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Predictive value of the triglyceride-glucose index for short- and long-term all-cause mortality in patients with critical coronary artery disease: a cohort study from the MIMIC-IV database

Huijian Wang[1†], Qingan Fu[1†], Shucai Xiao[1†], Xiaowei Ma[1], Yanhui Liao[1], Changlong Kang[1] and Renqiang Yang[1*]

Abstract

Background Triglyceride-glucose (TyG) index is linked to a poor prognosis for cardiovascular condition and is a valid indicator of insulin resistance. This study evaluated the potential predicting usefulness of the TyG index for all-cause mortality, both short- and long-term, for those concerning critical coronary artery disease (CAD).

Methods In this study, information from 5452 critically-ill individuals with CAD in intensive care units were gathered from the Medical Information Marketplace in Intensive Care (MIMIC-IV) database. Depending on the TyG index degree, the patients were categorized into three categories. Clinical outcomes included short-term (30-day) and long-term (365-day) all-cause mortality. The corresponding relationships involving the TyG index and clinical outcomes were examined by deploying restricted cubic spline (RCS) regression analysis and Cox proportional risk regression.

Results An increased TyG index was associated with increased 30-day (Tertile 1: 6.1%, Tertile 2: 7.3%, Tertile 3: 9.2%, $P=0.001$) and 365-day (Tertile 1: 15.2%, Tertile 2: 17.0%, Tertile 3: 19.6%, $P=0.002$) death rates across all causes. Cox regression with multiple variables indicates that higher TyG indices were linked to higher all-caused mortality hazard ratios throughout the short and long terms, with a larger predictive value for the former. RCS regression analyses suggested that the risk of death was notably and linearly that is associated with TyG index.

Conclusions The TyG index is a reliable predictor of all-cause mortality at different stages in critically ill CAD patients, with a higher predictive ability for short-term mortality. Early intervention in patients with elevated TyG index may improve their survival outcomes. Future research should delve into understanding its pathophysiological mechanisms and develop intervention strategies based on the TyG index, providing new insights and strategies to enhance the outlook for critically ill CAD patients.

†Huijian Wang, Qingan Fu and Shucai Xiao contributed equally to this work.

*Correspondence:
Renqiang Yang
Yang.RQ@ncu.edu.cn

Full list of author information is available at the end of the article

Keywords All-cause mortality, Coronary artery disease, Insulin resistance, MIMIC-IV, Triglyceride-glucose index

Introduction

Coronary artery disease (CAD) is a condition which heart muscle is deprived of blood and oxygen due to narrowing or blockage of the coronary arteries, is the top killer of death worldwide, with CAD causing a growing proportion of premature deaths [1]. This places heavy physical, health and financial burdens on patients and their families [2]. With the aging population, the incidence and death rate from cardiovascular disease (CVD) remaining rising, as does the demand for intensive cardiovascular care [3]. Patients with critical CAD often have more complicated conditions, more comorbidities and higher mortality rates, which will further increase the global public health burden. It is therefore important to investigate early risk stratification markers in patients with severe CAD to reduce their mortality.

Insulin resistance (IR), the incapacity of insulin in functioning as intended in target tissues that are insulin-sensitive [4], is a multifaceted syndrome associated with dyslipidemia, hypertension, hypercoagulable states and atherosclerosis, among other conditions, and significantly increases the likelihood of getting cardiovascular disease [5, 6]. Critically ill patients are marked by elevated mortality and a hypermetabolic state in which IR plays an important role [7]. Compared to healthy individuals, patients in the intensive care unit (ICU) are prone to severe IR, with a 70% reduction in insulin sensitivity of the body's tissues, suggesting that glucose uptake is severely compromised, adversely affecting prognosis [7]. Therefore, the assessment of IR in critically ill patients has far-reaching implications for their survival prognosis. Triglyceride-glucose (TyG) index has been a new instrument to assess IR with great specificity and sensitivity in comparison to the gold-standard technique hyperinsulinemic-normoglycemic clamp technique, and has the advantages of being convenient, accessible and reliable [8, 9]. Research has demonstrated that the TyG index has a solid link with unfavorable results in individuals with CVD and plays an integral part in the evolution of CVD [10–13]. In the ICU cohort containing 3036 patients, a high level of TyG index was considered an a standalone signal of increased in-hospital mortality in ICU patients, exhibiting a linear correlation with the outcome [14]. The same results were obtained in another cohort research involving critically ill CAD patients [15].

Currently, there are no studies on the relationship between the TyG index and long-term prognosis in patients with critical CAD, and studies comparing the predictive power of the TyG index for short- and long-term prognosis are very limited. This investigation aims to explore the association between the TyG index and the short- and long-term all-cause mortality in critical CAD patients, as well as the difference between short- and long-term survival prognoses.

