Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome

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Abstract

Background: The triglyceride-glucose index (TyG index) has been regarded as a reliable alternative marker of insulin resistance and an independent predictor of cardiovascular outcomes. Whether the TyG index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome (ACS) remains uncertain. The aim of this study was to investigate the prognostic value of the TyG index in patients with diabetes and ACS.

Methods: A total of 2531 consecutive patients with diabetes who underwent coronary angiography for ACS were enrolled in this study. Patients were divided into tertiles according to their TyG index. The primary outcomes included the occurrence of major adverse cardiovascular events (MACEs), defined as all-cause death, non-fatal myocardial infarction and non-fatal stroke. The TyG index was calculated as the ln (fasting triglyceride level [mg/dL] × fasting glucose level [mg/dL]/2).

Results: The incidence of MACE increased with TyG index tertiles at a 3-year follow-up. The Kaplan–Meier curves showed significant differences in event-free survival rates among TyG index tertiles (P = 0.005). Multivariate Cox hazards regression analysis revealed that the TyG index was an independent predictor of MACE (95% CI 1.201–1.746; P < 0.001). The optimal TyG index cut-off for predicting MACE was 9.323 (sensitivity 46.0%; specificity 63.6%; area under the curve 0.560; P = 0.001). Furthermore, adding the TyG index to the prognostic model for MACE improved the C-statistic value (P = 0.010), the integrated discrimination improvement value (P = 0.001) and the net reclassification improvement value (P = 0.019).

Conclusions: The TyG index predicts future MACE in patients with diabetes and ACS independently of known cardiovascular risk factors, suggesting that the TyG index may be a useful marker for risk stratification and prognosis in patients with diabetes and ACS.

Keywords: Triglyceride-glucose index, Cardiovascular events, Diabetes, Acute coronary syndrome

Background

Diabetes is one of the major risk factors for coronary artery disease (CAD) [1]. Up to 37% of patients presenting with acute coronary syndrome (ACS) suffer from diabetes mellitus in China [2]. Compared with those without diabetes, patients with diabetes and ACS remain at higher risk for recurrent ischemic cardiovascular events (CVEs) despite optimal treatment according to the current guidelines [2–4]. Therefore, it is crucial to identify patients at a high risk of developing future CVEs so that intense treatment can be provided. The identification of rapidly available and reliable markers may have great clinical significance in optimizing the risk stratification of recurrent cardiovascular risk.
The triglyceride-glucose index (TyG index), which is calculated from fasting glucose and triglycerides, has been proposed as a reliable marker of insulin resistance (IR) in clinical practice [5, 6]. The TyG index showed better performance for assessing IR than the homeostasis model assessment of IR (HOMA-IR) [7, 8]. Several studies have found a positive association between the TyG index and cardiovascular risk, including systematic CAD, carotid atherosclerosis, hypertension, metabolic syndrome, arterial stiffness and coronary artery calcification [9–15]. Furthermore, recent data suggest the TyG index could provide significant prognostic information in patients with established CAD [16–19]. The TyG index is associated with not only the incidence of cardiovascular disease (CVD) but also the development of Type 2 diabetes (T2DM) [6, 20–24]. Taken together, these results suggest that it may be plausible to use the TyG index as a predictor of future cardiovascular risk in patients with diabetes and CAD.

A previous study of patients with diabetes and stable CAD demonstrated that the TyG index was a useful marker for predicting clinical outcomes [19]. Another recent study found that the TyG index may be a valuable predictor of adverse cardiovascular outcomes after percutaneous coronary intervention (PCI) in patients with diabetes and ACS [25]. To date, no relevant study has focused on the impact of the TyG index on MACE in patients with diabetes and ACS who underwent non-invasive or invasive (PCI or CABG) treatment. To address the knowledge gap, this study aimed to specifically investigate whether the TyG index has a prognostic value for major adverse cardiovascular events (MACE) in patients with diabetes and ACS who received different treatments.

