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# Triglyceride-glucose index: a novel predictor of major adverse cardiovascular events and cerebrovascular events in patients with acute ST-segment elevation myocardial infarction

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## Abstract

**Introduction** Numerous studies have indicated the association of the triglyceride-glucose index (TyG) index with coronary artery disease, particularly myocardial infarction. However, limited mention exists regarding the predictive effects of major adverse cardiovascular events (MACE) and major adverse cardiac and cerebrovascular events (MACCE) in patients with ST-segment Elevation Myocardial Infarction (STEMI). This study aimed to investigate the predictive role of the TyG index on MACE and MACCE within 30 days in patients with STEMI.

**Methods** This study enrolled 586 patients with STEMI and conducted lipid, glucose, and myocardial biochemical testing. The TyG index was calculated; univariate analysis, multivariate analysis, and logistic regression analysis were employed to further investigate the correlation of the TyG index with MACE and MACCE. Subsequently, restricted cubic spline (RCS) analysis was conducted to determine whether they exhibit a linear correlation.

**Results** The study reported 105 MACCE patients. The results revealed a significant positive correlation between the TyG index and the occurrence of MACE and MACCE (odds ratio [OR] = 1.461, 95% confidence interval [CI] [1.091–1.956],  $p=0.011$  and OR = 1.427, 95%CI [1.064–1.914],  $p=0.017$ , respectively). In univariate and multivariate analysis, the TyG index remains correlated with MACE and MACCE even after adjusting for related variables. Subsequent RCS analysis, accounting for different factors such as age, white blood cell count, and N-terminal pro-B-type natriuretic peptide (NT-proBNP), indicated that the correlation of TyG index with MACE and MACCE remains linear ( $p$ -non-linear = 0.662,  $p$ -non-linear = 0.781, respectively).

**Conclusion** The TyG index effectively predicts MACE and MACCE in patients with STEMI within 30 days.

**Clinical trial number** Not applicable.

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**Keywords** Triglyceride-glucose index, ST elevation myocardial infarction, Major adverse cardiac events

## Introduction

The triglyceride-glucose (TyG) index, defined as the logarithm of the product of the fasting triglyceride level and one-half of the fasting blood glucose level, was initially introduced as a reliable and easily accessible alternative to the hyperinsulinemic-euglycemic clamp technique. It serves as a reproducible and credible surrogate marker for insulin resistance. Insulin resistance is a hallmark of various pathological conditions characterized by systemic inflammation, endothelial dysfunction, oxidative stress, and prothrombotic states [1–3]. Insulin resistance plays a pivotal role in the development of cardiovascular diseases. Insulin resistance, coupled with hyperinsulinemia, predisposes to vascular sclerosis, thereby increasing the risk of cardiovascular ailments [4]. A 13-year follow-up study demonstrated that metabolic syndrome, a condition closely linked to insulin resistance, is a significant risk factor for coronary heart disease (CHD) mortality, doubling the risk compared to those without metabolic syndrome [5]. Therefore, substantial interest is in exploring the potential association between the TyG index and cardiovascular diseases. Che et al., utilizing data from the UK Biobank, discovered that among 403,335 initially healthy participants, those with higher TyG values were more likely to develop subsequent cardiovascular diseases [6]. Similarly, Muhammad et al. observed that an elevated TyG index is associated with cardiovascular mortality and heart failure, with each unit increase in the TyG index correlating to an elevated risk of heart failure [7]. Remarkably, even among patients with rheumatoid arthritis, the TyG index remains predictive of cardiovascular disease occurrence, with its predictive capability enhanced when combined with rheumatoid factors [8]. The TyG index correlates with cardiovascular diseases and is strongly associated with myocardial infarction. Zhang et al. discovered a close correlation between the TyG index and adverse events in patients with acute myocardial infarction and diabetes [3]. Another study confirmed the predictive role of the TyG index in determining poor prognosis in patients with acute myocardial infarction [9]. However, the research cohorts of these investigations included patients with acute myocardial infarction accompanied by diabetes and acute non-ST-segment elevation myocardial infarction (STEMI), with less emphasis on patients specifically with acute STEMI. Studies on the TyG index in patients with STEMI have mainly concentrated on long-term mortality, with less attention given to short-term major adverse cardiovascular events (MACE), including cardiac death, non-fatal myocardial infarction and target-vessel revascularization, or major adverse cardiac and cerebrovascular events

(MACCE). However, these short-term events are critical factors influencing the immediate prognosis of patients with STEMI. Therefore, investigating the TyG index's role in predicting short-term MACE or MACCE in these critically ill patients could provide a novel prognostic indicator for individuals with acute STEMI.

