High Triglyceride-Glucose Index is Associated with Poor Cardiovascular Outcomes in Non-Diabetic ACS Patients with LDL-C Below 1.8mmol/L

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Research

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Abstract

Background: To evaluate the prognostic value of triglyceride glucose (TyG) index in non-diabetic acute coronary syndrome (ACS) patients with low-density lipoprotein cholesterol (LDL-C) below 1.8mmol/L.

Methods: A total of 1655 non-diabetic ACS patients with LDL-C below 1.8mmol/L were included in the analysis. Patients were stratified into 2 groups. Incidence of acute myocardial infarction (AMI), infarct size in patients with AMI, and major adverse cardiac and cerebral event (MACCE) during a median of 35.6-month follow-up were determined and compared between the 2 groups. The TyG index was calculated using the following formula: $\ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting plasma glucose (mg/dL)} / 2]$.

Results: Compared with the TyG index <8.33 group, the TyG index ≥ 8.33 group had significantly higher incidence of AMI (21.2% vs. 15.2%, $p = 0.014$) and larger infarct size in patients with AMI (pTNI: 10.4 vs. 4.8 ng/ml, $p = 0.003$; pCKMB: 52.8 vs. 22.0 ng/ml, $p = 0.006$; pMyo: 73.7 vs. 46.0 ng/ml, $p = 0.038$). Although there was no significant difference in mortality between the 2 groups, the incidence of revascularization of TyG index ≥ 8.33 group was significantly higher than that of TyG index <8.33 group (8.9% vs. 5.0%, $p = 0.035$). Multivariable Cox regression revealed that the TyG index was positively associated with revascularization [HR (95% CI): 1.67 (1.02, 2.75), $p = 0.043$].

Conclusion: In non-diabetic ACS patients with LDL-C below 1.8mmol/L, the high TyG index level was associated with higher incidence of AMI, larger infarct size, and higher incidence of revascularization. The high TyG index level might be a valid predictor of subsequent revascularization.

Trial registration: retrospectively registered.

Introduction

Acute coronary syndrome (ACS) is the leading cause of morbidity and mortality

from cardiovascular disease worldwide^[1, 2]. Therefore, it is crucial to identify patients at high risk of developing major adverse cardiac and cerebral event (MACCE) that may contribute to optimal management.

Insulin resistance (IR), a hallmark of metabolic syndrome (MetS), not only associated with an increased risk of cardiovascular disease, but also significantly correlated with a higher risk of MACCE^[3, 4]. However, direct measurement of IR, including the hyperinsulinemic-euglycemic clamp and the homeostasis model assessment of IR (HOMA-IR), are too complex and expensive to be used in large-scale epidemiological studies and clinical practice^[5]. Therefore, we urgently need a simple, accessible and reliable index to quantitatively evaluate IR.

High levels of triglyceride (TG) and fasting plasma glucose (FPG) are the important components of MetS. Recently, the triglyceride-glucose (TyG) index, which combines TG and FPG levels, has been proved as a reliable surrogate marker of IR in clinical practice^[6]. What's more, the TyG index has been found to be well correlated with coronary artery disease (CAD)^[7–9]. Luo et al. firstly reported a positive correlation between the TyG index level and the incidence of MACCE in patients with ST-elevation myocardial infarction (STEMI) who underwent percutaneous coronary intervention (PCI)^[10]. Mao et al. also found that in patients with non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS), high TyG index group showed significantly increased risk of major adverse cardiac event (MACE) compared with the low TyG index group^[11]. To the best of our knowledge, the relationship between TyG index and cardiovascular outcomes in non-diabetic ACS patients with LDL-C below 1.8 mmol/L, is still unknown. Our study was to fill this knowledge gap. Here, we aimed to investigate not only the relationship between TyG index and patient characteristics during hospitalization, but also the predictive value of TyG index on the cardiovascular outcomes.

