211.97±89.34	0.373	0.046	215.47±73.34	215.06±91.25	0.935	0.005
BUN (mg/dL)	19.91±13.85	33.84±22.01	<0.001	0.758	20.24±14.29	33.33±21.45	<0.001	0.718
Creatinine (mg/dL)	1.20±1.12	1.79±1.35	<0.001	0.476	1.21±1.12	1.82±1.40	<0.001	0.477
Glucose (mg/dL)	147.43±81.13	194.37±104.55	<0.001	0.502	147.91±81.25	206.29±111.17	<0.001	0.6
TC (mg/dL)	160.71±45.98	130.31±44.88	<0.001	0.669	160.13±46.10	132.29±47.03	<0.001	0.598
TG (mg/dL)	145.07±110.05	134.33±105.69	0.082	0.1	144.53±109.27	141.09±120.95	0.643	0.03
LDL-C (mg/dL)	93.76±39.82	141.22±885.88	0.002	0.076	93.36±39.82	180.85±1106.88	<0.001	0.112
HDL-C (mg/dL)	39.54±13.30	36.05±16.74	<0.001	0.231	39.49±13.36	35.87±16.97	<0.001	0.237
Potassium (mmol/L)	4.10±0.55	4.20±0.79	0.003	0.139	4.10±0.56	4.25±0.80	<0.001	0.217

Contd...

Table 1: Contd...

Variables	Hospital mortality				ICU mortality			
	Survivors (*n*=4899)	Nonsurvivors (*n*=338)	*P*	Effect size	Survivors (*n*=5008)	Nonsurvivors (*n*=229)	*P*	Effect size
Sodium (mmol/L)	137.70±3.65	138.11±5.53	0.053	0.088	137.72±3.69	137.91±5.73	0.45	0.04
Chloride (mmol/L)	104.19±4.62	104.20±6.92	0.974	0.002	104.19±4.66	104.14±7.22	0.89	0.007
BNP (mmol/L)	24.20±3.64	21.94±5.20	<0.001	0.503	24.18±3.67	21.29±5.39	<0.001	0.627
TyG index	9.02±0.72	9.17±0.79	<0.001	0.206	9.02±0.72	9.25±0.84	<0.001	0.293
Medication use								
Aspirin	2588 (52.83)	172 (50.89)	0.49	0.039	2646 (52.84)	114 (49.78)	0.365	0.061
Clopidogrel	132 (2.69)	5 (1.48)	0.176	0.085	133 (2.66)	4 (1.75)	0.399	0.062
Metoprolol	182 (3.72)	8 (2.37)	0.2	0.079	185 (3.69)	5 (2.18)	0.232	0.09
ACEIs	1211 (24.72)	45 (13.31)	<0.001	0.302	1229 (24.54)	27 (11.79)	<0.001	
ARBs	65 (1.33)	2 (0.59)	0.245	0.075	66 (1.32)	1 (0.44)	0.246	0.095
Statin	2272 (46.38)	124 (36.69)	<0.001	0.198	2314 (46.21)	82 (35.81)	0.002	0.213
Scoring systems								
APACHE IV	44.25±20.60	88.25±33.19	<0.001	1.593	44.99±21.39	93.23±34.01	<0.001	1.698

Continuous variables are presented as mean±SD or normally distributed variables or median (IQR) for nonnormally distributed variables, whereas categorical variables are presented as *n* (%). The effect size was calculated as the standardized mean difference. ICU=Intensive care unit; MBP=Mean blood pressure; LOS=Length of stay; WBC=White blood cell; RBC=Red blood cell; Hb=Hemoglobin; RDW=Red cell distribution width; BUN=Blood urea nitrogen; TC=Total cholesterol; TG=Triglycerides; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; BNP=B-type natriuretic peptide; TyG index=Triglyceride-glucose index; ACEIs=Angiotensin-converting enzyme inhibitors; ARBs=Angiotensin receptor blockers; prior MI=Prior myocardial infarction; AF=Atrial fibrillation; CHF=Chronic heart failure; CDK=Chronic kidney disease; COPD=Chronic obstructive pulmonary disease; APACHE=Acute physiology and chronic health evaluation; SD=Standard deviation; IQR=Interquartile range

model I (OR 1.73, 95% CI 1.45–2.06, $P < 0.001$), and model II (OR 2.53, 95% CI 1.59–4.03, $P < 0.001$).

Then, the TyG index was stratified by tertiles and quartiles to estimate whether the TyG index was an independent risk factor for hospital and ICU mortality in critically ill patients with ACS. A higher TyG index was significantly associated with increased risk of hospital and ICU mortality in univariate analysis, model I and model II logistic regression [P for trend < 0.05, Table 2]. The results in tertile groups were consistent with those in quartile groups. Moreover, the resulting trends were broadly in accordance with Supplementary Figure 1 ($P < 0.001$).