This study examined the TyG index's predictive ability for MACE and MACCE events in patients with acute STEMI.

## Methods

### Study population

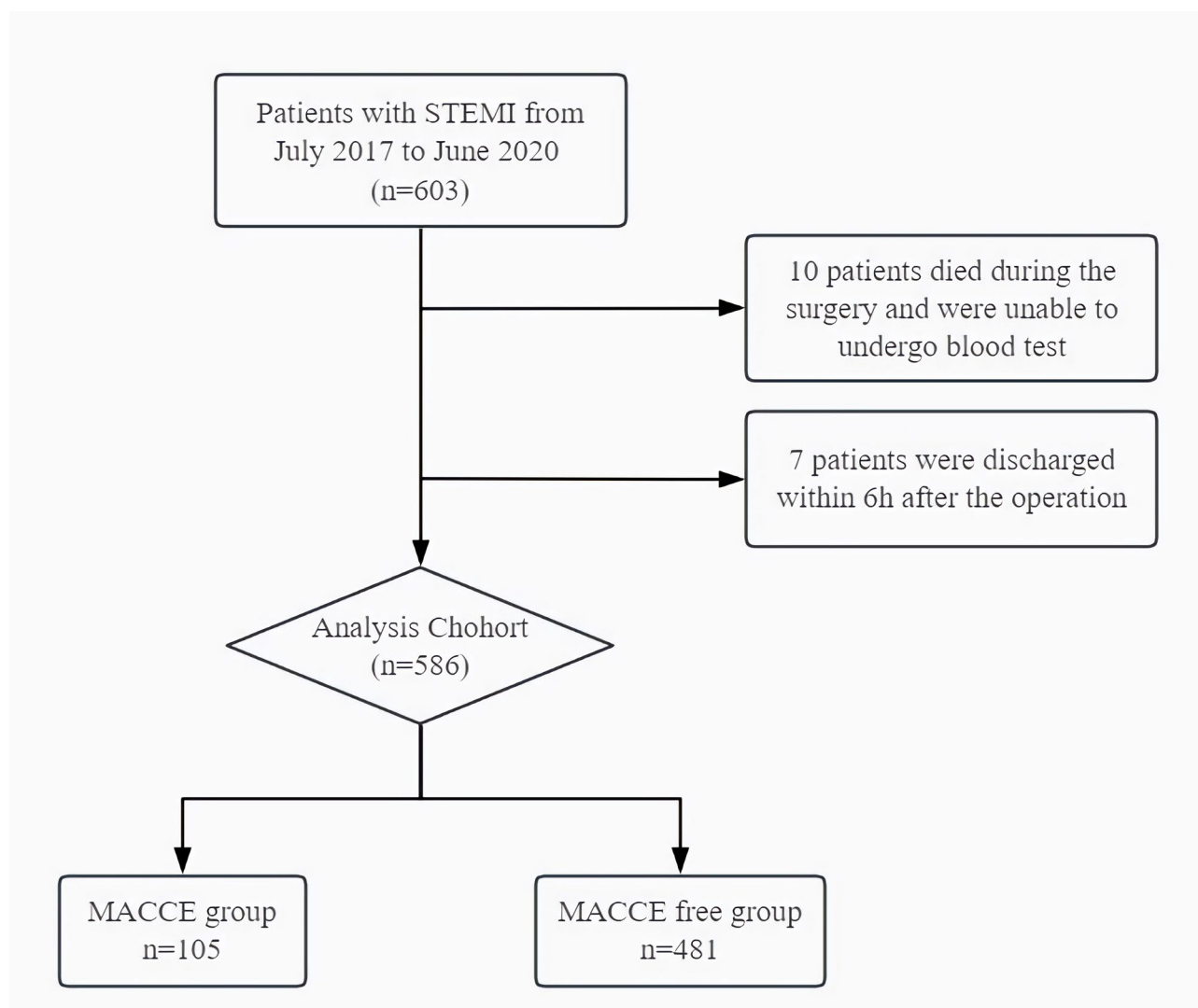
The study enrolled patients with acute STEMI who were admitted to The Affiliated Panyu Central Hospital of Guangzhou Medical University (formerly Guangzhou Panyu Central Hospital) between July 2017 and June 2020. All patients underwent emergency coronary angiography to identify acute coronary lesions, followed by primary percutaneous coronary intervention. Primary exclusion criteria excluded patients with normal coronary arteries on angiography, those diagnosed with acute STEMI unable to undergo surgical interventions due to shock, and patients with acute STEMI accompanied by cardiac mechanical complications or significant bleeding preventing antiplatelet therapy. STEMI diagnosis was based on established criteria: patients with acute chest pain (or chest pain-equivalent signs/symptoms) and persistent ST-segment elevation (or ST-segment elevation equivalents) on ECG; new ST elevation at the J-point in at least two contiguous leads:  $\geq 2.5$  mm in men aged  $< 40$  years,  $\geq 2$  mm in men aged  $\geq 40$  years, or  $\geq 1.5$  mm in women regardless of age in leads V2–V3 or  $\geq 1$  mm in the other leads or both (in the absence of left ventricular hypertrophy or left bundle branch block) [4]. The study received approval from the Ethics Committee of Guangzhou Panyu Central Hospital (approval number: PYRC-2023-378) and adhered to the principles outlined in the Helsinki Declaration of 2013 revised version.