Methods

Study population

Patients' records in the Cardiovascular Center of Beijing Friendship Hospital Database Bank were screened. As shown in **Figure 1**, the records of 10,216 ACS patients undergoing coronary angiography from December 2012 to March 2020 in our center were screened. Of the 11,110 patients, 9455 were excluded according to the exclusion criteria, which were 1) with diabetes mellitus, 2) with LDL-C ≥ 1.8 mmol/L, 3) with severe valvulopathy or cardiomyopathy, 4) with acute infectious disease, rheumatic disease, hematological disease, or neoplastic disease, and 5) lacking clinical or follow-up data. Finally, 1655 patients were included in this analysis. According to the median value of TyG index level, 1655 patients were stratified into 2 groups (TyG index < 8.33 group, $n = 829$ and TyG index ≥ 8.33 group, $n = 826$). All patients were followed up till April 30, 2020 with a median follow up of 35.6 (IQR: 13.2, 51.8) months.

Data collections and definitions

The data collection process was approved by the Institutional Review Board of Beijing Friendship Hospital affiliated to Capital Medical University and was in accordance with the Declaration of Helsinki.

Patients' demographics, medical and medication history, laboratory test results, echocardiographic and angiographic evaluation results were collected and verified using an electronic medical recording system. The outcomes from MACCE were collected and recorded during clinical follow-up visits.

ACS contains unstable angina pectoris (UAP) and acute myocardial infarction (AMI). UAP was diagnosed in patients with unstable chest discomfort (rest, new onset, or worsening of angina) and without the elevation of myocardial necrosis markers. AMI was defined as chest pain with new ST-segment changes and elevation of myocardial necrosis markers to at least twice of the upper limit of the normal range. MACCEs included all-cause death, non-fatal MI, non-fatal stroke, revascularization, and cardiac rehospitalization (admission because of angina or heart failure). All-cause death was defined as the incidence of cardiac death or non-cardiac death. Cardiovascular (CV) death was defined as fatal myocardial infarction, fatal stroke, sudden death, and other cardiovascular death. Non-fatal stroke, including ischemic and hemorrhagic stroke, was defined as cerebral dysfunction caused by cerebral vascular obstruction or sudden rupture and was diagnosed based on signs of neurological dysfunction or evidence of brain imaging. Any coronary revascularization was defined as a revascularization of the target vessel or non-target vessels. Cardiac rehospitalization refers to rehospitalization for angina pectoris or heart failure. The TyG index was calculated as $\ln [\text{fasting TG (mg/dL)} \times \text{fasting plasm glucose (FPG, mg/dL)}] / 2$ ^[12].

Statistical analyses

Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (IQR). Comparisons between the two study groups were analyzed by Student's t-test or Mann-Whitney U-test. Categorical variables are expressed as number and percentage and compared using the Pearson chi-square test or Fisher's exact test. To control confounding factors, we performed propensity score matching. The cumulative incidence of MACCE was estimated by Kaplan-Meier survival curves. A multivariable Cox regression analysis was performed to identify independent predictors for MACCE. Baseline variables that were significantly correlated with outcomes by univariate analysis were used in the multivariate model. Correlation analysis among variables was also taken into consideration in the multivariate analysis. All analyses were two-tailed and P value < 0.05 was considered statistically significant. Data were analyzed using the statistical analysis software IBM SPSS statistics 24.0.

Propensity score matching

Propensity score matching (PSM) was used to reduce selection bias in this study. The matching process was conducted with a minimum-distance scoring method and a 1-to-1 match between the TyG index ≥ 8.33 group and the TyG index < 8.33 group. In this study, propensity scores were calculated through a binary logistic regression model, including covariates of age, sex, body mass index (BMI), systolic blood pressure (SBP), hemoglobin (HGB), albumin, creatinine, glycated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), history of smoking and stroke, previous medication history including beta-blocker and statins, and statins treatment during hospitalization. Ultimately, 505 TyG index ≥ 8.33 patients were individually 1:1 matched to 505 TyG index < 8.33 controls using nearest available score matching. The statistical analysis software SPSS version 24.0 was used for the matching.

