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

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Abstract

Background: Triglyceride-glucose index (TyG index) has been regarded as a reliable alternative marker of insulin resistance and an independent predictor of cardiovascular outcomes. Whether TyG index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome (ACS) remains uncertain. The aim of the present study was to investigate the prognostic value of 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 the study. Patients were divided into 3 tertiles according to TyG index. The primary outcomes included the occurrence of major adverse cardiovascular events (MACE), defined as all-cause death, non-fatal myocardial infarction and non-fatal stroke. The TyG index was calculated as ln (fasting triglyceride level (mg/dL) ×fasting glucose level (mg/dL)/2).

Results: The incidence of MACE increased with TyG index tertiles after 3-year follow-up. 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 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 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 TyG index predicts future recurrent cardiovascular events in patients with diabetes and ACS, independently of known cardiovascular risk factors suggesting that TyG index may be a useful marker for risk stratification and prognosis in patients with diabetes and ACS.

Background

Diabetes is known one of the major risk factors for coronary artery disease (CAD) [1]. Up to 37% 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 current guidelines [2–4]. Therefore, it is crucial to identify patients at high risk of developing future CVEs so that intense treatment can be provided. Seeking rapidly available and reliable markers may have great clinical significance to optimize the risk stratification of recurrent cardiovascular risk.

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]. TyG index showed better performance for assessing IR than the homeostasis model assessment of IR(HOMA-IR) [7, 8]. A number of studies have found a positive association between TyG index and cardiovascular risk, including systematic CAD, carotid atherosclerosis, hypertension, metabolic syndrome, arterial stiffness and coronary calcification [9–15]. Furthermore, recent data suggest that TyG index could provide significant prognostic information in patients with established CAD [16–19]. In fact, TyG index is associated with not only the incidence of cardiovascular disease (CVD) but also the development of type 2 diabetes [20–25]. All these suggest that it is may be plausible to use the TyG index as a predictor for future cardiovascular risk in patients with diabetes and CAD.

Recent study was only focused on patients with diabetes and stable CAD and demonstrated that TyG index is a useful marker for predicting clinical outcomes [19]. To date, no relevant study has focused on the impact of TyG index on CVEs in patients with diabetes and ACS. To address the knowledge gap, the present study aimed to specifically investigate whether TyG index has prognostic value for recurrent CVEs in patients with diabetes and ACS.

Methods

Study population

This study was a single-center, retrospective, observational cohort study. From January 2016 to December 2016, a total of 3428 consecutive patients with Type 2 diabetes and ACS, who were admitted to Tianjin Chest Hospital for coronary angiography, were enrolled in this study.

Type 2 diabetes included those with history of type 2 diabetes, currently using insulin or hypoglycemic drugs, or fasting blood glucose(FBG)≥7.0 mmol/L or the 2-h plasma glucose of the oral glucose tolerance test≥11.1mmol/L. ACS was defined as 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), other severe medical illnesses or lacking complete clinical data(n=285) were excluded. Finally, a total of 2815 patients participated in the research. Patients were followed up from January 2017 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 3 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）.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 Definition

Clinical data were collected from all medical recorded by trained clinicians who blind to the purpose of the study. These included age, gender, duration of diabetes, newly diagnosed diabetes, 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 eject 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. The hemoglobin, FBG, Hemoglobin A1c(HbA1c), total cholesterol

(TC), triglyceride (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) were analyzed. The renal function was assessed by using the baseline estimated glomerular filtration rate (eGFR). Body mass index (BMI) was defined as weight (kg)/height (m^2). Angiographic significant stenosis was defined as >50% diameter stenosis. Multivessel disease was defined as 2 vessels with significant angiographic stenosis. The GRACE score was calculated according to 8 variables including age, SBP, HR, cardiac arrest during presentation, Killip class, ST-segment deviation, serum creatinine, positive cardiac biomarkers. The TyG index was calculated as ln (fasting TG level (mg/dL) ×FBG level (mg/dL)/2).

End points

The primary end point 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. Non-fatal MI referred to MI that did not result in death. Non-fatal stroke referred to stroke that did not result in death. The secondary end points included all-cause death, non-fatal MI, non-fatal stroke.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation when normally distributed, and as medians with interquartile ranges for results not normally distributed. Categorical variables were presented as frequencies. Baseline demographic characteristics, clinical presentation, laboratory findings, extent of CAD, revascularization, and medication data were compared between groups using analysis of variance or Kruskal-Wallis tests for continuous variables, and with chi-square test or Fisher's exact test for categorical variables.