In addition, Supplementary Table 1 indicated that after adjustment for all confounding factors, each 1-unit increase in the TyG index was associated with a 113% elevated risk of hospital mortality and a 138% elevated risk of ICU mortality.

The smoothing curves were used to further display the relationship between the TyG index and hospital and ICU mortality in critically ill patients with ACS [Figure 3]. There were continuous linear relations after adjusting for all covariates, both in hospital and ICU mortality. We found that the risk of hospital and ICU death increased with the higher TyG index.

Subgroup analysis

In most subgroups, no significant interaction was observed between the TyG index and hospital and ICU mortality in critically ill patients with ACS [Supplementary Tables 2 and 3].

DISCUSSION

The study discovered that despite adjustment for several variables, the TyG index still was an independent predictor of hospital and ICU mortality in critically ill patients with ACS. The TyG index of non-survivors was higher than that of survivors. There is a linear relationship between TyG index and hospital and ICU mortality, and with the increase of TyG index, the hospital and ICU mortality correspondingly increased. Furthermore, subgroup analysis illustrated that there was no evident interaction in most subgroups. Admittedly, it is the first time to study the relationship between short-term mortality and the TyG index in critically ill patients with ACS during hospitalization.

TyG index, as a new composite indicator, is closely related to IR.[10] The previous studies have showed that IR had a significant effect on organ-specific functions and organ crosstalk, leading to endothelial dysfunction, vascular damage and the development of CVD.[14,27,28] Patel *et al*.[14] found that as a risk factor of CVD, IR acts through hyperglycemia, oxidative stress, and dyslipidemia.

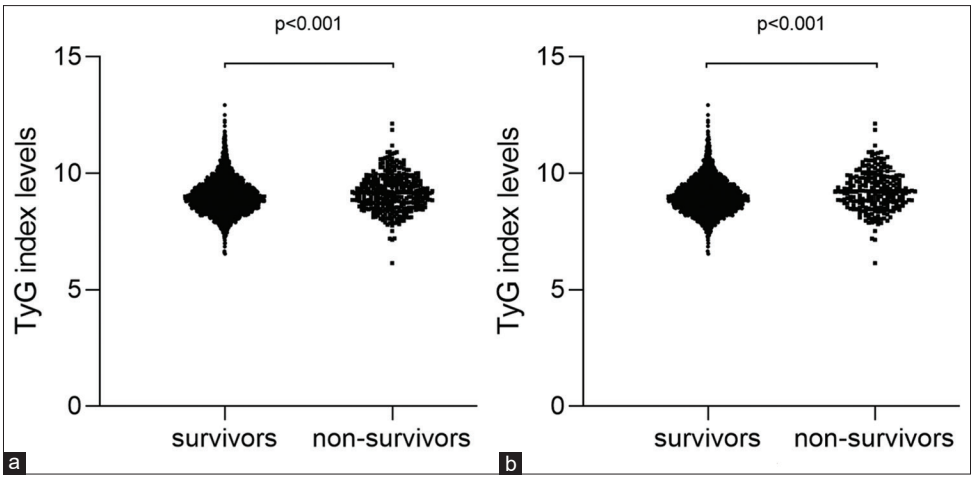

Figure 2: (a) Scatter plot showing triglyceride-glucose (TyG) index levels in critically ill acute coronary syndrome (ACS) patients with hospital survivor (left) and non-survivor (right). (b) Scatter plot showing TyG index levels in critically ill ACS patients with intensive care unit survivor (left) and non-survivor (right). TyG index = Triglyceride-glucose index

Table 2: The association between triglyceride-glucose index and hospital and intensive care unit mortality

	Univariate		Model I		Model II	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Hospital mortality						
Per 1-unit increase	1.33 (1.15–1.53)	<0.001	1.59 (1.36–1.85)	<0.001	2.23 (1.50–3.31)	<0.001
Tertiles						
<8.689	Reference		Reference		Reference	
≥8.689, <9.265	1.07 (0.80–1.42)	0.667	1.17 (0.87–1.57)	0.291	1.50 (0.92–2.45)	0.106
≥9.265	1.58 (1.21–2.06)	<0.001	2.05 (1.55–2.72)	<0.001	2.73 (1.50–4.97)	0.001
P for trend		<0.001		<0.001		0.001
Quartiles						
<8.534	Reference		Reference		Reference	
≥8.534, <8.968	0.95 (0.68–1.34)	0.782	1.03 (0.73–1.45)	0.863	1.60 (0.93–2.77)	0.092
≥8.968, <9.457	1.07 (0.77–1.49)	0.682	1.24 (0.89–1.74)	0.202	1.76 (0.97–3.21)	0.063
≥9.457	1.66 (1.22–2.24)	0.001	2.27 (1.66–3.11)	<0.001	3.05 (1.50–6.20)	0.002
P for trend		<0.001		<0.001		0.004
ICU mortality						
Per 1-unit increase	1.50 (1.26–1.78)	<0.001	1.73 (1.45–2.06)	<0.001	2.53 (1.59–4.03)	<0.001
Tertiles						
<8.689	Reference		Reference		Reference	
≥8.689, <9.265	1.22 (0.85–1.74)	0.281	1.31 (0.91–1.88)	0.143	1.72 (0.94–3.15)	0.077
≥9.265	1.86 (1.33–2.58)	<0.001	2.26 (1.61–3.18)	<0.001	3.03 (1.47–6.24)	0.002
P for trend		<0.001		<0.001		0.002
Quartiles						
<8.534	Reference		Reference		Reference	
≥8.534, <8.968	0.93 (0.61–1.42)	0.735	0.99 (0.65–1.51)	0.959	1.29 (0.66–2.54)	0.456
≥8.968, <9.457	1.13 (0.76–1.70)	0.542	1.27 (0.85–1.92)	0.247	1.58 (0.77–3.24)	0.210
≥9.457	1.97 (1.37–2.84)	<0.001	2.51 (1.73–3.66)	<0.001	2.68 (1.17–6.13)	0.019
P for trend		<0.001		<0.001		0.022