Results

Patient characteristics

As shown in **Figure 1**, of the 1655 eligible patients, 829 patients with the TyG index < 8.33 and 826 patients with the TyG index ≥ 8.33 . Comparing with the TyG index < 8.33 group, the TyG index ≥ 8.33 group showed significantly higher BMI, younger, lower SBP, higher percent of smoker, lower percent of stroke, and significantly more likely to receive beta-blocker or statins before the hospital admission for ACS. In-hospital medical and interventional treatments were similar between the 2 groups except that significantly higher patients treated with beta-blocker in the TyG index ≥ 8.33 group than in the TyG index < 8.33 group during hospitalization. Laboratory values showed that the TyG index ≥ 8.33 group had significantly higher white cell count, HGB, FPG, HbA1c, albumin, creatinine, TG and LDL-C than the TyG index < 8.33 group. The results of coronary angiography and echocardiography showed no significant difference between the 2 groups (**Table 1**).

Propensity score matching

Propensity scores of 505 TyG index ≥ 8.33 patients were 1:1 matched to 505 TyG index < 8.33 patients. There were no significant differences in baseline clinical characteristics and medical history between the PSM TyG index ≥ 8.33 and TyG index < 8.33 groups except that the PSM TyG index ≥ 8.33 group had significantly higher FPG and TG (**Table 1**).

The TyG index ≥ 8.33 group had a significantly higher incidence of AMI at the admission than the TyG index < 8.33 group (21.2% vs. 15.2%, $p = 0.014$, **Figure 2**). The peak levels of serum myoglobin (Myo), creatine kinase MB (CKMB), and cardiac troponin I (cTnI) were used to estimate infarct size. The peak levels of serum Myo, CKMB and cTnI were significantly higher in the TyG index ≥ 8.33 group (pMyo: 73.7 vs. 46.0 ng/ml, $p = 0.038$; pCKMB: 52.8 vs. 22.0 ng/ml, $p = 0.006$; pTnI: 10.4 vs. 4.8 ng/ml, $p = 0.003$, **Table 2**).

Subsequent MACCE and mortality

During a median of 35.6 months (IQR: 13.2-51.8 months) follow-up, composite MACCE occurred in 28.2% of patients in the TyG index ≥ 8.33 group and 24.3% in the TyG index < 8.33 group (HR=1.16, 95%CI: 0.96-1.40, $p = 0.117$). All-cause death was observed in 3.6% of the patients in the TyG index ≥ 8.33 group and 5.0% of the patients in the TyG index < 8.33 group (HR=0.71, 95%CI: 0.45-1.14, $p = 0.161$). CV death occurred in 2.7% of the patients in the TyG index ≥ 8.33 group and 3.4% in the TyG index < 8.33 group (HR=0.77, 95%CI: 0.44-1.35, $p = 0.364$). Revascularization occurred in 8.6% of the patients in the TyG index ≥ 8.33 group and 4.8% in the TyG index < 8.33 group (HR=1.82, 95%CI: 1.23-2.69, $p = 0.003$). Subsequent non-fatal MI, non-fatal stroke, and cardiac rehospitalization were not statistically different between the 2 groups (**Table 3**).

After propensity-score matching, composite MACCE occurred in 30.9% of the patients in the PSM TyG index ≥ 8.33 group and 24.6% in the PSM TyG index < 8.33 group (HR=1.14, 95%CI: 0.90-1.44, $p = 0.282$); all-cause death was observed in 4.4% of the patients in the PSM TyG index ≥ 8.33 group and 3.8% in the PSM TyG index < 8.33 group (HR=1.01, 95%CI: 0.55-1.87, $p = 0.976$); CV death was identified in 3.0% of PSM TyG index ≥ 8.33 group and 2.8% of the PSM TyG index < 8.33 group

(HR=0.96, 95%CI: 0.46-2.00, $p=0.920$); revascularization occurred in 8.9% of the PSM TyG index ≥ 8.33 group and 5.0% of the PSM TyG index < 8.33 group (HR=1.71, 95%CI: 1.04-2.81, $p=0.035$). Subsequent non-fatal MI, non-fatal stroke, and cardiac rehospitalization were not statistically different between the 2 groups (**Table 3**).

The Kaplan-Meier curves show that the TyG index ≥ 8.33 group had significantly higher cumulative rate of subsequent revascularization than the TyG index < 8.33 group (**Figure 3**). The cumulative rate of all cause death, CV death, non-fatal MI, non-fatal stroke, cardiac rehospitalization, and composite MACCE were not statistically different between the 2 groups.