**Methods**

**Study population**

This study was a single-center, retrospective, observational cohort study. From January 2016 to December 2016, 3428 consecutive patients with T2DM and ACS who were admitted to Tianjin Chest Hospital for coronary angiography were enrolled in this study. We included patients with a history of T2DM who were currently using insulin or hypoglycemic medications, or those with a fasting blood glucose (FBG) ≥ 7.0 mmol/L or a 2-h plasma glucose level on their oral glucose tolerance test (OGTT) ≥ 11.1 mmol/L. Patients with diabetic symptoms underwent the OGTT test during this hospitalization. ACS was defined as including either unstable angina pectoris (UAP), non-ST-segment elevation myocardial infarction (NSTEMI), or ST-segment elevation myocardial infarction (STEMI). Those with severe valvular disease or congenital heart disease requiring cardiac surgery (n = 42), acute infection (n = 76), malignancy (n = 14), severe hepatic dysfunction (n = 18), severe kidney dysfunction (n = 172), nutritional derangements (n = 8), or other severe medical illnesses, or those lacking complete clinical data (n = 285) were excluded. A total of 2815 patients participated in the research. Patients were followed up from January 2019 to December 2019 by telephone or outpatient clinical visit, and 2531 (89.9%) patients completed the 3-year clinical follow-up. The patients were divided into tertiles according to their admission TyG index levels: tertile 1 (n = 844, TyG index ≤ 8.848), tertile 2 (n = 843, 8.849 ≤ TyG index ≤ 9.382) and tertile 3 (n = 844, TyG index ≥ 9.383). This study was approved by the local research ethics committee and strictly adhered to the Declaration of Helsinki. Given the retrospective nature of the present research, no informed consent was required.

**Data collection and definitions**

Clinical data were collected from all of the medical records by trained clinicians who were blinded to the purpose of the study. The data included age, gender, duration of diabetes, whether diabetes had been newly diagnosed, smoking history, history of hypertension, family history of CAD, previous myocardial infarction (MI), previous percutaneous coronary intervention (PCI), previous coronary artery bypass graft (CABG), previous stroke, height, weight, systolic and diastolic blood pressure (SBP and DBP), heart rate (HR), left ventricle ejection fraction (LVEF) and medication at discharge. Peripheral venous blood samples were collected early in the morning after an overnight fast on admission and analyzed shortly after sampling. Hemoglobin, FBG, hemoglobin A1c (HbA1c), total cholesterol (TC), triglycerides (TG), low-density lipoprotein-C (LDL-C), high-density lipoprotein-C (HDL-C), serum creatinine, serum uric acid, high-sensitivity C-reactive protein (hs-CRP) and N-terminal proB-type natriuretic peptide (NT-proBNP) levels were analyzed. Renal function was assessed using the baseline estimated glomerular filtration rate (eGFR). Body mass index (BMI) was defined as weight (kg)/height (m²). All of the patients underwent coronary angiography during this hospitalization. Significant stenosis was defined as ≥ 50% diameter stenosis in at least one major coronary artery and multivessel disease was defined as ≥ 2 vessels with significant stenosis as observed during angiography. The Global Registry of Acute Coronary Events (GRACE) risk score was calculated for each patient according to eight variables on admission, including age, SBP, HR, presence of cardiac arrest during presentation, Killip class, ST-segment deviation, serum creatinine and positive cardiac biomarkers [26]. The TyG index was calculated as the ln (fasting TG level [mg/dL] × FBG level [mg/dL]/2).
Endpoints
The primary endpoint was new-onset major adverse cardiovascular event (MACE), defined as the composite of all-cause death, non-fatal MI and non-fatal stroke. All-cause death referred to death attributed to cardiovascular or non-cardiovascular causes. The secondary endpoints included all-cause death, non-fatal MI and non-fatal stroke.