Model I adjusted for: Age, gender and race, Model II adjusted for: Model I plus temperature, respiratory rate, heart rate, MBP, admission height, admission weight, WBC, RBC, Hb, RDW, platelet, BUN, creatinine, glucose, TC, LDL-C, HDL-C, potassium, sodium, chloride, prior MI, AF, CHF, diabetes, hepatic failure, CKD, COPD, hypertension, malignancy and stroke. OR=Odds Ratio; CI=Confidence interval; ICU=Intensive care unit; TyG index=Triglyceride-glucose index; MBP=Mean blood pressure; WBC=White blood cell; RBC=Red blood cell; Hb=Hemoglobin; RDW=Red cell distribution width; BUN=Blood urea nitrogen; TC=Total cholesterol; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; prior MI=Prior myocardial infarction; AF=Atrial fibrillation; AMI=Acute myocardial infarction; CHF=Chronic heart failure; CDK=Chronic kidney disease; COPD=Chronic obstructive pulmonary disease

Therefore, it is reasonable to confirm that the TyG index can replace IR as a potent indicator to evaluate the risk of CVD.

As it is well known, ACS is a major health care and one of the major causes of death, bringing a heavy economic burden to patients.[29] According to symptoms

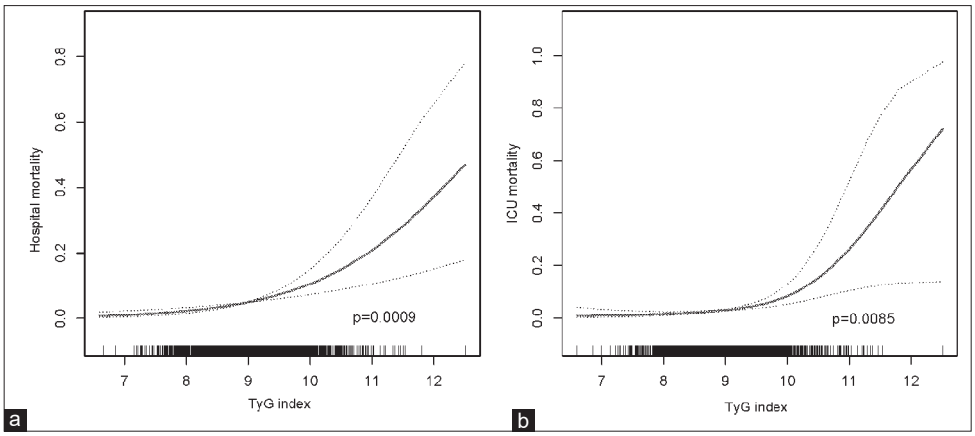

Figure 3: The linear association between the triglyceride-glucose index and hospital (a) and intensive care unit mortality. (b) TyG index = Triglyceride-glucose index; ICU = intensive care unit

and electrocardiographic changes, ACS is classified as unstable angina, non-ST elevation MI and ST elevation MI.[2] The occurrence of ACS involves a variety of complex pathophysiological mechanisms.[30] Currently, more attention is paid to the influence of gender and age on the mortality and prognosis of ACS patients.[31-34] Besides, owing to the special pathogenicity, blood glucose and lipids ought to be persistently focused.

An observational study of 791 patients with non-ST-segment elevation ACS[35] showed that the TyG index was an independent predictor of CAD severity and major adverse cardiovascular events. Wang *et al*.[36] manifested that for patients with diabetes and ACS, the TyG index may be a useful marker for risk stratification and prognosis. Another retrospective, cross-sectional, and observational study drew a similar conclusion, where the TyG index had significant value in predicting subclinical CAD and was independently associated with an increased risk of noncalcified or mixed coronary plaques.[37] Our study focused on critically ill patients with ACS and provided additional information to support previous studies, suggesting the clinical significance of the TyG index for predicting the hospital and ICU mortality.