### Blood sample collection

Fasting blood sample results obtained on the day after admission were collected for all enrolled patients in the study. Upon admission, the initial blood draw results were analyzed when patients required immediate blood tests, such as myocardial enzyme or troponin levels.

### Measurements

Baseline data for all enrolled patients, including age, gender, height, weight, medical history, and other relevant information, were extracted from medical records. Blood samples were analyzed using the testing instruments



**Fig. 1** Participant flow diagram illustrating the trial progression

available in our center's central laboratory. The TyG index was calculated using the following formula:  $\ln [\text{fasting triglyceride concentration (mg/dL)} \times \text{fasting plasma glucose concentration (mg/dL)} / 2]$  [10].

#### Endpoints and follow-up

The endpoint of this study refers to the incidence of MACE and MACCE. Follow-up encompasses 30 days after the onset of acute myocardial infarction symptoms. Follow-up was conducted through telephone interviews, outpatient visits, or hospital visits. The primary objective of the follow-up was to gather information regarding the occurrence of the previously mentioned adverse events from either the patient or their family members and to collect relevant event data from outpatient and inpatient medical records. The physicians conducting the follow-up were not privy to the surgical details, while the

medical professionals reporting the events were unaware of the patients' surgical circumstances.

#### Statistical analysis

Baseline blood test results were presented as Median (First Quartile, Third Quartile). Group comparisons were performed using Kruskal-Wallis H Tests, Pearson's chi-squared test and Fisher exact test. Logistic regression analysis, including univariate and multivariate analysis, was employed to assess the correlations. In various models, restricted cubic splines were applied to evaluate potential nonlinear associations between the TyG index and MACE or MACCE. Statistical analyses were primarily conducted using IBM SPSS (Version 27.0) software. R Statistical Software (<http://www.R-project.org>, The R Foundation) was utilized for restricted cubic splines statistical analysis. The statistical significance level was set at  $p < 0.05$ .

**Table 1** Logistic regression analysis of TyG index for MACE and MACCE in patients with acute ST-segment elevation myocardial infarction