Methods

Study population

The data for this study were obtained from the MIMIC-IV database (Medical Information Mart for Intensive Care IV), a publicly accessible and freely available repository of de-identified electronic medical files for Beth Israel Deaconess Medical Center patients who were admitted, including 509,200 patients admitted to the ICU from 2008 to 2019. One of the authors (HW) obtained access to the database (Record ID: 59123180). Authorization from the patient was not necessitate since the deidentified nature of these data. The included patients had severe coronary artery disease and were admitted to the intensive care unit. Following that were excluding standards: (1) Under the age of eighteen; (2) had multiple hospitalizations in the ICU for critical CAD, and just the information from their first admission was utilized out; (3) missing triglyceride and glucose data; (4) had malignant cancer or severe liver disease; and (5) had abnormal data. The study included a total of 5,452individuals who, according to their TyG index values, have been categorized into three groups (Fig. 1).

Data collection and definitions

Via the usage of PostgreSQL (version 16.0) and structured query language (SQL), baseline characteristics of the individuals being studied were collected. Including demographics, laboratory indicators, critical care scores, comorbidities, medications, survival information. Random forest interpolation was used to fill in missing values for variables less than 15%. The TyG index computation is done by employing glucose and triglycerides during fasting indicators utilizing the subsequent formula: Ln [(triglyceride (mg/dl) × glucose (mg/dl))/2] [16]. Diagnosis of comorbidities determined in accordance with ICD-9 and ICD-10 numbers from the International Classification of Diseases, and diabetes mellitus was determined by the Charlson comorbidity view in the MIMIC-IC database. Acute coronary syndrome (ACS), coronary artery bypass graft surgery, percutaneous coronary intervention, myocardial infarction, and ischemic heart disease are the definitions of CAD [17].

Clinical outcomes

The study's clinical outcomes included all-cause mortality during a 30-days (short-term) and 365-days (long-term) period. Final follow-up time of the MIMIC-IV database

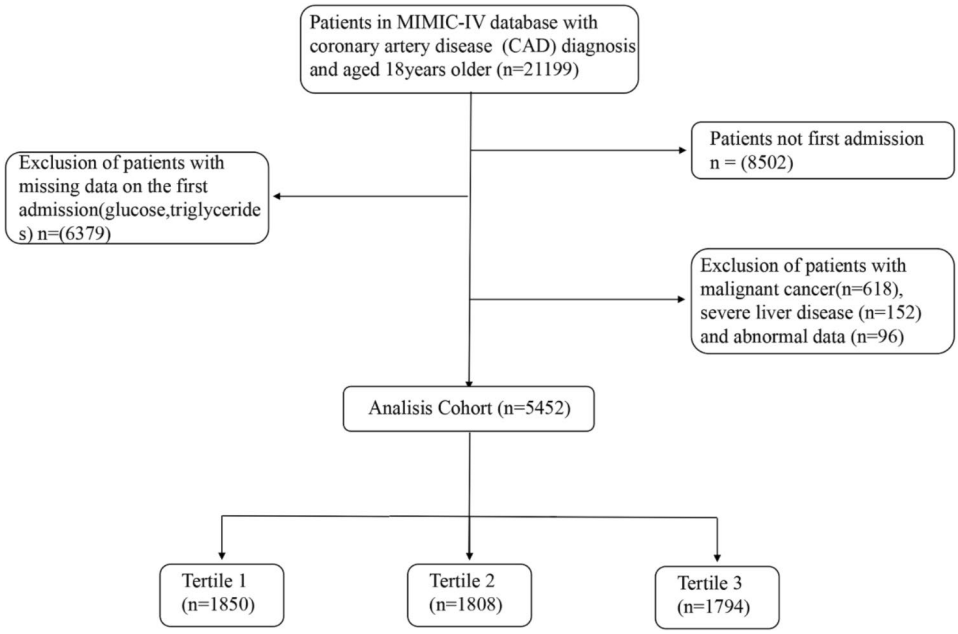

Fig. 1 Screening of the study population

was 1 year after the patient was discharged from the last hospitalization.

Statistical analysis

First, using chi-square or Fisher's test assess the categorical variables, and results are shown as percentages. Second, the Kolmogorov-Smirnov test was used to assess the normality of continuous numerical variables. All *P*-values were less than 0.05, indicating that the variables did not follow a normal distribution. Consequently, the results were expressed as interquartile ranges (IQR). Comparisons between the two groups were performed using the Kruskal-Wallis H test. Kaplan-Meyer (K-M) curves were used to perform survival analyses of the incidence of clinical outcomes at different TyG index levels. Next, cox regression analyses that were univariate made use of to further elucidate the connection relating the TyG index to all-cause mortality during a 30-day and 365-day timeframe. Subsequently, variables with *P*-values below the 0.05 significance level were extracted and incorporated into the multivariate Cox regression study for backward stepwise regression to obtain the final adjusted model. No variables were modified in the Model 1; Model 2 adjusted for gender and age; and heart rate, respiratory rate, blood oxygen saturation, red and white blood cells, creatinine, acute kidney failure, atrial fibrillation, cardiogenic shock, heart failure, myocardial infarction, aspirin, statin, and inhibitors of the angiotensin II receptor and angiotensin converting enzyme were all modified in Model 3 based on Model 2. In addition, a linear or nonlinear correlation of clinical outcomes and the TyG index was determined by restricted cubic spline (RCS), adjusting for Models 1 and 3 above. Finally, it was also analyzed whether the TyG index's predictive value varied depending on the subgroups. Subgroup analyses was conducted out for gender, age (<70 or >=70 years), diabetes mellitus, myocardial infarction, hypertension, and statin use, and an interaction effect of *P*-value was determined. These results are ultimately presented in the form of a forest plot. R software (version 4.3.3) was being employed to statistically analyze all of the data, and $P<0.05$ was considered significant for two-sided tests.