Our study showed that the TyG index was significantly elevated in nonsurvivors groups compared with the survivor groups ($P < 0.001$). With the increment of the TyG index, the risk of hospital and ICU mortality correspondingly rose up. We further performed subgroup analysis, and the trends were correlated with the previous. This was in accordance with the present findings, indicating an independent prognostic role of the TyG index for the critically ill ACS population.

Improving the ability to early identify the risk of death of critically ill patients with ACS and taking appropriate intervention measures is still an issue that we need to pay attention to. The TyG index has the advantage of being applicable in clinical practice compared with the homeostatic model assessment.[38] Regrettably, as a novel marker, the TyG index is currently not widely used yet. Whereas, it could quickly predict the risk of death of critically ill patients with ACS, since tests for TG and glucose concentrations are inexpensive and are routinely taken.

Although our study was based on a large-scale, multicenter ICU database, there were some limitations. Since the region is too single and the population is only from the US, the bias was inevitable. All data came from a publicly open clinical database, so it was difficult to extract some important variables, such as the history of smoking and drinking. Since both TG and glucose levels change dynamically, the study just chose the TyG index measured at the first time after admission. Random error may be inevitable. Due to missing values of more than 20%, it was difficult to obtain information about some important clinical or laboratory variables.

CONCLUSION

TyG index is an independent predictor of ICU and hospital mortality in critically ill patients with ACS and may contribute to the risk stratification and prognosis of such groups.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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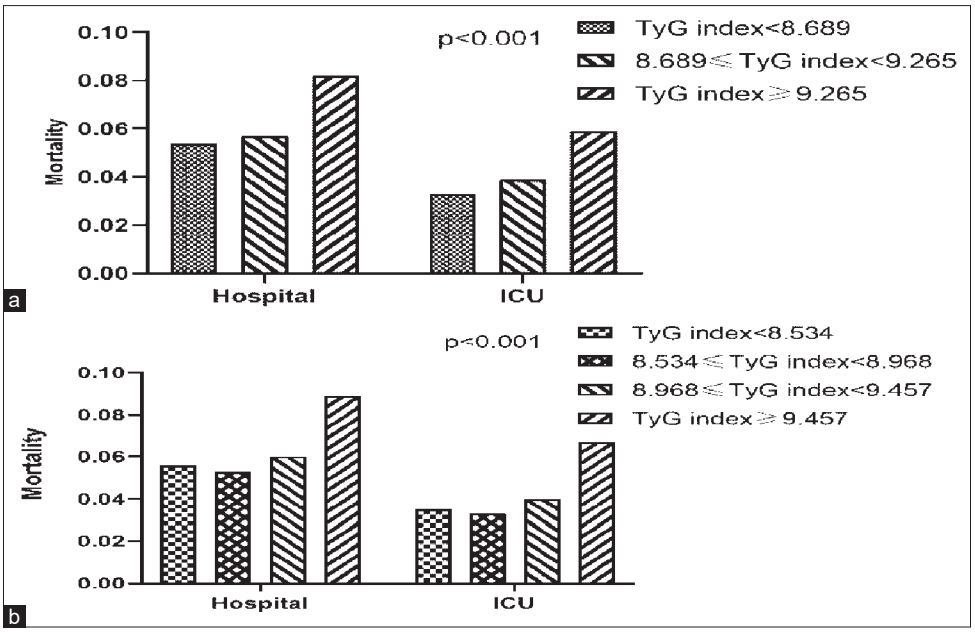

Supplementary Figure 1: The hospital and ICU mortality according to TyG index tertiles (a) and quartiles (b). TyG index = Triglyceride-Glucose index; ICU = Intensive care unit

Supplementary Table 1: Survival analysis of triglyceride-glucose index and hospital and intensive care unit mortality

	Univariate		Model I		Model II	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Hospital mortality	1.16 (1.01–1.32)	0.038	1.28 (1.12–1.48)	<0.001	2.13 (1.13–3.99)	0.019
ICU mortality	1.19 (1.01–1.39)	0.034	1.30 (1.11–1.53)	0.001	2.38 (1.06–5.34)	0.036