Categories	Univariate	Multivariate		
	OR (95%CI), <i>P</i>	Model 1 OR (95%CI), <i>P</i>	Model 2 OR (95%CI), <i>P</i>	Model 3 OR (95%CI), <i>P</i>
<b>MACE</b>				
Continuous variable per 1 unit	1.461 (1.091–1.956), <b>0.011</b>	1.916(1.381,2.658), <b>0.000</b>	1.686(1.195,2.378), <b>0.003</b>	1.545(1.057,2.259), <b>0.025</b>
Quartiles				
Quartile 1	Reference	Reference	Reference	Reference
Quartile 2	1.200(0.635,2.270), 0.574	1.285(0.665,2.484), 0.455	1.054(0.525,2.117), 0.882	0.827(0.391,1.752), 0.621
Quartile 3	1.181(0.629,2.219), 0.605	1.539(0.792,2.988), 0.203	1.161(0.572,2.354), 0.697	1.000(0.476,2.103), 0.999
Quartile 4	2.021(1.116,3.659) <b>0.020</b>	2.794(1.473,5.300) <b>0.002</b>	2.191(1.120,4.285) <b>0.022</b>	1.728(0.840,3.556) 0.137
<b>MACCE</b>				
Continuous variable per 1 unit	1.427 (1.064–1.914), <b>0.017</b>	1.838(1.324,2.552), <b>0.000</b>	1.611(1.141,2.276), <b>0.007</b>	1.459(0.998,2.132) 0.051
Quartiles				
Quartile 1	Reference	Reference	Reference	Reference
Quartile 2	1.137(0.605,2.136), 0.690	1.208(0.630,2.318), 0.570	0.982(0.492,1.962), 0.959	0.763(0.363,1.601), 0.474
Quartile 3	0.961(0.507,1.824), 0.904	1.215(0.622,2.376), 0.569	0.875(0.425,1.805), 0.719	0.746(0.350,1.587), 0.446
Quartile 4	1.913(1.064,3.441) <b>0.030</b>	2.582(1.372,4.857) <b>0.003</b>	2.018(1.039,3.922), <b>0.038</b>	1.578(0.775,3.215) 0.209

\*Statistically significant

Model 1: adjusted for Age, Gender, SBP

Model 2: adjusted for Age, Gender, SBP, DBP, WBC, NT-proBNP

Model 3: adjusted for Age, Gender, SBP, DBP, WBC, NT-proBNP, Creatinine, ALB, LVEF, Diabetes, Hypertension

## Results

A total of 603 patients with acute STEMI were included in the study. Among them, ten patients died intraoperatively and were consequently unable to undergo blood tests. Seven patients were discharged within 6 h after the operation, preventing them from completing blood tests. The final analysis included 586 patients (Fig. 1). These individuals were followed up for 30 days from the onset of symptoms, and any observed events during this period were promptly documented. Subsequently, the patients were categorized into two groups based on the occurrence of MACCE. The MACCE group comprised 105 patients, while the MACCE-free group included 481 patients. Table S1 (Supplemental Material) presents the baseline characteristics of these two groups. The baseline data revealed that patients in the MACCE group were substantially older than those in the MACCE-free group. Conversely, individuals in the MACCE-free group exhibited significantly higher blood pressure and lower heart rate than those in the MACCE group. Blood test results demonstrated significantly elevated levels of myocardial biochemical markers (such as troponin I, creatine kinase-MB (CK-MB), CK, and natriuretic peptide) in the MACCE group compared to the MACCE-free group.