Risk factors for subsequent revascularization

Univariate and multivariate analysis results and predictors for revascularization are presented in **Supplemental file**. Univariate analysis revealed that TyG index, FPG, multi-vessel/ left main (LM) coronary artery lesions, and PCI/Coronary Artery Bypass Graft (CABG) treatment during hospitalization were risk factors for revascularization in patients with ACS (all $p < 0.05$). Correlation analysis displayed that FPG and TyG index had a high correlation ($p < 0.001$). Therefore, FPG were not included in the multivariate model. In addition, PCI/CABG treatment during hospitalization was significantly correlated with multi-vessel/LM coronary artery lesions ($p < 0.001$). Therefore, PCI/CABG treatment during hospitalization was also not included in the multivariate model. After adjusting for confounding factors, multivariate analysis found that the TyG index [HR (95% CI): 1.67 (1.02,2.75), $p=0.043$] and multi-vessel/LM coronary artery lesions [HR (95% CI): 3.06 (1.23,7.62), $p=0.016$] were independent predictors of subsequent revascularization in patients with ACS.

Independent association of TyG index with subsequent revascularization in different subgroups

As shown in **Figure 4**, the independent predictive effect of TyG index on subsequent revascularization was mainly reflected in the subgroups of male gender, age < 65 years, BMI $< 25 \text{ kg/m}^2$, smoker, eGFR $\geq 60 \text{ ml/min/1.73m}^2$, HDL-C $< 1.01 \text{ mmol/L}$, and LVEF $\geq 50\%$.

Discussion

To the best of our knowledge, the current study was the first to investigate whether TyG index could be associated with patient characteristics during hospitalization and subsequent cardiovascular outcomes in non-diabetic ACS patients with LDL-C below 1.8 mmol/L. Our main findings include: in non-diabetic ACS patients with LDL-C below 1.8 mmol/L, (1) the high TyG index group had significantly higher incidence of AMI and larger infarct size than the low TyG index group, (2) the incidence of subsequent revascularization of the high TyG index group was significantly higher than that of the low TyG index group, (3) the high TyG index was an independent predictor of subsequent revascularization, and (4) Moreover, the independent predictive effect of TyG index on revascularization was mainly reflected in the subgroups of male gender, age < 65 years, BMI $< 25 \text{ kg/m}^2$, smoker, eGFR $\geq 60 \text{ ml/min/1.73 m}^2$, HDL-C $< 1.01 \text{ mmol/L}$, and LVEF $\geq 50\%$.

IR, a hallmark of MetS, is defined as a decrease in the efficiency of insulin in promoting glucose uptake and utilization. IR can induce glucose metabolism imbalance, which leads to chronic hyperglycemia and then in turn triggers oxidative stress and causes inflammatory responses. In addition, IR can alter systemic lipid metabolism, including increased TGs levels, decreased HDL-C levels, increased small dense low-density lipoproteins, and excessive postprandial lipemia. Moreover, IR can also cause endothelial dysfunction by decreasing nitric oxide production from endothelial cells and increasing procoagulant factor release. Therefore, it is easy to understand that IR has been proven to contribute to the progression of cardiovascular disease^[13, 14] due to above mechanisms. However, traditional measurement of IR, including the hyperinsulinemic-euglycemic clamp and HOMA-IR, are too complex and expensive to be used in clinic practice on a large scale. In recent years, researchers have tried to find a simpler and more valid surrogate marker of IR.

As is known to all, high levels of TG and FPG are the components of MetS. Recently, the TyG index, a composite indicator composed of TG and FPG, has been demonstrated as a reliable marker of IR^[6, 12, 15] and has a high sensitivity and