CI=Confidence interval; HR=Hazard ratio; ICU=Intensive care unit

Supplementary Table 2: The association between three triglyceride-glucose index groups and hospital mortality in subgroup analysis

	n	TyG index <8.689 (reference)	8.689≤TyG index <9.265 OR (95% CI)	TyG index ≥9.265 OR (95% CI)	*P* for interaction
Age (years)					0.577
<64.00	2592	1 (reference)	1.58 (0.84–3.00)	2.08 (1.14–3.78)	
≥64.00	2645	1 (reference)	1.04 (0.74–1.45)	1.90 (1.39–2.59)	
Male					0.31
No	1844	1 (reference)	0.99 (0.63–1.55)	1.74 (1.16–2.61)	
Yes	3393	1 (reference)	1.12 (0.77–1.63)	1.45 (1.01–2.07)	
Race					0.094
White	4114	1 (reference)	1.06 (0.78–1.46)	1.49 (1.10–2.01)	
Black	464	1 (reference)	0.77 (0.19–3.13)	3.41 (1.23–9.48)	
Other	659	1 (reference)	0.97 (0.41–2.29)	1.34 (0.62–2.88)	
Aspirin					0.556
No	2477	1 (reference)	1.21 (0.79–1.85)	1.80 (1.21–2.67)	
Yes	2760	1 (reference)	0.95 (0.64–1.42)	1.40 (0.97–2.02)	
ACEIs					0.608
No	3981	1 (reference)	1.17 (0.86–1.60)	1.68 (1.26–2.26)	
Yes	1256	1 (reference)	0.66 (0.30–1.44)	1.18 (0.59–2.35)	
ARBs					0.355
No	2841	1 (reference)	1.20 (0.83–1.73)	1.62 (1.15–2.29)	
Yes	2396	1 (reference)	0.89 (0.55–1.44)	1.52 (0.98–2.34)	
Diabetes					<0.001
No	4098	1 (reference)	1.28 (0.93–1.78)	2.09 (1.52–2.86)	
Yes	1139	1 (reference)	0.43 (0.23–0.83)	0.54 (0.32–0.91)	
AF					0.283
No	4892	1 (reference)	1.13 (0.81–1.56)	1.81 (1.35–2.44)	
Yes	345	1 (reference)	0.75 (0.39–1.47)	0.77 (0.38–1.52)	
AMI					0.237
No	1530	1 (reference)	1.01 (0.63–1.61)	1.37 (0.87–2.14)	
Yes	3707	1 (reference)	1.12 (0.78–1.63)	1.75 (1.25–2.46)	
CHF					0.515
No	4782	1 (reference)	1.14 (0.83–1.58)	1.66 (1.23–2.24)	
Yes	455	1 (reference)	0.68 (0.34–1.37)	1.14 (0.61–2.15)	
CKD					0.452
No	4914	1 (reference)	1.21 (0.89–1.66)	1.73 (1.28–2.33)	
Yes	323	1 (reference)	0.54 (0.24–1.22)	0.85 (0.43–1.66)	
COPD					0.614
No	4980	1 (reference)	1.03 (0.76–1.39)	1.59 (1.20–2.09)	
Yes	257	1 (reference)	1.70 (0.58–5.01)	1.47 (0.49–4.44)	
Hypertension					0.331
No	4429	1 (reference)	0.96 (0.70–1.31)	1.52 (1.14–2.01)	
Yes	808	1 (reference)	2.19 (0.94–5.13)	2.27 (0.97–5.31)	
Stroke					0.153
No	5068	1 (reference)	1.02 (0.75–1.38)	1.46 (1.10–1.93)	
Yes	169	1 (reference)	1.98 (0.67–5.91)	3.77 (1.38–10.30)	
BNP (mmol/L)					0.172
<24.00	2071	1 (reference)	1.22 (0.83–1.80)	1.72 (1.21–2.45)	
≥24.00	2914	1 (reference)	0.83 (0.52–1.31)	1.17 (0.75–1.82)	
BUN (mg/dL)					0.859
<16.00	2384	1 (reference)	1.56 (0.79–3.07)	1.30 (0.63–2.68)	
≥16.00	2848	1 (reference)	0.99 (0.71–1.37)	1.51 (1.13–2.03)	
WBC (10^9/L)					0.023
<10.60	2467	1 (reference)	0.74 (0.44–1.25)	0.93 (0.56–1.55)	
≥10.60	2539	1 (reference)	1.09 (0.76–1.56)	1.54 (1.10–2.16)	
RBC (10^{12}/L)					0.846
<4.28	2492	1 (reference)	1.29 (0.90–1.83)	1.86 (1.33–2.61)	

Contd...

Supplementary Table 2: Contd...