Results

Baseline characteristics

After screening the study population, 5,452 patients with critical CAD were ultimately included. Three groups of patients have been split into established on the TyG index when the patient was admitted [Tertile 1 (5.8–8.6), Tertile 2 (8.6–9.2), and Tertile 3 (9.2–13.4)]. The medians for the three groups were 8.3, 8.9, and 9.7, respectively. Table 1 shows their baseline characteristics, 3,410 patients (62.5%) were male, and the patients' median age was 69 years. Patients in this study having the greatest TyG index were generally younger and had a faster heart rate and greater systolic blood pressure. The patients were admitted with increased levels of low density lipoprotein, total cholesterol, red blood cells, creatinine, potassium, glycosylated hemoglobin and white blood cells and comparatively low high density lipoprotein and sodium values. Additionally, those whose TyG index is higher demonstrated a greater incidence of hypertension, acute kidney failure, diabetes mellitus, and chronic kidney disease; greater use of statins; and a lower incidence of atrial

Table 1 Baseline characteristics of patients with critical CAD classified by the TyG index

Variables	Overall(*n* = 5452)	T1(*n* = 1850)	T2(*n* = 1808)	T3(*n* = 1794)	*P*-value
Age, years	69.0 [60.0, 78.0]	71.0 [62.0, 81.0]	69.0 [60.0, 78.0]	66.0 [57.0, 74.0]	< 0.001
Male, n(%)	3410 (62.5)	1169 (63.2)	1127 (62.3)	1114 (62.1)	0.772
Vital signs					
Temperature,°C	36.7 [36.4, 37.0]	36.7 [36.4, 36.9]	36.7 [36.4, 37.0]	36.7 [36.5, 37.1]	< 0.001
HR, bpm	82.0 [73.0, 94.0]	81.0 [71.0, 93.0]	82.0 [72.0, 94.0]	83.0 [74.0, 96.0]	< 0.001
RR, insp/min	18.0 [14.0, 22.0]	17.0 [14.0, 21.0]	18.0 [14.0, 22.0]	18.0 [14.0, 22.0]	0.009
SBP, mmhg	121.0 [106.0, 138.0]	120.0 [105.0, 137.8]	121.0 [104.0, 138.0]	124.0 [107.0, 140.0]	0.002
DBP, mmhg	66.0 [56.0, 79.0]	67.0 [56.0, 79.0]	66.0 [56.0, 78.0]	66.0 [56.0, 79.0]	0.339
Laboratory indicators					
RBC, m/uL	4.3 [3.9, 4.7]	4.3 [3.9, 4.7]	4.3 [3.9, 4.8]	4.4 [3.9, 4.8]	0.006
WBC, K/uL	8.1 [6.4, 10.6]	7.8 [6.1, 10.2]	8.1 [6.5, 10.6]	8.4 [6.8, 10.9]	< 0.001
Platelet, K/uL	230.0 [184.0, 283.0]	223.0 [177.0, 277.0]	234.0 [188.0, 285.0]	231.5 [189.0, 286.0]	< 0.001
Creatinine, mg/dL	1.0 [0.8, 1.4]	1.0 [0.8, 1.3]	1.0 [0.8, 1.4]	1.1 [0.9, 1.4]	< 0.001
TC, mg/dL	160.0 [131.0, 196.0]	150.0 [124.0, 180.0]	158.0 [131.0, 190.0]	177.0 [144.0, 215.0]	< 0.001
HDL, mg/dL	45.0 [36.0, 57.0]	51.0 [41.0, 63.0]	45.0 [37.0, 56.0]	40.0 [33.0, 49.0]	< 0.001
LDL, mg/dL	83.0 [61.0, 110.0]	78.0 [57.0, 103.0]	83.0 [62.0, 108.0]	88.0 [64.0, 121.0]	< 0.001
TG, mg/dL	122.0 [87.0, 178.0]	79.0 [63.0, 96.0]	127.5 [104.8, 152.0]	210.0 [157.2, 285.0]	< 0.001
Glu, mg/dL	112.0 [95.0, 149.0]	96.0 [87.0, 109.0]	113.0 [97.0, 139.2]	151.0 [115.0, 203.0]	< 0.001
TyG index	8.9 [8.5, 9.4]	8.3 [8.1, 8.5]	8.9 [8.8, 9.0]	9.6 [9.4, 10.0]	< 0.001
HbA1c,%	5.9 [5.5, 6.9]	5.7 [5.4, 6.1]	5.9 [5.5, 6.7]	6.5 [5.8, 7.9]	< 0.001
Sodium, mEq/L	139.0 [137.0, 141.0]	139.0 [137.0, 141.0]	139.0 [137.0, 141.0]	139.0 [137.0, 141.0]	< 0.001
Potassium, mEq/L	4.2 [3.9, 4.6]	4.2 [3.9, 4.5]	4.2 [3.9, 4.6]	4.3 [3.9, 4.7]	0.001
Sp02,%	98.0 [96.0, 100.0]	98.0 [96.0, 100.0]	98.0 [96.0, 100.0]	98.0 [96.0, 100.0]	0.008
Gcs	15.0 [15.0, 15.0]	15.0 [15.0, 15.0]	15.0 [15.0, 15.0]	15.0 [15.0, 15.0]	0.237
SOFA	1.0 [0.0, 3.0]	1.0 [0.0, 3.0]	1.0 [0.0, 3.0]	1.0 [0.0, 3.0]	0.077
Comorbidities, n (%)					
AKF	1905 (34.9)	576 (31.1)	601 (33.2)	728 (40.6)	< 0.001
CKD	1601 (29.4)	444 (24.0)	528 (29.2)	629 (35.1)	< 0.001
AF	1905 (34.9)	746 (40.3)	610 (33.7)	549 (30.6)	< 0.001
HTN	4374 (80.2)	1414 (76.4)	1456 (80.5)	1504 (83.8)	< 0.001
CS	407 (7.5)	137 (7.4)	135 (7.5)	135 (7.5)	0.991
MI	1460 (26.8)	494 (26.7)	486 (26.9)	480 (26.8)	0.992
HF	2320 (42.6)	803 (43.4)	742 (41.0)	775 (43.2)	0.279
DM	2345 (43.0)	485 (26.2)	734 (40.6)	1126 (62.8)	< 0.001
Drugs, n (%)					
Aspirin	4395 (80.6)	1498 (81.0)	1431 (79.1)	1466 (81.7)	0.133
Insulin	2947 (54.1)	774 (41.8)	950 (52.5)	1223 (68.2)	< 0.001
Statin	1177 (21.6)	359 (19.4)	394 (21.8)	424 (23.6)	0.008
ACEI/ARB	2140 (39.3)	702 (37.9)	737 (40.8)	701 (39.1)	0.215
Betablocker	4088 (75.0)	1392 (75.2)	1347 (74.5)	1349 (75.2)	0.847
Clinical outcomes, n (%)					
30-day mortality	409 (7.5)	112 (6.1)	132 (7.3)	165 (9.2)	0.001
365-day mortality	941 (17.3)	282 (15.2)	308 (17.0)	351 (19.6)	0.002