Statistical analysis
Continuous variables were expressed as mean±standard deviation when normally distributed. The GRACE score, TG, hs-CRP and NT-proBNP were not normally distributed; therefore, those variables were expressed as medians with interquartile ranges. Categorical variables were presented as frequencies. Baseline demographic characteristics, clinical presentation, laboratory findings, extent of CAD, revascularization and medication data were compared between groups by analysis of variance or Kruskal–Wallis tests for continuous variables, and with a Chi square test or Fisher’s exact test for categorical variables. Multivariate linear regression analyses based on the stepwise method were performed to reveal the factors associated with the TyG index. The Kaplan–Meier event-free survival curves associated with TyG index tertiles were compared using log-rank tests. A multivariate stepwise Cox proportional hazards regression analysis with entry/stay criteria of 0.1/0.1 was constructed to identify independent predictors of MACE. The possible factors included age, sex, duration of diabetes, smoking history, hypertension, previous MI, previous PCI, previous CABG, previous stroke, BMI, AMI, LVEF, left main disease, multi-vessel disease, revascularization, HbA1c, LDL-C, uric acid, hs-CRP, NT-proBNP, eGFR, statin use, insulin use and TyG index. The area under the receiver operating characteristic (ROC) curves was used to indicate the predictive value of the TyG index for MACE. To evaluate whether an increased TyG index had incremental predictive value for MACE, C-statistics, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were compared between models. A two-sided analysis with a P value <0.05 was considered significant. All of the analyses were performed using SPSS version 20.0 (IBM Corp, Armonk, NY, USA) and SAS version 9.1.3 (Cary, NC, USA).

Results
Baseline characteristics of patients
Baseline clinical characteristics and clinical events data were fully recorded for 2531 patients (89.9%). Patient characteristics are listed in Table 1. The study patients had an average age of 66.3±6.8 years and 1415 (55.9%) patients were male. Patients were divided into tertiles according to the admission TyG index levels (tertile 1: n=844, TyG index ≤ 8.848; tertile 2: n=843, 8.849 ≤ TyG index ≤ 9.382; and tertile 3: n=844, TyG index ≥ 9.383). The mean levels of TyG index of the three groups were 8.467±0.293, 9.114±0.152 and 9.841±0.403, respectively. There were significant differences (P<0.05) among the three groups in terms of duration of diabetes, previous PCI, previous stroke, BMI, SBP, DBP, HR, GRACE score, multi-vessel disease, treatment strategy, FBG, HbA1c, HDL-C, Uric acid, NT-proBNP, eGFR and the use of medications at discharge including clopidogrel or ticagrelor, β-blocker, angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin II receptor blocker (ARB) and insulin, and no significant difference was found in the other indicators. The associations between the TyG index and cardiovascular risk factors were examined using linear regression analysis. As shown in Table 2, TyG index levels were positively associated with BMI, hemoglobin A1c (HbA1c) and uric acid and negatively associated with age, male sex, HDL-C and eGFR in the multivariate linear regression analysis (P<0.05)

TyG index and cardiovascular events
During the 3-year follow-up, 289 (11.4%) MACEs were recorded, including 142 (49.1%) all-cause death, 101 (34.9%) non-fatal MI and 46 (16.0%) non-fatal stroke. Table 3 shows the 3-year event rate and Cox proportional hazard analysis for all-cause death, non-fatal MI, non-fatal stroke and MACE. Rates of all-cause death, non-fatal MI, non-fatal stroke and MACE increased progressively with a higher TyG index. On unadjusted Cox modeling, only the rate of MACE rose significantly with elevated TyG index levels (P=0.005 for trend). Multivariate-adjusted hazard ratio (HR) also increased with rising TyG index levels after adjusting for age, male, smoking history, previous MI, previous CABG, BMI, AMI, LVEF, left main disease, multi-vessel disease, HbA1c, hs-CRP, statin use and insulin use (P=0.019 for the trend). As shown in Fig. 1, Kaplan–Meier survival analysis showed that the cumulative incidence of MACE increased with higher tertiles of the TyG index (log-rank test, P=0.005).