specificity for identifying MetS^[16]. Previous studies reported that the TyG index is a simple, cost-effective surrogate marker of IR compared to HOMA-IR^[17, 18]. It was demonstrated that TyG index was a useful predictor of Type 2 diabetes mellitus (T₂DM)^[19, 20] which contributed to cardiovascular disease risk. Studies have also shown an association of TyG index with arterial stiffness^[21, 22], stroke^[23], carotid atherosclerosis^[24], coronary artery calcification^[7] and coronary artery stenosis^[8]. Subsequently, several studies were conducted and found a positive relationship between TyG index and cardiovascular disease. It has been reported that the TyG index may contribute to the early identification of apparently healthy individuals at high risk for cardiovascular events^[25–27]. Jin et al. revealed that TyG index was positively associated with cardiovascular events risk [HR(95% CI): 1.36(1.10,1.69), $p = 0.005$] in patients with stable CAD^[28]. The findings of Luo et al. showed that the TyG index was significantly associated with an increased risk of MACCE in STEMI patients within 1 year after PCI [HR(95% CI):1.53(1.01,2.06), $p = 0.003$]^[10]. It was demonstrated that the TyG index was an independent predictor of MACEs [HR(95% CI):1.88(1.13,3.12), $p = 0.015$] in patients with NSTEMI-ACS^[11]. Jin et al.^[29] and Su et al.^[30] found that both TyG index and HbA1c could predict cardiovascular outcomes in T₂DM patients while TyG index might be better. Unfortunately, no data is currently available with regard to the effects of TyG index on clinical outcomes in non-diabetic ACS patients, especially those with LDL-C lower than 1.8 mmol/L. Recently, Alizargar et al. questioned the conclusion that TyG index can be used to predict cardiovascular events in patients with CAD, considering that it might be influenced by diabetes and the hyperlipidemic state that led to cardiovascular disease^[31]. Therefore, in order to avoid the mixed effects of diabetes and hyperlipemia on cardiovascular events, we only analyzed ACS patients with non-diabetic and LDL-C below 1.8 mmol/L, which was the novelty of this study.

Although we found that higher TyG index levels had no significant effect on the incidence of all-cause death, CV death and composite MACCE. However, our study indicated an association between higher TyG index levels and an increased risk of subsequent revascularization for the first time, and the TyG index might be a valid predictor of subsequent revascularization in non-diabetic ACS patients with LDL-C below 1.8 mmol/L. This finding might be greatly of interest. A high TyG index level still has a significant impact on the risk of subsequent revascularization, after all, patients without diabetes and with LDL-C below 1.8 mmol/L seem to be a relatively low-risk group for cardiovascular events in follow-up. In addition, we found that the independent predictive effect of TyG index on subsequent revascularization was mainly reflected in the subgroups of male gender, age < 65 years, BMI < 25 kg/m², smoker, eGFR ≥ 60 ml/min/1.73 m², HDL-C < 1.01 mmol/L, and LVEF ≥ 50%.

This finding implied that using TyG index for early risk stratification in the above subgroups may have more important clinical significance. Moreover, we also found that the high TyG index group had significantly higher incidence of AMI and larger infarct size compared with the low TyG index group, which were not reported in previous studies.

Luo et al^[10] and Mao et al^[11] demonstrated that the TyG index was an independent predictor of cardiovascular events in STEMI and NSTEMI-ACS population, respectively. The cut-off value of the former was TyG ≥ 9.608 and the latter was TyG ≥ 8.805. In this study, we found that the high TyG index level was an independent predictor of subsequent revascularization in non-diabetic ACS patients with LDL-C < 1.8 mmol/L. We proposed the cut-off point of TyG ≥ 8.33, which was significantly lower than that in previous studies. The main reason is that patients with diabetes and hyperlipemia have been excluded in this study, whereas previous studies have not. Therefore, the cut-off value of the TyG index in this study might be lower than that in previous studies.

Limitations

There were several limitations in the present study. Firstly, this was a single-center study, the sample size might be not large enough and the follow-up time might be not long enough; thus, generalization of the findings should be cautious. Secondly, laboratory parameters were only measured once after hospital admission, which could cause potential bias due to measurement error. Thirdly, this was a retrospective observational study. The information on the levels of TyG index during

follow-up was limited. Hence, prospective cohort studies with larger sample and longer follow-up time are required to confirm our findings.

Conclusions

In non-diabetic ACS patients with LDL-C below 1.8 mmol/L, the high TyG index group had significantly higher incidence of AMI and larger infarct size than the low TyG index group. In addition, the incidence of subsequent revascularization of the high TyG index group was significantly higher than that of the low TyG index group, and the high TyG index level was an independent predictor of subsequent revascularization.