	n	TyG index <8.689 (reference)	8.689≤TyG index <9.265 OR (95% CI)	TyG index ≥9.265 OR (95% CI)	*P* for interaction
≥4.28	2520	1 (reference)	0.87 (0.52–1.46)	1.48 (0.93–2.34)	
Chloride (mmol/L)					0.005
<104.00	2129	1 (reference)	1.02 (0.66–1.57)	1.22 (0.82–1.82)	
≥104.00	3104	1 (reference)	1.09 (0.73–1.61)	1.88 (1.30–2.71)	
Creatinine (mg/dL)					0.467
<0.95	2611	1 (reference)	1.29 (0.72–2.31)	1.84 (1.05–3.22)	
≥0.95	2622	1 (reference)	0.97 (0.69–1.37)	1.34 (0.98–1.83)	
Hb (g/dL)					0.506
<12.90	2437	1 (reference)	1.24 (0.86–1.78)	1.87 (1.32–2.63)	
≥12.90	2595	1 (reference)	0.92 (0.56–1.49)	1.43 (0.92–2.22)	
Glucose (mg/dL)					<0.001
<126.00	2605	1 (reference)	0.50 (0.30–0.84)	0.34 (0.14–0.78)	
≥126.00	2632	1 (reference)	1.12 (0.74–1.68)	1.23 (0.84–1.80)	
LDL-C (mg/dL)					0.016
<88.00	1847	1 (reference)	1.10 (0.70–1.74)	1.44 (0.93–2.23)	
≥88.00	1893	1 (reference)	1.71 (0.73–3.99)	3.12 (1.40–6.95)	
HDL-C (mg/dL)					0.4
<37.00	2292	1 (reference)	0.58 (0.35–0.95)	1.01 (0.67–1.54)	
≥37.00	2646	1 (reference)	1.57 (0.99–2.50)	1.62 (0.98–2.69)	
TC (mg/dL)					0.84
<138.00	2439	1 (reference)	1.26 (0.86–1.85)	1.91 (1.32–2.78)	
≥138.00	2495	1 (reference)	1.33 (0.63–2.81)	2.06 (1.04–4.10)	
TG (mg/dL)		1 (reference)			0.226
<116.00	2587	1 (reference)	1.88 (1.36–2.60)	4.03 (2.66–6.11)	
≥116.00	2650	1 (reference)	0.59 (0.20–1.71)	1.48 (0.53–4.13)	
Platelet (10^9/L)					0.233
<208.00	2488	1 (reference)	1.06 (0.72–1.57)	1.29 (0.89–1.88)	
≥208.00	2538	1 (reference)	1.09 (0.71–1.69)	1.93 (1.30–2.87)	
Potassium (mmol/L)					0.683
<4.10	2576	1 (reference)	1.03 (0.67–1.59)	1.59 (1.06–2.38)	
≥4.10	2659	1 (reference)	1.10 (0.74–1.63)	1.54 (1.08–2.22)	
Sodium (mmol/L)					0.003
<138.00	2369	1 (reference)	1.21 (0.79–1.86)	1.29 (0.86–1.94)	
≥138.00	2865	1 (reference)	0.95 (0.64–1.42)	1.88 (1.32–2.69)	
RDW (%)					0.948
<13.80	2296	1 (reference)	1.17 (0.68–2.01)	1.76 (1.07–2.88)	
≥13.80	2410	1 (reference)	1.00 (0.70–1.43)	1.56 (1.12–2.18)	
Temperature (℃)					0.345
<36.50	2425	1 (reference)	1.25 (0.85–1.84)	1.88 (1.31–2.68)	
≥36.50	2610	1 (reference)	0.91 (0.57–1.45)	1.26 (0.81–1.97)	
Respiratory rate (beats/min)					0.869
<26.00	2510	1 (reference)	1.29 (0.77–2.16)	1.52 (0.92–2.52)	
≥26.00	2699	1 (reference)	0.94 (0.66–1.34)	1.56 (1.13–2.15)	
Heart rate (beats/minute)					0.274
<95.00	2548	1 (reference)	0.77 (0.43–1.38)	1.67 (1.01–2.77)	
≥95.00	2688	1 (reference)	1.11 (0.79–1.56)	1.34 (0.97–1.85)	
MBP (mmHg)					0.792
<68.00	2553	1 (reference)	1.00 (0.69–1.45)	1.62 (1.15–2.27)	
≥68.00	2680	1 (reference)	1.23 (0.77–1.96)	1.65 (1.06–2.57)	
APACHE IV					0.217
<42.00	2581	1 (reference)	0.50 (0.09–2.71)	2.05 (0.61–6.83)	
≥42.00	2613	1 (reference)	1.21 (0.83–1.75)	1.81 (1.28–2.56)	

OR=Odds ratio; CI=Confidence interval; TyG index=Triglyceride-glucose index; ACEIs=Angiotensin-converting enzyme inhibitors; ARBs=Angiotensin receptor blockers; AF=Atrial fibrillation; AMI=Acute myocardial infarction; CHF=Chronic heart failure; CDK=Chronic kidney disease; COPD=Chronic obstructive pulmonary disease; BNP=B-type natriuretic peptide; BUN=Blood urea nitrogen; WBC=White blood cell; RBC=Red blood cell; Hb=Hemoglobin; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; TC=Total cholesterol; TG=Triglycerides; RDW=Red cell distribution width; MBP=Mean blood pressure; APACHE=Acute physiology and chronic health evaluation