Univariate and multivariate Cox proportional hazards regression analyses and predictors for MACE are presented in Table 4. In the univariate analysis, the criteria associated with MACE occurrence were TyG index, age, previous MI, BMI, AMI, LVEF, left main disease, multi-vessel disease, hs-CRP and statin use. After adjusting for BMI and other confounding factors, multivariate Cox proportional hazards regression analysis showed that TyG index, age, previous MI, LVEF, hs-CRP and statin use independently predicted the occurrence of MACE in patients with diabetes and ACS.
| Variable                               | Tertile 1 (n = 844) | Tertile 2 (n = 843) | Tertile 3 (n = 844) | P value |
|----------------------------------------|---------------------|---------------------|---------------------|---------|
| TyG index                              | 8.467 ± 0.293       | 9.114 ± 0.152       | 9.841 ± 0.403       | <0.001  |
| Age, years                             | 67.2 ± 6.9          | 66.2 ± 6.7          | 65.6 ± 6.8          | <0.001  |
| Male                                   | 519 (61.5)          | 446 (52.9)          | 450 (53.3)          | <0.001  |
| Duration of diabetes, years            | 10.2 ± 8.0          | 9.3 ± 7.3           | 10.0 ± 7.7          | 0.030   |
| Newly diagnosed diabetes               | 47 (5.6)            | 53 (6.3)            | 57 (6.8)            | 0.596   |
| Smoker                                 | 338 (40.0)          | 323 (38.3)          | 338 (40.4)          | 0.703   |
| Hypertension                           | 627 (74.3)          | 656 (77.8)          | 661 (78.3)          | 0.102   |
| Family history                         | 101 (12.0)          | 93 (11.0)           | 77 (9.1)            | 0.157   |
| Previous MI                            | 119 (14.1)          | 95 (11.3)           | 94 (11.1)           | 0.110   |
| Previous PCI                           | 193 (22.9)          | 156 (18.5)          | 149 (17.7)          | 0.015   |
| Previous CABG                          | 44 (5.2)            | 29 (3.4)            | 29 (3.4)            | 0.101   |
| Previous stroke                        | 138 (16.4)          | 187 (22.2)          | 190 (22.5)          | 0.002   |
| BMI, kg/m²                              | 25.4 ± 2.7          | 25.9 ± 2.7          | 26.4 ± 3.3          | <0.001  |
| SBP, mmHg                               | 134.9 ± 11.8        | 135.8 ± 12.0        | 136.9 ± 11.4        | 0.003   |
| DBP, mmHg                               | 74.0 ± 10.4         | 74.8 ± 10.6         | 75.9 ± 10.1         | 0.001   |
| HR, bpm                                 | 72.9 ± 12.2         | 73.6 ± 12.1         | 74.9 ± 11.5         | 0.003   |
| LVEF                                    | 58 ± 8              | 58 ± 8              | 57 ± 9              | 0.294   |
| GRACE score                             | 135 (129–140)       | 135 (130–141)       | 136 (131–142)       | <0.001  |
| Clinical presentation                   |                     |                     |                     | 0.236   |
| UAP                                     | 692 (82.0)          | 672 (79.7)          | 654 (77.5)          |         |
| NSTEMI                                  | 73 (8.6)            | 86 (10.2)           | 91 (10.8)           |         |
| STEMI                                   | 79 (9.4)            | 85 (10.1)           | 99 (11.7)           |         |
| Left main disease                      | 82 (9.7)            | 94 (11.2)           | 87 (10.3)           | 0.624   |
| Multi-vessel disease                    | 658 (78.0)          | 689 (81.7)          | 697 (82.5)          | 0.037   |