Multivariate linear regression analyses based on stepwise method was performed to reveal the factors associated with the TyG index. Kaplan-Meier event-free survival curves associated with TyG index tertiles were compared using log-rank tests. Possible factors associated with MACE were determined by using univariate Cox regression analysis. Then, variables with significant association (P values <0.10) with MACE were included in multivariate Cox proportional hazards regression analysis as two models. 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 2-sided analysis with a P value <0 .05 was considered significant. All analyses were performed using SPSS version 20.0 (IBM Corp, Armonk, New York) 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%). Patients characteristics are listed in Table 1. The study patients had an average age of 66.3±6.8 and 1415 (55.9%)patients were male. Patients were divided into 3 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 3 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 3 groups in terms of duration of diabetes, previous PCI, previous stroke, BMI, SBP, DBP, HR, GRACE score, mutil-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, ACEI or ARB, and insulin, and no significant difference was found in the other indicators. The associations between TyG index and cardiovascular risk factors were examined using liner regression analysis. As shown in Table2, TyG index levels were positively associated with BMI, hemoglobin A1c (HbA1c) and uric acid and negatively associated with age, male, HDL-C and eGFR in the multivariate liner regression analysis (P <0 .05)

TyG index and cardiovascular events

During 3-year follow-up, 289 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 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, smoker, previous MI, previous CABG, BMI, AMI, LVEF, left main disease, multi-vessel disease, HbA1c, hs-CRP, statin, insulin (P=0.019 for trend). As shown in Figure 1, Kaplan-Meier survival analysis showed that the cumulative incidence of MACE increased with higher tertiles of 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 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 analyses 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.

The ROC analysis showed that the optimal cutoff value of TyG index level for predicting MACE was 9.323 (sensitivity 46.0% and specificity 63.6%), with AUC of 0.560 (95% CI: 0.524-0.595, P=0.001). The incremental predictive value of TyG index for MACE is shown in Table 6. Adding TyG index to the model of established risk factors improved the prediction of MACE (P=0.01). Moreover, the addition of TyG index has 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.

Discussion

This study investigated the association between TyG index and adverse CVEs in patients with diabetes and ACS. The results showed that TyG index was positively associated with increased CVEs. After adjusting for confounding factors, TyG index was independently associated with increased risk of MACE. Furthermore, our results showed that adding 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 TyG index for CVEs in patients with diabetes and ACS. To the best of our knowledge, this study, for the first time, demonstrated TyG index is a potential predictor for adverse CVEs in patients with diabetes and ACS. Most important, the present study suggests that a simple method by estimating IR may optimize the risk stratification of recurrent cardiovascular risk in patients with diabetes and ACS.

IR is a major characteristic of type 2 diabetes and has been recognized as a risk factor for CVD [26]. 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 [27–28]. Therefore, identification of IR will have great clinical signification to improve 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 [29–31]. 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 [32]. 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. TyG index is superior to HOMA-IR for the purpose of predicting IR [7, 8]. Compared with HOMA-IR, TyG index does not require quantification of insulin and may apply to patients treated with insulin. It is well established that TyG index is associated with increased risks of type 2 diabetes and CVD. Moreover, 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 cause of death in patients with diabetes. Therefore, it is necessary to determine whether TyG index predicts future cardiovascular risk in patients with type 2 diabetes and ACS.

However, it is controversial whether TyG index predict cardiovascular outcomes in patients with established type 2 diabetes. Su et al found that TyG index was positively associated with CVEs including MI, UAP, stroke, hospitalization for CAD, peripheral artery disease, and cardiovascular-related death, suggesting that TyG index may be a useful marker for predicting clinical outcomes in 3524 patients with type 2 diabetes and may provide more additional prognostic benefit than HbA1c[33]. Data from Jin et al indicated that TyG index could predict cardiovascular outcomes defined by cardiovascular mortality, non-fatal MI, stroke, post-discharge revascularization and hospitalized UAP and TyG index may have better prognostic value for CVEs than hemoglobin glycation indexes (HGIs) in 1282 type 2 diabetes with new-onset, stable CAD during 3846-person-year follow-up[19]. All these findings suggested that TyG index is strongly correlated with the development of CVD in patients with diabetes. Contrary to these studies, several studies failed to demonstrate any association between TyG index and CVEs. Laura et al demonstrated that TyG index was not associated with a 10-year CVD risk defined by coronary heart disease (CHD), cerebrovascular disease and peripheral arterial disease in 258 subjects with type 2 diabetes [20]. Cho et al. failed to find an independent association between TyG index and CAD or obstructive CAD in 996 established diabetic patients after adjusting for traditional cardiovascular risk factors [35]. The differences in subject selection, event definition or research methods may contribute to the disparity of these results. Of the note, there is a paucity of data on the issue focused on patients with diabetes and ACS.