Supplementary Table 3: The association between three triglyceride-glucose index groups and intensive care unit mortality in subgroup analysis

	n	TyG index <8.689 (reference)	8.689≤ TyG index <9.265 OR (95% CI)	TyG index ≥9.265 OR (95% CI)	*P* for interaction
Age (years)					0.706
<64.00	2592	1 (reference)	1.55 (0.78–3.09)	1.76 (0.91–3.38)	
≥64.00	2645	1 (reference)	1.18 (0.77–1.80)	2.38 (1.62–3.51)	
Male					0.245
No	1844	1 (reference)	0.85 (0.48–1.50)	2.00 (1.23–3.25)	
Yes	3393	1 (reference)	1.53 (0.96–2.43)	1.71 (1.09–2.69)	
Race					0.221
White	4114	1 (reference)	1.25 (0.84–1.85)	1.77 (1.22–2.56)	
Black	464	1 (reference)	0.77 (0.14–4.27)	4.16 (1.25–13.80)	
Other	659	1 (reference)	0.97 (0.33–2.82)	1.43 (0.56–3.67)	
Aspirin					0.472
No	2477	1 (reference)	1.14 (0.68–1.91)	1.91 (1.19–3.04)	
Yes	2760	1 (reference)	1.29 (0.78–2.12)	1.79 (1.12–2.87)	
ACEIs					0.714
No	3981	1 (reference)	1.31 (0.90–1.92)	1.88 (1.32–2.68)	
Yes	1256	1 (reference)	0.77 (0.26–2.32)	1.87 (0.75–4.69)	
ARBs					0.287
No	2841	1 (reference)	1.25 (0.80–1.94)	1.75 (1.16–2.64)	
Yes	2396	1 (reference)	1.20 (0.65–2.21)	2.08 (1.19–3.63)	
Diabetes					<0.001
No	4098	1 (reference)	1.51 (1.00–2.26)	2.69 (1.82–3.96)	
Yes	1139	1 (reference)	0.47 (0.22–1.02)	0.51 (0.27–0.96)	
AF					0.639
No	4892	1 (reference)	1.28 (0.86–1.90)	2.04 (1.42–2.92)	
Yes	345	1 (reference)	0.86 (0.36–2.07)	1.08 (0.45–2.56)	
AMI					0.7
No	1530	1 (reference)	1.44 (0.79–2.62)	1.97 (1.12–3.49)	
Yes	3707	1 (reference)	1.12 (0.72–1.75)	1.82 (1.21–2.74)	
CHF					0.964
No	4782	1 (reference)	1.35 (0.91–2.01)	1.99 (1.37–2.88)	
Yes	455	1 (reference)	0.69 (0.30–1.60)	1.29 (0.61–2.73)	
CKD					0.871
No	4914	1 (reference)	1.45 (0.98–2.13)	1.97 (1.36–2.85)	
Yes	323	1 (reference)	0.37 (0.11–1.18)	1.22 (0.56–2.67)	
COPD					0.252
No	4980	1 (reference)	1.19 (0.82–1.72)	1.91 (1.36–2.69)	
Yes	257	1 (reference)	1.68 (0.46–6.16)	1.07 (0.26–4.44)	
Hypertension					0.065
No	4429	1 (reference)	1.11 (0.76–1.61)	1.68 (1.19–2.38)	
Yes	808	1 (reference)	4.33 (0.93–20.24)	6.58 (1.47–29.43)	
Stroke					0.147
No	5068	1 (reference)	1.13 (0.78–1.63)	1.66 (1.17–2.33)	
Yes	169	1 (reference)	4.20 (0.83–21.23)	8.04 (1.74–37.23)	
BNP (mmol/L)					0.24
<24.00	2071	1 (reference)	1.27 (0.80–2.00)	1.98 (1.31–2.99)	
≥24.00	2914	1 (reference)	1.05 (0.57–1.92)	1.22 (0.67–2.24)	
BUN (mg/dL)					0.923
<16.00	2384	1 (reference)	1.28 (0.56–2.95)	1.36 (0.59–3.17)	
≥16.00	2848	1 (reference)	1.22 (0.82–1.82)	1.83 (1.27–2.63)	
WBC (10^9/L)					0.075
<10.60	2467	1 (reference)	0.90 (0.48–1.70)	1.14 (0.61–2.13)	
≥10.60	2539	1 (reference)	1.23 (0.79–1.91)	1.78 (1.18–2.69)	
RBC (10^{12}/L)					0.522
<4.28	2492	1 (reference)	1.35 (0.88–2.09)	2.07 (1.37–3.11)	

Contd...