| Treatment strategy                      |                     |                     |                     | 0.001   |
| Medicine therapy                        | 310 (36.7)          | 249 (29.5)          | 241 (28.6)          |         |
| PCI                                     | 436 (51.7)          | 497 (59.0)          | 514 (60.9)          |         |
| CABG                                    | 98 (11.6)           | 97 (11.5)           | 89 (10.5)           |         |
| Laboratory findings                     |                     |                     |                     |         |
| Hemoglobin, g/dl                        | 132.1 ± 15.8        | 133.0 ± 15.4        | 132.5 ± 15.3        | 0.490   |
| FBG, mmol/L                             | 7.7 ± 2.8           | 7.9 ± 2.8           | 8.4 ± 3.4           | <0.001  |
| HbA1c, %                                | 7.5 ± 1.4           | 7.6 ± 1.4           | 7.8 ± 1.4           | <0.001  |
| TC, mmol/L                              | 4.40 ± 1.21         | 4.46 ± 1.06         | 4.39 ± 1.10         | 0.367   |
| TG, mmol/L                              | 1.50 (1.11–2.04)    | 1.53 (1.12–2.07)    | 1.54 (1.11–2.15)    | 0.699   |
| LDL-C, mmol/L                           | 2.88 ± 0.10         | 2.92 ± 0.93         | 2.90 ± 0.95         | 0.759   |
| HDL-C, mmol/L                           | 1.10 ± 0.32         | 1.08 ± 0.29         | 1.02 ± 0.28         | <0.001  |
| Uric acid, umol/L                       | 305.4 ± 78.4        | 306.4 ± 88.2        | 325.5 ± 106.1       | <0.001  |
| hs-CRP, mg/L                            | 1.89 (0.83–4.61)    | 1.64 (0.71–4.78)    | 1.85 (0.79–4.63)    | 0.325   |
| NT-proBNP, pg/ml                        | 1081 (497–2786)     | 1178 (856–170.7)    | 1608 (95.8–363.2)   | <0.001  |
| eGFR, mL/min                            | 97.8 ± 20.8         | 96.2 ± 23.7         | 85.5 ± 24.6         | <0.001  |
| Medications at discharge                |                     |                     |                     |         |
| Aspirin                                 | 817 (96.8)          | 811 (96.2)          | 814 (96.4)          | 0.799   |
| Clopidogrel/Ticagrelor                  | 666 (78.9)          | 689 (81.7)          | 707 (83.8)          | 0.036   |
| β-blocker                               | 513 (60.8)          | 545 (64.7)          | 586 (69.4)          | 0.001   |
| ACEI/ARB                                | 455 (53.9)          | 490 (58.1)          | 500 (59.2)          | 0.066   |
| Statin                                  | 802 (95.0)          | 807 (95.7)          | 797 (94.4)          | 0.468   |
| CCB                                     | 241 (28.6)          | 253 (30.0)          | 231 (27.4)          | 0.485   |
| Nitrate                                 | 478 (56.6)          | 459 (54.4)          | 453 (53.7)          | 0.447   |
| Insulin                                 | 321 (38.0)          | 327 (38.8)          | 377 (44.7)          | 0.010   |
The ROC analysis showed that the optimal cutoff value of the TyG index level for predicting MACE was 9.323 (sensitivity 46.0% and specificity 63.6%), with an area under the curve (AUC) of 0.560 (95% CI: 0.524–0.595, \( P = 0.001 \)). The incremental predictive value of the TyG index for MACE is shown in Table 5. Adding the TyG index to the model of established risk factors improved the prediction of MACE (\( P = 0.01 \)). Moreover, the addition of the TyG index has an incremental prognostic value for predicting MACE in terms of NRI (14.7%...
improvement, \( P = 0.019 \) and IDI (8.9% improvement, \( P = 0.001 \)), especially when comparing the baseline model with established risk factors.