To our knowledge our study population represents the first cohort of patients with diabetes and ACS in which the association between TyG index and long-term MACE has been investigated. Moreover, our study is the first study to take all-cause death, non-fatal MI, and non-fatal stroke as the composite endpoint events. Our study demonstrated that a higher TyG index was significantly associated with a higher risk of MACE. The higher risk of MACE persisted after adjusting for traditional cardiovascular risk factors, burden of comorbidities, disease severity and medications. We also found that after adjusting for important variables, TyG index remain independently predict adverse cardiovascular outcomes. Thus, our findings extend the findings of previous studies, and highlight the role of TyG index in predicting CVEs [16–19]. In addition, we also identified the optimal cut-off of TyG index for predicting MACE. We found the AUC of the optimal cut-off value 9.456 is poor, suggesting that it is difficult to predict hard endpoint events based on TyG index alone. However, by adding TyG index into established risk factors of MACE, we found a significant improvement in risk prediction in terms of the C-statistic value, NRI and IDI. Although previous studies have showed that a higher TyG index is associated with worse cardiovascular outcomes, none have discriminated the incremental prognostic value of TyG index in terms of hard clinical endpoints. Our study implied that the use of TyG index may refine the risk stratification of cardiovascular risk. Routinely introducing TyG index into clinical practice could more accurately identify patients with higher cardiovascular risk, and therefore a more rational treatment or preventing strategy could be provided.

The exact mechanisms accounting for the association between TyG index and CVEs remain unclear. As a reliable maker of severity of IR, the proatherogenic property may partly account for the association [35, 36]. In the present 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 TyG index and poor prognosis may be explained by the presence of cardiovascular risk factors. Consistent with previous studies [17, 37], TyG index was positively associated with the severity of coronary disease, suggesting that a difference in the extent of coronary atherosclerosis may contribute to the graded TyG index-MACE relationship. In addition, TyG index has been shown to be correlated with micro- and macrovascular damage, such as arterial stiffness, nephric microvascular damage, cardiac autonomic neuropathy, and cerebrovascular disease [38–40], all these conditions known to increase the risk of adverse CVEs. Nevertheless, in the present study, patients with higher TyG index were younger and less likely to have PCI history and prior MI. Therefore, more efforts need to be made to elucidate the exact mechanism on the association between TyG index and CVEs.

Study Limitations

The present study has several potential limitations. First, as the present study was a single-center retrospective study, it is difficult to exclude influence from unmeasured and residual confounding factors. Second, FPG and triglyceride levels were only measured at the baseline.

The levels of FPG and triglyceride might change during follow-up; therefore, it is unknown whether the change of TyG index could predict cardiovascular outcomes. Third, our research did not include HOMA-IR index. Further study on the comparison of the predictive value of TyG index and HOMA-IR needs to be explored. We also did not compare the predictive value of TyG index and HbA1c because only the predictive value of TyG index kept significant when the two variables were in the same model. Fourth, the study was based on Chinese patients; therefore, these results require replications in other ethnic cohorts. Finally, we did not observe significant differences in secondary end points among the TyG index tertiles, which may be attributed to secondary prevention; these treatments may affect the impact of TyG index on MACE. Despite these limitations, the presents study has important clinical implication because it is the first research to investigate the association between TyG index and cardiovascular risk in patients with established diabetes and ACS.

Conclusion

In conclusion, a high TyG index was independently associated with an increased risk of recurrent CVEs in patients with diabetes and ACS. Adding TyG index to the basic model provided has incremental prognostic value for prediction of MACE. These findings suggested that TyG index may be a useful marker for risk stratification and prognosis in patients with diabetes and ACS.

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; 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 eject 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.

Declarations

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Authors' contributions

LW, HLC and JXZ participated in the study design. LW, YCH, AW, YYZ, HY, LBR, WQ, RZ and JHX participated in data collection. LW, HY and LBR performed the statistical analysis. LW drafted the article.

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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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Tables

Table 1 Baseline characteristics of 3 groups

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
Intensive medicine	310(36.7)	249(29.5)	241(28.6)	
PCI	436(51.7)	497(59.0)	514(60.9)	

Table 1 (continued)

Variable	Tertile 1 (n=844)	Tertile 2 (n=843)	Tertile 3 (n=844)	P value
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±1.05	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	108.1(49.7-278.6)	117.8(85.6-170.7)	160.8(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

Data are expressed as mean ± SD, medians with interquartile ranges or percentage.