Data: Median (IQR). TyG: triglyceride glucose, SOFA: sequential organ failure assessment, Gcs: Glasgow Coma Scale, HR: heart rate, RR: respiratory rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, SpO2: oxyhemoglobin saturation, RBC: red blood cell, WBC: white blood cell, TG: triglyceride, TC: total cholesterol, LDL: low density lipoprotein, HDL: high density lipoprotein, Glu: glucose, HbA1c: glycosylated hemoglobin, AKF: acute kidney failure, AF: atrial fibrillation, CKD: chronic kidney disease, HTN: hypertension, CS: cardiogenic shock, MI: acute myocardial infarction, DM: diabetes mellitus, HF: heart failure, AECI/ARB: angiotensin converting enzyme inhibitors/angiotensin II receptor antagonists

fibrillation. The higher the TyG index of the patient, the higher the 30-day all-cause mortality rate (6.1% vs. 7.3% vs. 9.2%, $P=0.001$) and the 365-day all-cause mortality rate (15.2% vs. 17.0% vs. 19.6%, $P=0.002$).

Survival analysis

The K–M survival analysis was took on to compare patients' all-cause mortality who stratified by different TyG index. The upper TyG index group showed noticeably higher all-cause death rates for 30 and 365 days than

did the group with a lower TyG index. Furthermore, a notable disparity was observed in all-cause mortality across the three groups (log-rank $P = 0.0012$, log-rank $P = 0.0015$). The findings of the preceding analysis are presented in great detail in Fig. 2.

The associations between clinical outcomes and the TyG index

To further explore in detail the TyG index's autonomous influence on the prognosis for both short- and long-term survival for those with critical CAD, there were three Cox proportional hazard models in use. Specifically, in three models, as TyG index increased, the critical CAD patients' 30-day all-cause mortality gradually increased [Model 1: Ref. vs. 1.22 (0.95–1.57, $P=0.125$) vs. 1.55 (1.22–1.97, $P<0.001$)]. Model 2: Ref. vs. 1.32 (1.02–1.70, $P=0.031$) vs. 2.00 (1.57–2.55, $P<0.001$); Model 3: Ref. vs. 1.39 (1.07–1.79, $P=0.012$) vs. 2.02 (1.58–2.59, $P<0.001$)] (Table 2). The same findings were found for 365-day all-cause mortality. When comparing the all-cause mortality across 30 and 365 days, it was found that 30-day all-cause mortality hazard ratio was greater than 365-day all-cause mortality in any model, especially in the T3 group [Model 1: 1.55 (1.22–1.97, $P<0.001$) vs. 1.33 (1.14–1.55, $P<0.001$)); Model 2: 2.00 (1.57–2.55, $P<0.001$) vs. 1.67 (1.43–1.96, $P<0.001$); Model 3: 2.02 (1.58–2.59, $P<0.001$) vs. 1.64 (1.40–1.93, $P<0.001$)]. The results were statistically significant.