The prognostic values of the TyG index in various subgroups for MACE are presented in Table 6. After adjusting for age, sex, duration of diabetes, smoking status, hypertension, previous MI, previous PCI, previous CABG, previous stroke, BMI, LVEF, left main disease, multi-vessel disease, HbA1c, LDL-C, uric acid, hs-CRP, NT-proBNP, eGFR, statin use and insulin use, the TyG index still independently predicted the occurrence of MACE in patients with diabetes and ACS irrespective of treatment strategy. The TyG index independently predicted the occurrence of MACE in the UAP subgroup, while it could not independently predict the occurrence of MACE in NSTEMI and STEMI subgroups.

**Discussion**

This study investigated the association between the TyG index and MACE in patients with diabetes and ACS. The results showed the TyG index was positively associated

![Kaplan–Meier survival curve for MACE (major adverse cardiovascular events) across TyG index terciles](image)

**Table 4** Univariate and multivariate Cox regression analysis for predicting MACE

| Variables                  | HR  | 95% CI       | P value | HR  | 95% CI       | P value |
|----------------------------|-----|--------------|---------|-----|--------------|---------|
| TyG index                  | 1.471 | 1.238–1.748 | <0.001 | 1.455 | 1.208–1.753 | <0.001 |
| Age                       | 1.041 | 1.024–1.058 | <0.001 | 1.039 | 1.022–1.057 | <0.001 |
| Male                      | 1.227 | 0.969–1.554 | 0.089  |     |              |         |
| Duration of diabetes      | 1.012 | 0.997–1.026 | 0.117  |     |              |         |
| Smoker                    | 1.253 | 0.994–1.581 | 0.056  |     |              |         |
| Hypertension              | 0.965 | 0.736–1.265 | 0.796  |     |              |         |
| Previous MI               | 1.807 | 1.350–2.419 | <0.001 | 1.439 | 1.048–1.975 | 0.024  |
| Previous PCI              | 1.221 | 0.928–1.607 | 0.154  |     |              |         |
| Previous CABG             | 1.842 | 1.170–2.901 | 0.008  |     |              |         |
| Previous stroke           | 0.991 | 0.745–1.319 | 0.951  |     |              |         |
| BMI                       | 1.045 | 1.005–1.086 | 0.027  |     |              |         |
| AMI                       | 1.939 | 1.514–2.484 | <0.001 |     |              |         |
| LVEF                      | 0.955 | 0.945–0.966 | <0.001 | 0.968 | 0.955–0.981 | <0.001 |
| Left main disease         | 1.600 | 1.161–2.206 | 0.004  |     |              |         |
| Multi-vessel disease      | 1.568 | 1.119–2.197 | 0.009  |     |              |         |
| Revascularization         | 0.873 | 0.677–1.125 | 0.294  |     |              |         |
| HbA1c                     | 1.077 | 0.997–1.164 | 0.061  |     |              |         |
| LDL-C                     | 1.085 | 0.966–1.218 | 0.171  |     |              |         |
| Uric acid                 | 1.001 | 0.999–1.002 | 0.276  |     |              |         |
| hs-CRP                    | 1.009 | 1.005–1.012 | <0.001 | 1.004 | 1.000–1.008 | 0.031  |
| NT-proBNP                 | 1.001 | 0.999–1.003 | 0.331  |     |              |         |
| eGFR                      | 0.997 | 0.992–1.002 | 0.247  |     |              |         |
| Statin                    | 0.599 | 0.388–0.926 | 0.021  | 0.578 | 0.371–0.901 | 0.015  |
| Insulin                   | 1.210 | 0.960–1.526 | 0.107  |     |              |         |

TyG index triglyceride-glucose index, MI myocardial infarction, PCI percutaneous coronary intervention, AMI acute myocardial infarction, LVEF left ventricle ejection fraction, HbA1c Hemoglobin A1c, LDL-C low-density lipoprotein cholesterol, hs-CRP high-sensitivity C-reactive protein, NT-proBNP N-terminal proB-type natriuretic peptide, eGFR estimated glomerular filtration rate, MACE major adverse cardiovascular event, HR hazard ratio, CI confidential interval
with increased MACE. After adjusting for confounding factors, the TyG index was an independent predictor of MACE irrespective of treatment strategy. Furthermore, our results showed that adding the TyG index to the model may improve the discrimination of risk prediction for MACE in patients with diabetes and ACS. These findings revealed the prognostic value of the TyG index for MACE in patients with diabetes and ACS. To the best of our knowledge, this study demonstrated, for the first time, that the TyG index is a potential predictor for MACE in patients with diabetes and ACS who received different treatments. Most importantly, this study suggests that a simple method of estimating IR may optimize the risk stratification of recurrent cardiovascular risk in patients with diabetes and ACS.