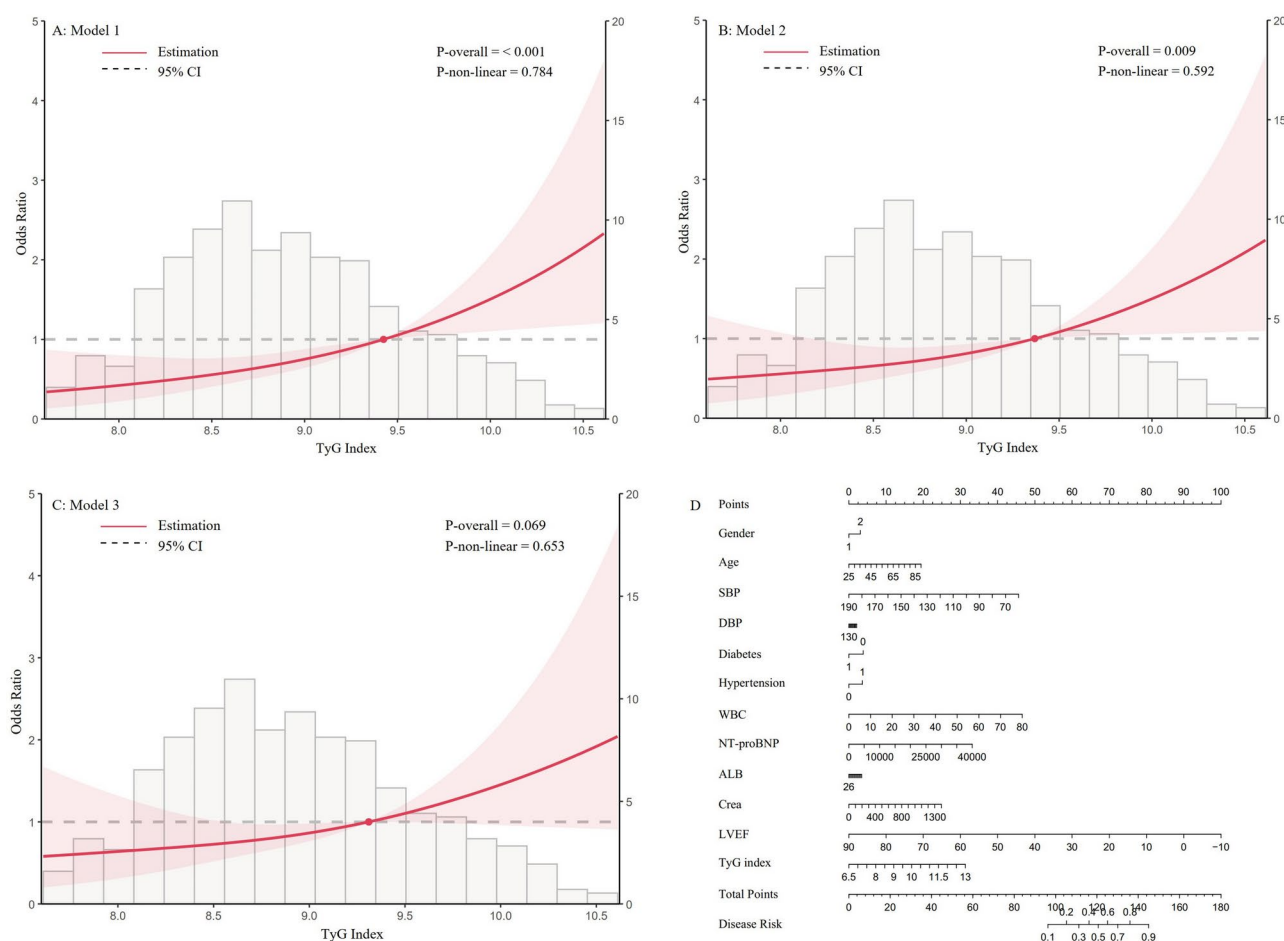
Moreover, indicators reflecting liver and kidney function, such as creatinine and transaminase levels, were significantly higher in the MACCE group than in the MACCE-free group. Regarding specific indices, the TyG index exhibited a significant difference between the two groups, with the MACCE group demonstrating a higher TyG index than the MACCE-free group ( $p=0.046$ ).

Univariate logistic regression was conducted to assess the relationship between baseline variables and both MACE and MACCE. The TyG index positively correlated with MACE and MACCE (odds ratio [OR]: 1.461, 95% confidence interval [CI] [1.091–1.956],  $p=0.011$  and OR: 1.427, 95%CI [1.064–1.914],  $p=0.017$ , respectively) (Table S2). Meanwhile, correlations were observed between patients' age, blood pressure, heart rate levels, and MACE and MACCE. Markers reflecting inflammation, such as white blood cell count (WBC) and C-reactive protein (CRP), were associated with these events. Furthermore, indicators reflecting myocardial injury area, cardiac function, and liver and kidney function, such as CK-MB, N-terminal pro-B-type natriuretic peptide, serum albumin (ALB), and creatinine, were all correlated with MACE and MACCE (all  $p<0.05$ ) (Table S2). When adjusted for relevant factors such as age, gender, blood