List Of Abbreviations

Triglyceride-glucose: TyG; IR: Insulin resistance; ACS: Acute coronary syndrome; LDL-C: Low-density lipoprotein cholesterol; AMI: Acute myocardial infarction; MACCE: Major adverse cardiac and cerebral event; cTNI: Cardiac troponin I; CKMB: Creatine kinase MB; Myo: Myoglobin; MetS: Metabolic syndrome; HOMA-IR: the Homeostasis model assessment of IR; TG: Triglyceride; FPG: Fasting plasma glucose; STEMI: ST-elevation myocardial infarction; PCI: Percutaneous coronary intervention; NSTEMI: non-ST-segment elevation acute coronary syndrome; MACE: Major adverse cardiac event; UAP: Unstable angina pectoris; CV: Cardiovascular; PSM: Propensity score matching; BMI: Body mass index; SBP: Systolic blood pressure; HGB: Hemoglobin; HbA1c: Glycated hemoglobin; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LM: left main coronary artery; CABG: Coronary Artery Bypass Grafting; CAD: Coronary artery disease; T₂DM: Type 2 diabetes mellitus.

Declarations

Ethics approval and consent to participate

The study data collections were approved by the Institutional Review Board of Beijing Friendship Hospital affiliated to Capital Medical University, and written informed consent was obtained from all patients.

Consent for publication

Consent to publish from the participant to report individual patient data: not applicable (no patient identifier or personalized data shown).

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

YZ performed study, statistical analysis and wrote manuscript. XSD, BH, QBL and HG participated in study data collection. HC contributed discussion and edited manuscript. XQZ designed study and revised manuscript. WPL designed study, performed statistical analysis and edited manuscript. HWL provided funding support, designed study and reviewed manuscript. 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.

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Tables

Table 1. Baseline clinical characteristics.

Characteristics	Before PS match			After PS match		
	TyG < 8.33	TyG ≥ 8.33	p value	TyG < 8.33	TyG ≥ 8.33	p value
	(n: 829)	(n: 826)		(n: 505)	(n: 505)	
TyG index	8.0 ± 0.2	8.8 ± 0.7	< 0.001	8.0 ± 0.2	8.7 ± 0.4	< 0.001
Age, years	67.4 ± 10.2	63.9 ± 10.2	< 0.001	65.6 ± 10.5	65.9 ± 9.7	0.674
Male gender	604(73.1)	619(74.7)	0.474	364(72.1)	371(73.5)	0.621
BMI, kg/m ²	24.8 ± 3.6	26.0 ± 3.2	< 0.001	25.5 ± 3.6	25.6 ± 3.1	0.720
SBP, mmHg	129.2 ± 17.7	127.1 ± 17.8	0.013	128.2 ± 17.6	127.6 ± 17.7	0.599
DBP, mmHg	74.5 ± 11.5	74.6 ± 11.2	0.769	74.7 ± 11.7	74.3 ± 10.5	0.550
Heart rate, bpm	68.9 ± 12.8	68.8 ± 11.5	0.901	68.1 ± 12.3	68.8 ± 11.3	0.398
Medical history						
Current/ex-Smoker	445(53.9)	491(59.2)	0.028	276(54.7)	286(56.6)	0.526
Hypertension	586(70.9)	615(74.2)	0.139	357(70.7)	376(74.5)	0.180
Stroke	194(23.5)	148(17.9)	0.005	97(19.2)	107(21.2)	0.433
Previous PCI/CABG	298(36.1)	295(35.6)	0.835	199(39.4)	171(33.9)	0.067
Medication used before admission						
Antiplatelet agent	518(62.7)	521(62.8)	0.955	330(65.3)	304(60.2)	0.091
ACEI/ARB	299(36.2)	329(39.7)	0.144	183(36.2)	204(40.4)	0.174
Beta-blocker	213(25.8)	275(33.2)	0.001	149(29.5)	138(27.3)	0.443
CCB	297(36.0)	314(37.9)	0.418	184(36.4)	189(37.4)	0.744
Diuretics	42(5.1)	57(6.9)	0.124	25(5.0)	26(5.1)	0.886
Statins	348(42.1)	397(47.9)	0.019	233(46.1)	224(44.4)	0.569
Laboratory values						
WBC, 10 ⁹ /L	6.4 ± 2.0	6.9 ± 2.3	< 0.001	6.4 ± 1.9	6.6 ± 2.2	0.215
Neutrophil ratio, %	66.6 ± 9.0	65.8 ± 9.0	0.065	66.3 ± 8.9	66.1 ± 9.3	0.775
Hemoglobin, g/L	134.2 ± 15.1	137.6 ± 15.6	< 0.001	135.9 ± 15.1	135.8 ± 15.7	0.912