IR is a major characteristic of T2DM and has been recognized as a risk factor for CVD [27]. IR not only contributes to the development of CVD in both the general population and patients with diabetes but also predicts cardiovascular outcomes in patients with CVD [28, 29]. Therefore, identification of IR will have great clinical significance for improving cardiovascular risk stratification in primary and secondary prevention. However, there is no consensus on whether IR predicts cardiovascular risks in patients with established diabetes, with or without CVD [30–32]. A recent study demonstrated that the degree of IR, reflected by HOMA-IR, was not associated with CVEs in patients with diabetes and ACS who are not treated with insulin [33]. The TyG index, as the product of FPG and triglycerides, is a novel index that has been suggested as a simple and reliable surrogate of IR and has been shown to be superior to HOMA-IR in predicting IR [7, 8]. Compared with the HOMA-IR, the TyG index does not require quantification of insulin and may apply to all of the patients treated with insulin. It is well established that an increased TyG index is associated with increased risks of T2DM and CVD [6, 20–24]. Moreover, the TyG index has been recognized as an independent predictor for the risk of CVEs in patients with CVD [16–19]. Atherosclerotic CVD is the most common cause of death in patients with diabetes. Therefore, it is necessary to determine whether the TyG index predicts future cardiovascular risk in patients with T2DM and ACS.

Whether the TyG index is able to predict cardiovascular outcomes in patients with established T2DM remains controversial. In a study of 3524 patients with T2DM, Su et al. found the TyG index was positively associated with CVD in both the general population and patients with diabetes but also predicts cardiovascular outcomes in patients with CVD [28, 29]. Therefore, identification of IR will have great clinical significance for improving cardiovascular risk stratification in primary and secondary prevention. However, there is no consensus on whether IR predicts cardiovascular risks in patients with established diabetes, with or without CVD [30–32]. A recent study demonstrated that the degree of IR, reflected by HOMA-IR, was not associated with CVEs in patients with diabetes and ACS who are not treated with insulin [33]. The TyG index, as the product of FPG and triglycerides, is a novel index that has been suggested as a simple and reliable surrogate of IR and has been shown to be superior to HOMA-IR in predicting IR [7, 8]. Compared with the HOMA-IR, the TyG index does not require quantification of insulin and may apply to all of the patients treated with insulin. It is well established that an increased TyG index is associated with increased risks of T2DM and CVD [6, 20–24]. Moreover, the TyG index has been recognized as an independent predictor for the risk of CVEs in patients with CVD [16–19]. Atherosclerotic CVD is the most common cause of death in patients with diabetes. Therefore, it is necessary to determine whether the TyG index predicts future cardiovascular risk in patients with T2DM and ACS.

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### Table 5 Evaluation of Predictive Models for MACE

| Variables              | C-Statistic | P value | NRI (95% CI) | P value | IDI (95% CI) | P value |
|------------------------|-------------|---------|--------------|---------|--------------|---------|
| Established risk factors | 0.649 (0.613–0.686) | Ref. | Ref.         | Ref.    | Ref.         | Ref.    |
| Established risk factors + TyG index | 0.677 (0.644–0.711) | <0.001 | 0.147 (0.025–0.270) | 0.019 | 0.009 (0.004–0.014) | 0.001 |

**TyG index** triglyceride-glucose index, MACE major adverse cardiovascular event, NRI net reclassification improvement, IDI integrated discrimination improvement. Established risk factors included age, previous MI, LVEF, hs-CRP and statin

### Table 6 Prognostic value of TyG index for MACE in various subgroups

| Variables              | TyG index |
|------------------------|-----------|
|                        | Medicine therapy | PCI | CABG | UAP | NSTEMI | STEMI |
| Adjusted HR (95% CI)   | 1.854 (1.262–2.723) | 1.315 (1.014–1.705) | 2.014 (1.093–3.708) | 1.604 (1.270–2.027) | 1.261 (0.754–2.109) | 1.195 (0.639–2.235) |
| P value                | 0.002 | 0.039 | 0.025 | <0.001 | 0.377 | 0.577 |