pressure, WBC, NT-proBNP, creatinine, albumin, ejection fraction, diabetes, and hypertension, the TyG index remained significantly correlated with MACE in patients with STEMI (Model 3, OR: 1.545, 95% CI [1.057–2.259],  $p=0.025$ ). With fewer adjustment factors (Model 1,2), the correlation (Table 1) was more pronounced. Furthermore, the TyG index correlated with MACCE in patients with STEMI (Table 1, Model 1 OR: 1.838, 95%CI [1.324–2.552],  $p<0.001$ , Model 2 OR: 1.611, 95%CI [1.141–2.276],  $p=0.007$  and Model 3 OR: 1.459, 95%CI [0.998–2.132],  $p=0.051$ , respectively). Intriguingly, when we categorized participants into quartiles based on their TyG index and designated the lowest quartile as the reference group, our analysis revealed a consistent and dose-dependent association between increasing TyG index levels and the risk of MACE and MACCE in both Model 1 (Table 1MACE, Q4 vs. Q1: OR, 2.794, 95%CI [1.473–5.300],  $p=0.002$ ; Table 1MACCE, Q4 vs. Q1:

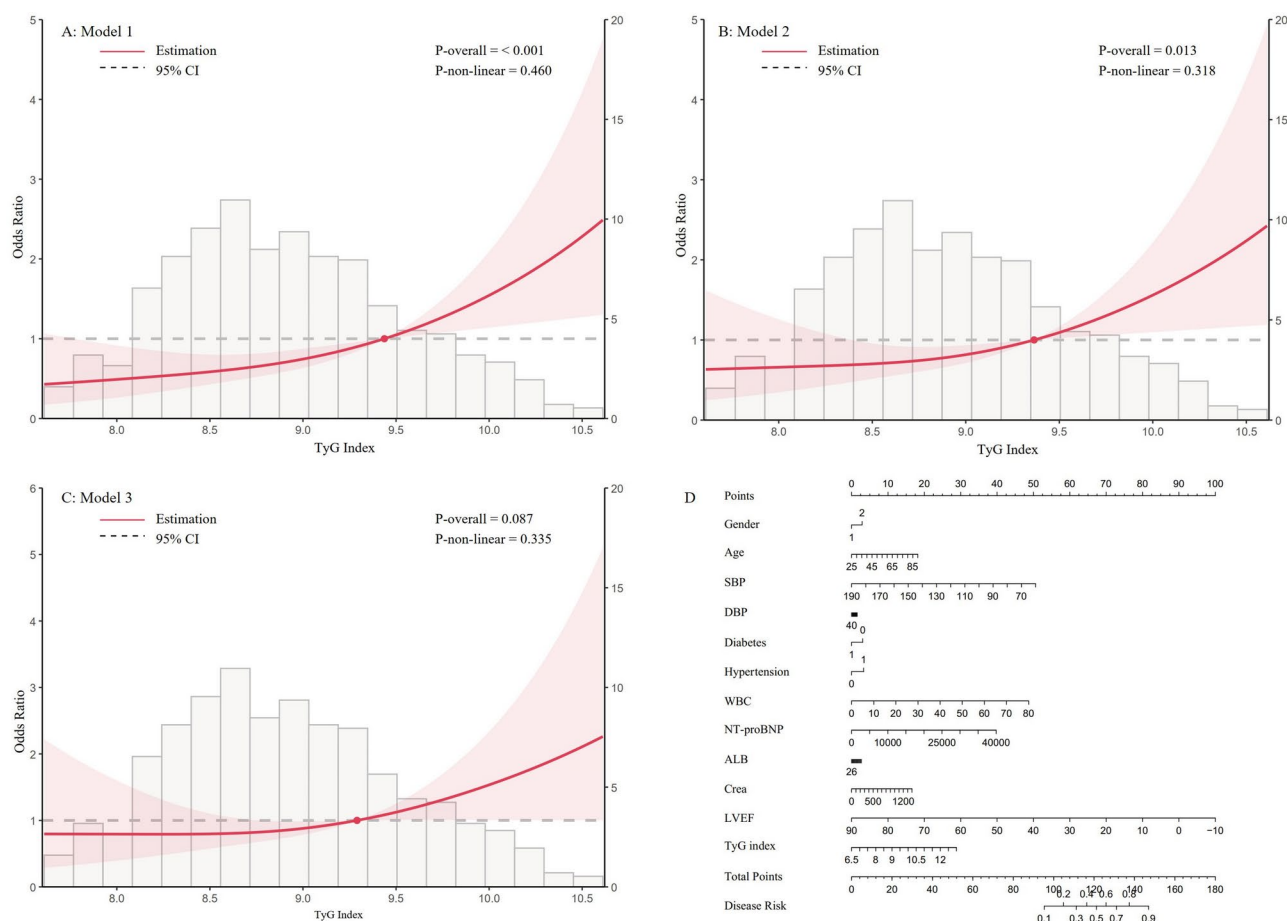
OR, 2.582, 95%CI [1.372–4.857],  $p=0.003$ ) and Model 2 (Table 1MACE, Q4 vs. Q1: OR, 2.582, 95%CI [1.120–4.285],  $p=0.022$ ; Table 1MACCE, Q4 vs. Q1: OR, 2.018, 95%CI [1.039–3.922],  $p=0.038$ ). Specifically, higher TyG quartiles demonstrated a progressive escalation in risk, underscoring a graded relationship. However, this pattern was no longer evident in Model 3 (Table 1MACE, Q4 vs. Q1: OR, 1.728,  $p=0.137$ ; Table 1MACCE, Q4 vs. Q1: OR, 1.578,  $p=0.209$ ), suggesting that adjustments for additional covariates may attenuate or nullify this association.