According to the RCS regression model, as the TyG index increased, the risk of 30-day and 365-day all-cause death increased linearly (P for nonlinearity = 0.2446 and P for nonlinearity = 0.552, respectively) (Fig. 3).

Subgroup analysis

With regard to 30-day all-cause mortality, there were differences in the impact of the TyG index with the hypertension, myocardial infarction, and statin subgroups. The TyG index shown a significant connection with 30-day all-cause mortality in the patient subgroups with combined hypertension, combined myocardial infarction, and no statin. There were not any notable variations among the patient subgroups without hypertension, without myocardial infarction or who were taking statins. However, no significant interactions were found (P interaction greater than 0.05). For 365-day all-cause mortality, the TyG index had different effects on hypertension, myocardial infarction, diabetes, and statin use. In the subgroups of patients with hypertension, with myocardial infarction, without diabetes mellitus, and not taking statins, there was a significant correlation between 365-day all-cause mortality risk and TyG index. In the subgroups without hypertension, without myocardial infarction, with diabetes mellitus, and with statins, there was no significant difference in the 365-day all-cause mortality risk. Interestingly, 365-day all-cause mortality appeared to be more accurately predicted by the TyG index among those who combined myocardial infarction

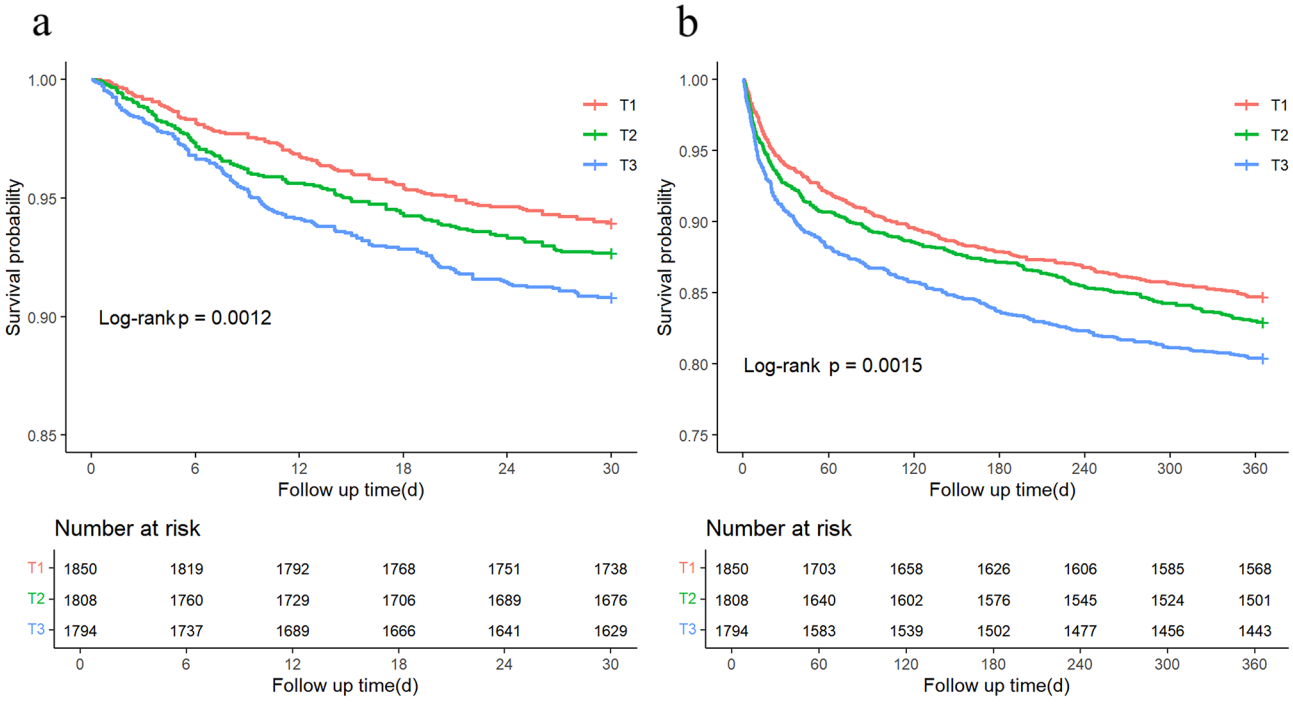

Fig. 2 KM survival analysis curves **a**: Comparison of all-cause mortality between groups at 30 days; **b**: Comparison of mortality between groups at 365 days

Table 2 Multivariate Cox proportional hazards modeling of 30- and 365-day all-cause mortality