**TyG index** triglyceride-glucose index, PCI percutaneous coronary intervention, CABG coronary artery bypass graft, UAP unstable angina pectoris, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-segment elevation myocardial infarction, MACE major adverse cardiovascular event, HR hazard ratio, CI confidential interval
The exact mechanisms accounting for the association between the TyG index and MACE remain unclear. As a reliable marker of the severity of IR, proatherogenic properties of IR may partly account for the association [36, 37]. In this study, TyG index levels were positively associated with BMI, HbA1c and uric acid, and were negatively associated with HDL-C and eGFR, suggesting that the observed association between the TyG index and poor prognosis may be explained by the presence of cardiovascular risk factors. Consistent with previous studies [17, 38], the TyG index was positively associated with the severity of CAD, suggesting that a difference in the extent of coronary atherosclerosis may contribute to the graded TyG index-MACE relationship. Moreover, the TyG index has been strongly associated with coronary artery calcification progression [39]. In addition, the TyG index has been correlated with micro- and macrovascular damage, such as arterial stiffness, nephric microvascular damage, cardiac autonomic neuropathy and cerebrovascular disease.
has an incremental prognostic value for the prediction of ACS. Adding the TyG index to the basic model provided increased risk of MACE in patients with diabetes and MACE in patients with established diabetes and ACS first to investigate the association between the TyG index and CV events. Second, the diagnosis of diabetes was made by the attending physician and only those with diabetic symptoms underwent the OGTT test. Therefore, some patients with diabetes may have remained unidentified. Third, FPG and triglyceride levels were only measured at the baseline. The levels of FPG and triglyceride might have changed by the follow-up; therefore, it is unknown whether the change in the TyG index could have predicted cardiovascular outcomes. Fourth, the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) score was not routinely calculated in our cardiac catheterization lab, so the association between the TyG index and the SYNTAX score was not evaluated. Therefore, future studies should explore the impact of the TyG index on the SYNTAX score in patients with diabetes and ACS. Our research also did not include the HOMA-IR index. Further study on the comparison of the predictive value of the TyG index and HOMA-IR must be explored. We also did not compare the predictive value of the TyG index and HbA1c because the predictive value of the TyG index only remained significant when the two variables were in the same multivariate Cox regression model. Fifth, the study was based on Chinese patients; therefore, these results require replications in other ethnic cohorts. Finally, although our study did not demonstrate the prognostic value of the TyG index in patients with diabetes and AMI, this finding requires further evaluation in a larger, prospective study. Despite these limitations, this study has important clinical implications because it is the first to investigate the association between the TyG index and MACE in patients with established diabetes and ACS who received different treatments.

**Conclusion**

A high TyG index was independently associated with an increased risk of MACE in patients with diabetes and ACS. Adding the TyG index to the basic model provided an incremental prognostic value for the prediction of MACE. These findings suggested that the TyG index may be a useful marker for risk stratification and prognosis in patients with diabetes and ACS who have received different ACS treatments.

**Abbreviations**

CAD: Coronary artery disease; ACS: Acute coronary syndrome; CVEs: Cardiovascular events; TyG index: Triglyceride-glucose index; IR: Insulin resistance; HOMA-IR: Homeostasis model assessment of IR; CVD: Cardiovascular disease; T2DM: Type 2 diabetes mellitus; FBG: Fasting blood glucose; UAP: Unstable angina pectoris; NSTEMI: Non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; LVEF: Left ventricle ejection fraction; Hba1c: Hemoglobin A1c; TC: Total cholesterol; TG: Triglyceride; LDL-C: Low density lipoprotein-C; HDL-C: High density lipoprotein-C; hs‑CRP: High-sensitivity C-reactive protein; NT‑proBNP: N-terminal proB-type natriuretic peptide; eGFR: Estimated glomerular filtration rate; BMI: Body mass index; MACE: Major adverse cardiovascular event; NRI: Net reclassification improvement; IDI: Integrated discrimination improvement; ROC: Receiver operating characteristic; AUCs: Area under the receiver operating characteristic curves; SYNTAX: The Synergy Between PCI With Taxus and Cardiac Surgery.

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**Authors’ contributions**

LW, HLC and JXZ participated in the study design. LW, YCH, AW, YYZ, HY, LBR, WQ, WYL, RZ and JHX participated in data collection. LW, HY and LBR performed the statistical analysis. LW drafted the article. All authors read and approved the final manuscript.

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**Availability of data and materials**

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

**Ethics approval and consent to participate**

The study was approved by our local ethical committee. No informed consent was required.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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