To further investigate whether the correlation of the TyG index with MACE and MACCE follows a linear pattern, analyses were conducted using restricted cubic spline curves. Model 3 showed no significant association between the TyG index and MACE ( $p=0.069$ , P-non-linear=0.653, Fig. 2C). However, in Models 1 and 2, the TyG index exhibited a linear correlation with the incidence of



**Fig. 2** Restricted cubic spline analysis and nomogram depicting the relationship between the TyG index and MACE. **A** corresponds to Table 1, Model 1, with adjustments for Age, Gender, SBP. **B** corresponds to Table 1, Model 2, with adjustments for Age, Gender, SBP, DBP, WBC, NT-proBNP. **C** corresponds to Table 1, Model 3, with adjustments for Age, Gender, SBP, DBP, WBC, NT-proBNP, creatinine, ALB, LVEF, and the presence of diabetes and hypertension. **D** represents the nomogram derived from the logistic regression analysis of the TyG index and MACE. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; NT-proBNP, N-terminal pro-brain natriuretic peptide; ALB, serum albumin; LVEF, left ventricular fraction; MACE, major adverse cardiovascular event; TyG index, triglyceride-glucose index





**Fig. 3** Restricted cubic spline analysis and nomogram illustrating the relationship between the TyG index and MACCE. **A** corresponds to Table 1, Model 1, with adjustments for Age, Gender, SBP. **B** corresponds to Table 1, Model 2, with adjustments for Age, Gender, SBP, DBP, WBC, NT-proBNP. **C** corresponds to Table 1, Model 3, with adjustments for Age, Gender, SBP, DBP, WBC, NT-proBNP, creatinine, ALB, LVEF, and the presence of diabetes and hypertension. **D** represents the nomogram derived from the logistic regression analysis of the TyG index and MACCE

MACE ( $p < 0.001$  and  $p = 0.009$ , Fig. 2A and B) rather than a nonlinear correlation ( $p\text{-non-linear} = 0.784$ ,  $p\text{-non-linear} = 0.592$ , respectively). Similarly, similar results were obtained when further exploring the correlation between the TyG index and MACCE. In Model 3, there was no association between the TyG index and MACCE, whereas in Model 1 and 2, the TyG index showed a linear correlation with MACCE (Fig. 3A, B, & C). A nomogram was developed to predict MACE or MACCE based on the model to enhance the model's usability. Each variable was assigned a score, calculated by summing all the individual scores (Figs. 2D and 3D).

## Discussion

This study observed a considerable association of the TyG index with MACE and MACCE in patients with STEMI, identifying it as an independent prognostic indicator. The TyG index was positively correlated with the WBC, hemoglobin (HGB), CK-MB, CK, ALB, and creatinine while negatively associated with age and left ventricular

ejection fraction (LVEF). Models incorporating the TyG index were evaluated for clinical application using RCS analysis.