Supplementary Table 3: Contd...

	n	TyG index <8.689 (reference)	8.689≤ TyG index <9.265 OR (95% CI)	TyG index ≥9.265 OR (95% CI)	*P* for interaction
≥4.28	2520	1 (reference)	1.18 (0.62–2.26)	1.97 (1.09–3.54)	
Chloride (mmol/L)					0.01
<104.00	2129	1 (reference)	1.00 (0.59–1.71)	1.32 (0.82–2.15)	
≥104.00	3104	1 (reference)	1.41 (0.87–2.27)	2.37 (1.51–3.73)	
Creatinine (mg/dL)					0.396
<0.95	2611	1 (reference)	1.71 (0.80–3.64)	2.41 (1.16–5.01)	
≥0.95	2622	1 (reference)	1.07 (0.71–1.61)	1.54 (1.06–2.23)	
Hb (g/dL)					0.812
<12.90	2437	1 (reference)	1.38 (0.88–2.14)	2.16 (1.43–3.28)	
≥12.90	2595	1 (reference)	1.10 (0.60–2.02)	1.76 (1.01–3.05)	
Glucose (mg/dL)					0.001
<126.00	2605	1 (reference)	0.61 (0.32–1.17)	0.31 (0.09–1.03)	
≥126.00	2632	1 (reference)	1.11 (0.69–1.79)	1.26 (0.81–1.97)	
LDL-C (mg/dL)					0.003
<88.00	1847	1 (reference)	1.31 (0.75–2.29)	1.27 (0.72–2.25)	
≥88.00	1893	1 (reference)	1.44 (0.48–4.32)	4.42 (1.67–11.71)	
HDL-C (mg/dL)					0.93
<37.00	2292	1 (reference)	0.80 (0.43–1.49)	1.49 (0.87–2.55)	
≥37.00	2646	1 (reference)	1.61 (0.90–2.87)	1.90 (1.03–3.50)	
TC (mg/dL)					0.793
<138.00	2439	1 (reference)	1.59 (0.99–2.58)	2.36 (1.47–3.80)	
≥138.00	2495	1 (reference)	0.95 (0.37–2.43)	2.42 (1.10–5.33)	
TG (mg/dL)					0.659
<116.00	2587	1 (reference)	2.10 (1.41–3.12)	4.63 (2.85–7.54)	
≥116.00	2650	1 (reference)	0.82 (0.19–3.58)	2.12 (0.51–8.77)	
Platelet (10^9/L)					0.241
<208.00	2488	1 (reference)	1.23 (0.76–1.98)	1.45 (0.91–2.29)	
≥208.00	2538	1 (reference)	1.24 (0.72–2.14)	2.42 (1.48–3.95)	
Potassium (mmol/L)					0.868
<4.10	2576	1 (reference)	1.28 (0.75–2.21)	1.89 (1.13–3.16)	
≥4.10	2659	1 (reference)	1.17 (0.73–1.89)	1.79 (1.16–2.75)	
Sodium (mmol/L)					<0.001
<138.00	2369	1 (reference)	1.08 (0.65–1.80)	1.18 (0.73–1.91)	
≥138.00	2865	1 (reference)	1.36 (0.82–2.26)	2.75 (1.73–4.37)	
RDW (%)					0.294
<13.80	2296	1 (reference)	1.12 (0.60–2.10)	1.62 (0.92–2.87)	
≥13.80	2410	1 (reference)	1.25 (0.80–1.95)	2.01 (1.33–3.05)	
Temperature (℃)					0.422
<36.50	2425	1 (reference)	1.36 (0.85–2.18)	2.23 (1.45–3.43)	
≥36.50	2610	1 (reference)	1.07 (0.60–1.91)	1.39 (0.79–2.42)	
Respiratory rate (beats/min)					0.396
<26.00	2510	1 (reference)	0.99 (0.51–1.89)	1.47 (0.81–2.68)	
≥26.00	2699	1 (reference)	1.28 (0.83–1.97)	2.00 (1.34–2.98)	
Heart rate (beats/min)					0.045
<95.00	2548	1 (reference)	1.01 (0.47–2.16)	2.32 (1.20–4.50)	
≥95.00	2688	1 (reference)	1.20 (0.79–1.80)	1.48 (1.01–2.18)	
MBP (mmHg)					0.389
<68.00	2553	1 (reference)	1.20 (0.76–1.89)	2.16 (1.43–3.26)	
≥68.00	2680	1 (reference)	1.31 (0.73–2.34)	1.56 (0.89–2.73)	
APACHE IV					0.219
<42.00	2581	1 (reference)	0.50 (0.04–5.48)	2.56 (0.50–13.23)	
≥42.00	2613	1 (reference)	1.21 (0.83–1.75)	1.81 (1.28–2.56)	

OR=Odds ratio; CI=Confidence interval; TyG index=Triglyceride-glucose index; ACEIs=Angiotensin-converting enzyme inhibitors; ARBs=Angiotensin receptor blockers; AF=Atrial fibrillation; AMI=Acute myocardial infarction; CHF=Chronic heart failure; CDK=Chronic kidney disease; COPD=Chronic obstructive pulmonary disease; BNP=B-type natriuretic peptide; BUN=Blood urea nitrogen; WBC=White blood cell; RBC=Red blood cell; Hb=Hemoglobin; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; TC=Total cholesterol; TG=Triglycerides; RDW=Red cell distribution width; MBP=Mean blood pressure; APACHE=Acute physiology and chronic health evaluation