Dates are presented as mean ± SD, median (IQR) or number (%).

TyG, triglyceride-glucose index; BMI, body mass index; SBP, systolic blood pressure; DBP,

diastolic blood pressure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft;

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; CCB, calcium channel blocker; WBC, white blood cell; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; eGFR, estimated glomerular filtration rate; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LM, left main coronary artery; LAD, left anterior descending.

FPG, mmol/L	4.8 ± 0.6	5.4 ± 0.9	< 0.001	4.8 ± 0.5	5.4 ± 0.9	< 0.001
HbA1c, %	5.7 ± 0.4	5.8 ± 0.5	< 0.001	5.7 ± 0.5	5.6 ± 0.6	0.538
Albumin, g/L	39.9 ± 3.6	40.7 ± 3.7	< 0.001	40.4 ± 3.5	40.4 ± 3.9	0.926
Creatinine, umol/L	74.1(65.2,86.0)	76.0(66.0,88.6)	0.038	74.2(64.9,86.0)	75.3(66.0,88.0)	0.176
eGFR,ml/min/1.73 m ²	84.8(70.9,98.2)	85.3(71.5,98.2)	0.664	85.5(72.5,99.9)	83.3(70.5,96.0)	0.077
TC, mmol/L	3.1 ± 0.4	3.1 ± 0.4	0.102	3.1 ± 0.4	3.1 ± 0.4	0.611
TG, mmol/L	0.8 ± 0.2	1.6 ± 0.7	<0.001	0.8 ± 0.2	1.4 ± 0.4	< 0.001
LDL-C, mmol/L	1.5 ± 0.1	1.6 ± 0.2	<0.001	1.5 ± 0.2	1.5 ± 0.2	0.311
HDL-C, mmol/L	1.2 ± 0.3	1.0 ± 0.3	<0.001	1.1 ± 0.3	1.1 ± 0.2	0.878
Echocardiography						
LVEF,%	63.9 ± 9.7	64.6 ± 8.4	0.094	63.9 ± 9.4	64.3 ± 8.7	0.554
Angiography findings						
Multi-vessel/LM	665(80.5)	683(82.4)	0.325	279(55.2)	287(56.8)	0.612
Proximal LAD	382(46.2)	399(48.1)	0.443	230(45.5)	249(49.3)	0.231
In-hospital treatment						
PCI/CABG	461(55.8)	484(58.4)	0.290	279(55.2)	287(56.8)	0.612
Antiplatelet agent	794(96.1)	800(96.5)	0.685	485(96.0)	489(96.8)	0.497
ACEI/ARB	415(50.2)	418(50.4)	0.942	250(49.5)	253(50.1)	0.850
Beta-blocker	534(64.6)	579(69.8)	0.024	347(68.7)	336(66.5)	0.459
CCB	297(36.0)	316(38.1)	0.363	184(36.4)	191(37.8)	0.648
Diuretics	72(8.7)	71(8.6)	0.912	39(7.7)	41(8.1)	0.816
Statins	742(89.8)	754(91.0)	0.438	454(89.9)	458(90.7)	0.671
Hospital stay, day	5(4,7)	5(4,7)	0.778	5(4,7)	6(4,7)	0.938
Dates are presented as mean ± SD, median (IQR) or number (%).						
TyG, triglyceride-glucose index; BMI, body mass index; SBP, systolic blood pressure; DBP,						
diastolic blood pressure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft;						
ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; CCB; calcium channel blocker; WBC, white blood cell; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; eGFR, estimated glomerular filtration rate; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LM, left main coronary artery; LAD, left anterior descending.						