The TyG index has been closely associated with atherosclerosis [11], demonstrating its ability to predict the short-term prognosis of patients with STEMI and the probability of myocardial infarction in the general population [12]. Moreover, it has been associated with quantitative flow ratio (QFR) and synergy between PCI with Taxus and cardiac surgery (SYNTAX) scores in patients with myocardial infarction [13]. Consequently, the TyG index may serve as a prognostic indicator for patients with myocardial infarction, irrespective of coronary artery occlusion [14] or diabetic status [15, 16]. Our study revealed an association of the TyG index with short-term MACE or MACCE in patients with STEMI, confirming its crucial role in the prognosis of atherosclerosis patients (Table S1-S2, Figs. 2 and 3). These findings provide clinicians with a tool for predicting the prognosis of patients with STEMI.

The ability of the TyG index to reflect the prognosis of coronary heart disease primarily stems from its role as a surrogate marker for insulin resistance. Insulin resistance is a fundamental clinical characteristic of severe metabolic syndrome and indicates a pathological state associated with systemic inflammation, endothelial dysfunction, oxidative stress, and a prothrombotic state [1, 2]. Furthermore, cytokines released post-myocardial infarction could induce hyperglycemia, leading to post-infarction insulin resistance, a recognized risk factor for post-infarction complications [17]. This mechanism could trigger oxidative stress, aggravate inflammatory responses, enhance foam cell formation, impair endothelial function, and promote smooth muscle cell proliferation [18]; it could increase sympathetic nervous system excitability and renal sodium retention, elevating cardiac workload and impacting prognosis [19]. Not all insulin resistance markers effectively predict adverse cardiovascular events. The homeostasis model assessment (HOMA-IR), calculated as (fasting insulin [mU/mL] × FPG [mmol/L])/22.5, has recently been shown to lack correlation with thrombus burden in STEMI patients. In univariate analysis, HOMA-IR was associated with higher thrombus burden, but in multivariate analysis, adjusting for confounders such as lipid profiles, uric acid, and renal function, this relationship became insignificant ( $p=0.112$ ) [20]. Given that thrombus burden is a critical determinant of surgical outcomes and prognosis in STEMI, HOMA-IR may not predict patient prognosis. This discrepancy may arise from three factors: (1) the formula excludes lipid levels, limiting its accuracy in assessing coronary artery conditions; (2) it may poorly reflect insulin resistance in specific populations, such as adolescents [21], Han Chinese women with polycystic ovary syndrome [22], and African-American or European individuals [23]; (3) Bland-Altman analysis reveals significant proportional biases in STEMI patients [24]. Thus, not all insulin resistance markers are equally effective in predicting STEMI prognosis, with the TyG index likely playing a unique role. However, further studies are needed to validate this hypothesis. While numerous studies have confirmed the impact of the TyG index on the prognosis of patients with coronary heart disease, most have focused on long-term effects. However, MACE and MACCE predominantly manifest in the short term following disease onset [25]. Therefore, this study emphasizes the short-term occurrence of MACE or MACCE, which aligns more closely with clinical priorities.

This study has several limitations. Firstly, it was a single-center clinical study with a relatively small sample size. Moreover, the lack of a long-term follow-up period poses a restriction. Future research could involve larger sample sizes and multicenter studies with extended follow-up periods.

In summary, the TyG index has demonstrated predictive value for short-term MACE or MACCE in patients with STEMI, and its value is linearly correlated with the occurrence of these events. Further research is warranted to determine whether reducing the TyG index could decrease the incidence of cardiovascular events.

### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12872-025-04801-w>.

Supplementary Material 1

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### Author contributions

Ruibin Wei, Qiang Xie and Jianhao Li led the design and development of the project. Ruibin Wei was responsible for drafting, revising, and refining the manuscript. Bingquan Chen and Dayu Wang collected relevant patient data. Jian Hou performed statistical analyses, derived the results, and generated the corresponding figures. Yingqing Feng oversaw overall coordination and served as a consultant, addressing challenges encountered during the study.

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### Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

#### Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Guangzhou Panyu Central Hospital (Date: November 21, 2023 / No. PYRC-2023-378). Written informed consent was obtained from individual or guardian participants.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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