Categories	TyG index		
	T1	T2	T3
30-day mortality			
Number of deaths (%)	112(27.4)	132(32.3)	165(40.3)
Model 1 HR (95% CI), *P*-value	Ref.	1.22 (0.95–1.57, $P=0.125$)	1.55 (1.22–1.97, $P<0.001$)
Model 2 HR (95% CI), *P*-value	Ref.	1.32 (1.02–1.70, $P=0.031$)	2.00 (1.57–2.55, $P<0.001$)
Model 3 HR (95% CI), *P*-value	Ref.	1.39 (1.07–1.79, $P=0.012$)	2.02 (1.58–2.59, $P<0.001$)
365-day mortality			
Number of deaths (%)	282(30.0)	308(32.7)	351(37.3)
Model 1 HR (95% CI), *P*-value	Ref.	1.13 (0.96–1.33, $P=0.135$)	1.33 (1.14–1.55, $P<0.001$)
Model 2 HR (95% CI), *P*-value	Ref.	1.21 (1.03–1.43, $P=0.019$)	1.67 (1.43–1.96, $P<0.001$)
Model 3 HR (95% CI), *P*-value	Ref.	1.27 (1.08–1.50, $P=0.004$)	1.64 (1.40–1.93, $P<0.001$)

Cox proportional hazard models were used to estimate HR and 95% CI.

Model 1 was unadjusted

Model 2 was adjusted for age and sex

Model 3 was adjusted for age, sex, HR, RR, SpO2, SOFA score, RBC, WBC, creatinine, AKI, AF, CS, MI, HF, aspirin, statin, and ACEI/ARB.

HR: hazard ratio, CI: confidence interval

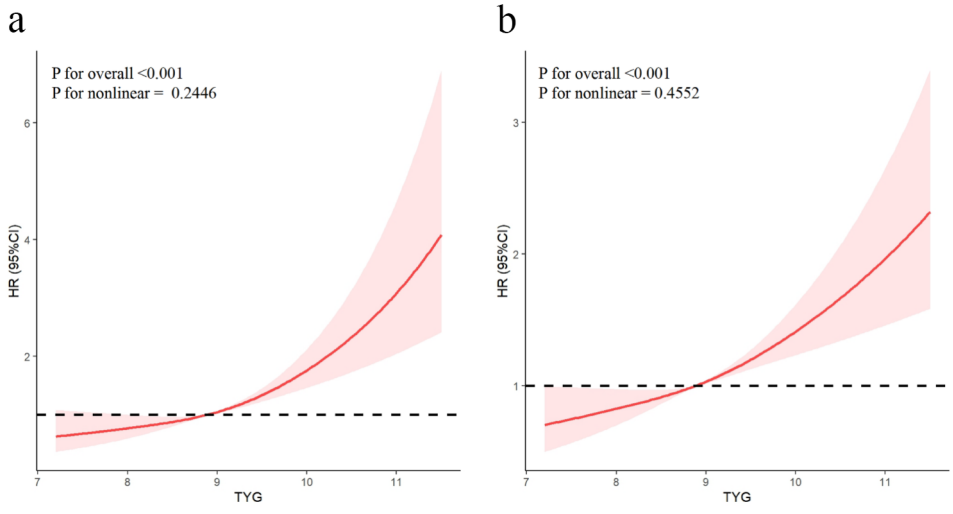

Fig. 3 RCS regression analysis of the TyG index and 30-day (**a**) and 365-day (**b**) all-cause mortality

than in patients without myocardial infarction [HR (95% CI) combined with myocardial infarction 1.33 (1.15, 1.54) vs. no myocardial infarction 1.07 (0.96, 1.2), *P* interaction = 0.016] (Fig. 4).

Discussion

This study represents the first evaluation of the connection between the clinical outcomes in the short and long term and the TyG index in a United States (US) cohort of critical CAD patients. The findings demonstrated that higher TyG index values were linked to greater long- and short-term all-cause death and had greater predictive power for short-term all-cause death. The same results were obtained following confounding factor adjustment. Furthermore, it has a significant linear relationship with both long- and short-term all-cause death according to the RCS regression analysis. According to the subgroup analyses, no significant interaction effect was found for short-term all-cause death. However, for long-term all-cause death, a significant interaction effect was found for the myocardial infarction subgroup.

Several investigations have proven the TyG index exists as a trustworthy substitute for IR. Not only does it have high sensitivity and specificity, but it also has the