Table 2
The estimated infarction size in patients with AMI.

The peak value of myocardial enzyme	Before PS match		P value	After PS match		P value
	TyG < 8.33	TyG ≥ 8.33		TyG < 8.33	TyG ≥ 8.33	
	(n: 135)	(n: 168)		(n:77)	(n:107)	
pMyo,ng/ml	51.5(23.8,143.8)	73.7(26.8,189.0)	0.123	46.0(22.1,136.5)	73.7(27.7,176.0)	0.038
pCK-MB,ng/ml	26.5(5.9,78.8)	54.1(8.5,156.0)	0.017	22.0(6.0,73.3)	52.8(12.8,153.0)	0.006
pTNI,ng/ml	5.5(0.9,18.8)	10.5(1.7,32.3)	0.008	4.8(0.7,16.1)	10.4(2.4,36.3)	0.003
Data are presented as IQR						
AMI, acute myocardial infarction; TyG, triglyceride-glucose index; pMyo, The peak value of myoglobin; pCK-MB, The peak value of Creatine kinase MB; pTNI, The peak value of troponin I.						

Table 3
Clinical events during long-term follow-up.

	TyG < 8.33	TyG ≥ 8.33	HR(95%CI)	p value
Overall population				
Number	829	826		
Composite MACCE	201(24.3)	234(28.2)	1.16(0.96,1.40)	0.117
All cause death	41(5.0)	30(3.6)	0.71(0.45,1.14)	0.161
CV death	28(3.4)	22(2.7)	0.77(0.44,1.35)	0.364
Non-fatal MI	21(2.5)	25(3.0)	1.15(0.64,2.06)	0.635
Non-fatal stroke	17(2.1)	21(2.5)	1.19(0.63,2.26)	0.596
Revascularization	40(4.8)	71(8.6)	1.82(1.23,2.69)	0.003
Cardiac rehospitalization	158(19.1)	186(22.4)	1.16(0.94,1.44)	0.168
Matched population				
Number	505	505		
Composite MACCE	124(24.6)	156(30.9)	1.14(0.90,1.44)	0.282
All cause death	19(3.8)	22(4.4)	1.01(0.55,1.87)	0.976
CV death	14(2.8)	15(3.0)	0.96(0.46,2.00)	0.920
Non-fatal MI	9(1.8)	16(3.2)	1.56(0.69,3.54)	0.288
Non-fatal stroke	9(1.8)	16(3.2)	1.53(0.67,3.46)	0.312
Revascularization	25(5.0)	45(8.9)	1.71(1.04,2.81)	0.035
Cardiac rehospitalization	101(20.0)	121(24.0)	1.07(0.82,1.39)	0.629
Dates are presented as number (%) or median (IQR).				
TyG, triglyceride-glucose index; MACCE, major adverse cardiac and cerebral event;				
CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.				

Figures

Figure 1

The flow chart of study subject enrollment. CBD, Cardiovascular Center of Beijing Friendship Hospital Database; ACS, acute coronary syndrome; CAG, coronary angiography; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose index.

Figure 2

Percentages of patients with UAP and AMI in 2 groups. TyG, triglyceride-glucose index; UAP, unstable angina pectoris; AMI, acute myocardial infarction.

Figure 3

Kaplan-Meier curves for all-cause death(A), CV death(B), non-fatal MI(C), non-fatal stroke(D), cardiac rehospitalization(E), revascularization(F) and composite MACCEs(G) of the TyG < 8.33 group(green line) versus the TyG ≥ 8.33 group(red line). TyG, triglyceride-glucose index; CV: cardiovascular ; MI, myocardial infarction; MACCEs, major adverse cardiac and cerebral event; HR, hazard ratio; CI, confidence interval.

Figure 4

Forest plot of revascularization according to different subgroups. Prespecified subgroups of interest in this analysis are sex, age, BMI, smoker, hypertension, eGFR, HDL-C and LVEF. The dashed vertical line represents the hazard ratio for the overall study population. The box sizes are proportional to the precision of the estimates (with larger boxes indicating a greater degree of precision). TyG, triglyceride-glucose index; BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; LM, left main coronary artery; HR, hazard ratio; CI, confidence interval.

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