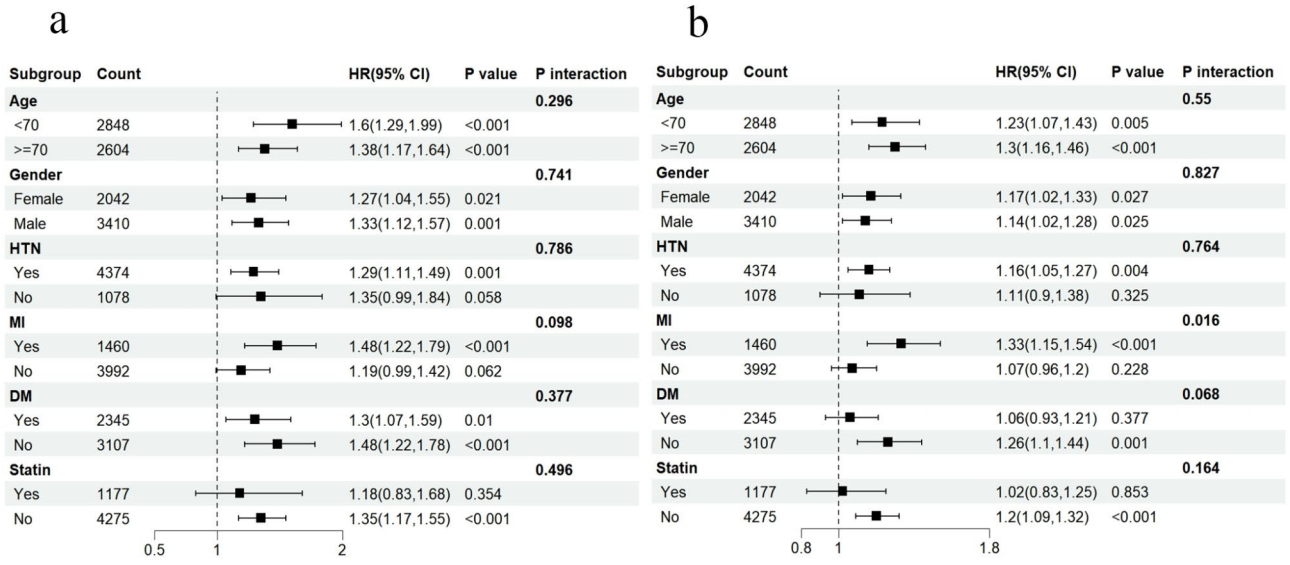

Fig. 4 Forest plot of subgroup analyses of the TyG index versus 30-day all-cause mortality (**a**) and 365-day all-cause mortality (**b**). HTN: hypertension; MI: myocardial infarction; DM: diabetes mellitus

following advantages: it is based on fasting glucose and triglyceride measurements; it is low cost; it is a routine clinical test; and it does not require serum insulin measurements. CAD risk in the general population is linked to the TyG index, according to earlier research [18], and is still relevant in patients without traditional risk factors [19]. In terms of predicting poor prognosis, Ma et al. first discovered that the TyG index can predict unfavourable cardiovascular events after ACS patients have undergone percutaneous coronary intervention (PCI) who have diabetes mellitus [20]. Numerous later research has indicated that TyG index has significant significance in predicting poor prognosis in patients with CAD [21, 22], including those with premature CAD [23]. These findings indicate it is an invaluable tool for CAD patients' risk stratification. The TyG index is valuable for forecasting the occurrence of severe CAD. Recurrent revascularization owing to restenosis from a drug-eluting stent (DES-ISR) or the progression of coronary lesions is a critical condition for patients with CAD and can seriously endanger their life. Individuals with an elevated TyG index in ACS have a greater likelihood of DES-ISR after PCI and are linked to a higher risk of DES-ISR [24]. In type 2 diabetic ACS patients, the greater the TyG index value, the more likely they are to have repeat revascularisation, and this index has a high predictive value for repeat revascularisation [25]. The associations between an increased TyG index and morbidity and death from other diseases in critically ill patients and in the general population have been investigated in many clinical studies. In one study, for those aged 65 years and older, a higher TyG index was discovered to be positively and independently connected to a greater danger of critical delirium, suggesting that the TyG index is a validated metabolic indicator for the cardiovascular and cerebral systems that facilitates risk categorization and management in high-risk elderly populations [26]. In-hospital mortality and severely altered mental status in individuals suffering from severe cerebrovascular illness are also predicted by the TyG index and may help to further identify and intervene in high-risk patients [27]. In studies of the general population, the TyG index has been shown to possess a U-shaped links that involves all causes and cardiovascular disease mortality in patients with metabolic syndrome [28]. In patients with intermediate-risk chronic coronary syndromes, those with elevated TyG values had significantly higher odds of cerebrovascular events, hospitalization for heart failure, nonfatal myocardial infarction, and noncardiac death [29]. There is a linkage of the TyG index and the possibility for getting new illnesses, such as chronic kidney disease, first stroke in elderly hypertensive patients and central obesity in older and middle-aged individuals [30–32]. Fluctuations in the TyG index were shown to be related to all-cause mortality during hospitalization and all-cause mortality within one year in individuals suffering from serious illnesses, and multiple TyG index measurements may be superior to a single measurement [33].

While the precise mechanism underneath the links of the TyG index with poor prognosis in CAD patients is unknown, this correlation may correspond with IR given that it is a valid IR surrogate marker. First, specifically impairs the insulin-stimulated phosphatidylinositol 3-kinase (PI3K) signalling pathway. In both humans and animals, preferential action by less impaired pathways, such as the pathway of vascular mitogen-activated

protein kinase (MAPK), occurs When there is a selective impairment of the PI3K pathway. However, compensatory hyperinsulinaemia may in turn activate the MAPK pathway, which has a deleterious effect by encouraging atherosclerosis and causing endothelial dysfunction in the vascular wall [34]. Second, the abnormal renin-angiotensin system activation caused by IR can lead to fluid retention, causing increased blood pressure as well as elevated cardiac workload [35]. In addition, metabolic changes caused by IR, such as chronic hyperglycaemia and dyslipidaemia, function in concert with increased blood pressure to further damage the cardiovascular system and can also cause oxidative stress and aggravate the reaction of inflammation, harm the role of endothelium and encourage the growth of cells of smooth muscle [4, 36]. Finally, IR can lead to an increase in platelet tissue factor (TF) synthesis, and increased TF synthesis is associated with a hypercoagulable state and an increased risk of thrombosis [37]. Overall, the potential mechanisms linking the TyG index to poor prognosis in CAD patients can be summarized as follows: (1) endothelial damage; (2) fluid retention and increased cardiac load; (3) metabolic abnormalities, oxidative stress, and pro-inflammatory responses; and (4) increased blood viscosity.

Comparison with and addition to other related studies. Zhang et al. were the first to report that in patients with severe CAD, the TyG index and in-hospital mortality were linearly correlated, regardless of whether the patients had myocardial infarction [15]. On this basis, the present study further revealed that in patients with critical CAD, the TyG index has a linear combination with both long- and short-term all-cause death and that having a myocardial infarction seemed to have greater predictive value for long-term all-cause death than not having one. This difference is due to both the variation in the percentage among myocardial infarction patients in the two studies (69.65% versus 26.7%) and the difference in the duration of follow-up. This discovering also illustrates that the TyG index might exist more effective in predicting outcomes for patients with more severe disease. According to Hao et al., the TyG index is nonlinearly in relation to long-term prognosis in individuals with CAD who have steady hemodynamics [38]. However, in patients with critical CAD, the present study revealed that it was linearly related to prognosis, which may be due to the different severities of CAD in the study groups, as the severity of IR is related to the severity of CAD [7]. Furthermore, in line with the results of two additional studies on critical illnesses, the TyG index appears to be a more accurate indicator of short-term all-cause mortality [39, 40]. This may be related to improvements in IR or decreases in the severity of the condition in subsequent treatments by health care professional. In summary, the TyG index shows a significant linear relations with all-cause mortality over the short and long terms in critical CAD patients and exhibits superior predictive ability in short-term. Clinicians need to improve their knowledge and understanding of this index and enhance their ability to apply the TyG index for early risk assessment and therapeutic intervention in clinical practice. Thus, individualized treatment plans can be formulated to improve treatment effects and reduce unnecessary waste of medical resources. For patients with high TyG index, condition monitoring and clinical care should be strengthened during hospitalization, and their vital signs and condition changes should be closely monitored, so that timely measures can be taken to prevent deterioration of the condition. Meanwhile, follow-up management should be strengthened after discharge. Patients should be instructed to continue to monitor their triglyceride and glucose levels at home, maintain a healthy lifestyle, and be retested on time in order to detect and manage potential problems in a timely manner and reduce the risk of long-term mortality.

Strengths and limitations

This is the initial investigation focused on assessing the TyG index's predictive capability in the short- and long-term outcome of those with critical CAD. This comprehensive analysis contributes to a comprehensive understanding of the predictive validity of the TyG index across time periods. However, this study is not without its shortcomings. First, this was a retrospective study, which does not allow the determination of causality. Second, despite the adjustment for sufficient variables and the implementation of rigorous statistical analyses, there may have been unmeasured confounders. Such as some oral medications that improve insulin resistance may affect the linear relationship between TyG and clinical outcomes. In addition, the study was conducted only with individuals in the U.S. population, and further research involving larger populations is necessary to confirm whether the results are applicable to other populations. Finally, in this research, only assessed the baseline TyG index and did not dynamically track the TyG index during hospitalization or subsequent multiple hospitalizations. Therefore, the prognostic impact of the TyG index's dynamic fluctuations remains to be investigated.

Conclusion

TyG index is a vital forecast tool in assessing short- and long-term all-cause mortality in those with critical CAD. In particular, it has shown higher validity in the prediction of short-term all-cause mortality. By monitoring this index, clinicians can better manage critical CAD patients' conditions, identify high-risk patients early, rationalize the allocation of medical resources, and provide timely

intervention and treatment, which can help reduce patient mortality.

Abbreviations

CAD	Coronary Artery Disease
IR	Insulin resistance
TyG	Triglyceride-glucose
ACS	Acute coronary syndrome
CVD	Cardiovascular disease
ICU	Intensive Care Unit
SQL	Structured query language
MIMIC-IV	Medical Information Mart for Intensive Care IV
RCS	Restricted Cubic Spline
PCI	Percutaneous Coronary Intervention
TF	Tissue Factor

Supplementary Information

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Supplementary Material 1

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Author contributions
HW wrote the main manuscript text and performed the data analysis. QF: data curation and creation of tables. SX: data analysis. XM and YL: study design. CK: prepared figures. RY: revised the manuscript. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Cardiovascular Medicine, The Second Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, China

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