TyG index triglyceride-glucose index, *MI* myocardial infarction, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass graft, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *LVEF* left ventricle ejection fraction, *GRACE Score* Global Registry of Acute Coronary Events Score, *UAP* unstable angina pectoris, *NSTEMI* non-ST-segment elevation myocardial infarction, *STEMI* ST-segment elevation myocardial infarction, *FBG* fasting blood glucose, *HbA1c* Hemoglobin A1c, *TC* total cholesterol, *TG* triglycerides, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *hs-CRP* high-sensitivity C-reactive protein, *NT-proBNP* N-terminal proB-type natriuretic peptide, *eGFR* estimated glomerular filtration rate, *ACEI* angiotensin II coenzyme inhibitor, *ARB* angiotensin II receptor blocker, *CCB* calcium channel blocker; SD, standard deviation.

Table 2 Univariate and multivariate liner regression analysis for TyG index

Variable	Univariate			Multivariate		
	β	Standard β	P value	β	Standard β	P value
Age	-0.11	-0.114	<0.001	-0.010	-0.106	<0.001
Male	-0.096	-0.075	<0.001	-0.114	-0.089	<0.001
Smoker	0.019	0.015	0.454			
Hypertension	0.016	0.010	0.601			
BMI	0.051	0.235	<0.001	0.046	0.209	<0.001
HbA1c	0.041	0.090	<0.001	0.030	0.065	0.001
LDL-C	0.001	0.002	0.914			
HDL-C	-0.298	-0.138	<0.001	-0.202	-0.094	<0.001
Uric acid	0.001	0.212	<0.001	0.001	0.088	<0.001
hs-CRP	0.001	0.027	0.182			
eGFR	-0.008	-0.295	<0.001	-0.006	-0.226	<0.001

BMI body mass index, *HbA1c* Hemoglobin A1c, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *hs-CRP* high-sensitivity C-reactive protein, *eGFR* estimated glomerular filtration rate

Table 3 Baseline TyG index and Prediction of Cardiovascular Events

End point	Baseline TyG index	Events, n/Total	3-year Event Rate, %	Unadjusted HR (95%CI)	P for trend	Adjusted HR (95%CI)	P for trend
All-cause death	Tertile 1	41/844	4.86	Ref.	0.238	Ref.	0.518
	Tertile 2	45/843	5.34	1.114(0.730-1.701)		1.071(0.694-1.651)	
	Tertile 3	56/844	6.64	1.397(0.934-2.091)		1.266(0.828-1.936)	
Non-fatal MI	Tertile 1	23/844	2.73	Ref.	0.067	Ref.	0.117
	Tertile 2	38/843	4.51	1.680(1.001-2.819)		1.591(0.939-2.697)	
	Tertile 3	40/844	4.74	1.782(1.067-2.976)		1.709(1.006-2.903)	
Non-fatal stroke	Tertile 1	11/844	1.30	Ref.	0.101	Ref.	0.115
	Tertile 2	13/843	1.54	1.200(0.538-2.679)		1.237(0.550-2.781)	
	Tertile 3	22/844	2.61	2.050(0.994-4.227)		2.065(0.983-4.341)	
MACE	Tertile1	75/844	8.89	Ref.	0.005	Ref.	0.019
	Tertile 2	96/843	11.39	1.300(0.961-1.758)		1.267(0.932-1.723)	
	Tertile 3	118/844	13.98	1.611(1.206-2.152)		1.537(1.138-2.076)	

Adjusted variables were age, male, smoker, previous MI, previous CABG, BMI, AMI, LVEF, left main disease, multi-vessel disease, HbA1c, hs-CRP, statin, insulin.

MI myocardial infarction, *MACE* major adverse cardiovascular event, *HR* hazard ratio, *CI* confidential interval

Table 4 Univariate and multivariate Cox regression analysis for predicting MACE

Variables	Univariate			Multivariate		
	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			
Smoker	1.253	0.994-1.581	0.056			
Previous MI	1.807	1.350-2.419	<0.001	1.439	1.048-1.975	0.024
Previous CABG	1.842	1.170-2.901	0.008			
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			
HbA1c	1.077	0.997-1.164	0.061			
hs-CRP	1.009	1.005-1.012	<0.001	1.004	1.000-1.008	0.031
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, *AMI* acute myocardial infarction, *LVEF* left ventricle ejection fraction, *HbA1c* Hemoglobin A1c, *hs-CRP* high-sensitivity C-reactive protein, *HR* hazard ratio, *CI* confidential interval

Table5 Evaluation of Predictive Models for MACE

	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.
Established risk factors+TyG index	0.677(0.644-0.711)	0.010	0.147(0.025-0.270)	0.019	0.090(0.004-0.014)	0.001

TyG index triglyceride-glucose index, *MACE* major adverse cardiovascular event, *NRI* net reclassification improvement, *IDI* integrated discrimination improvement

Figures

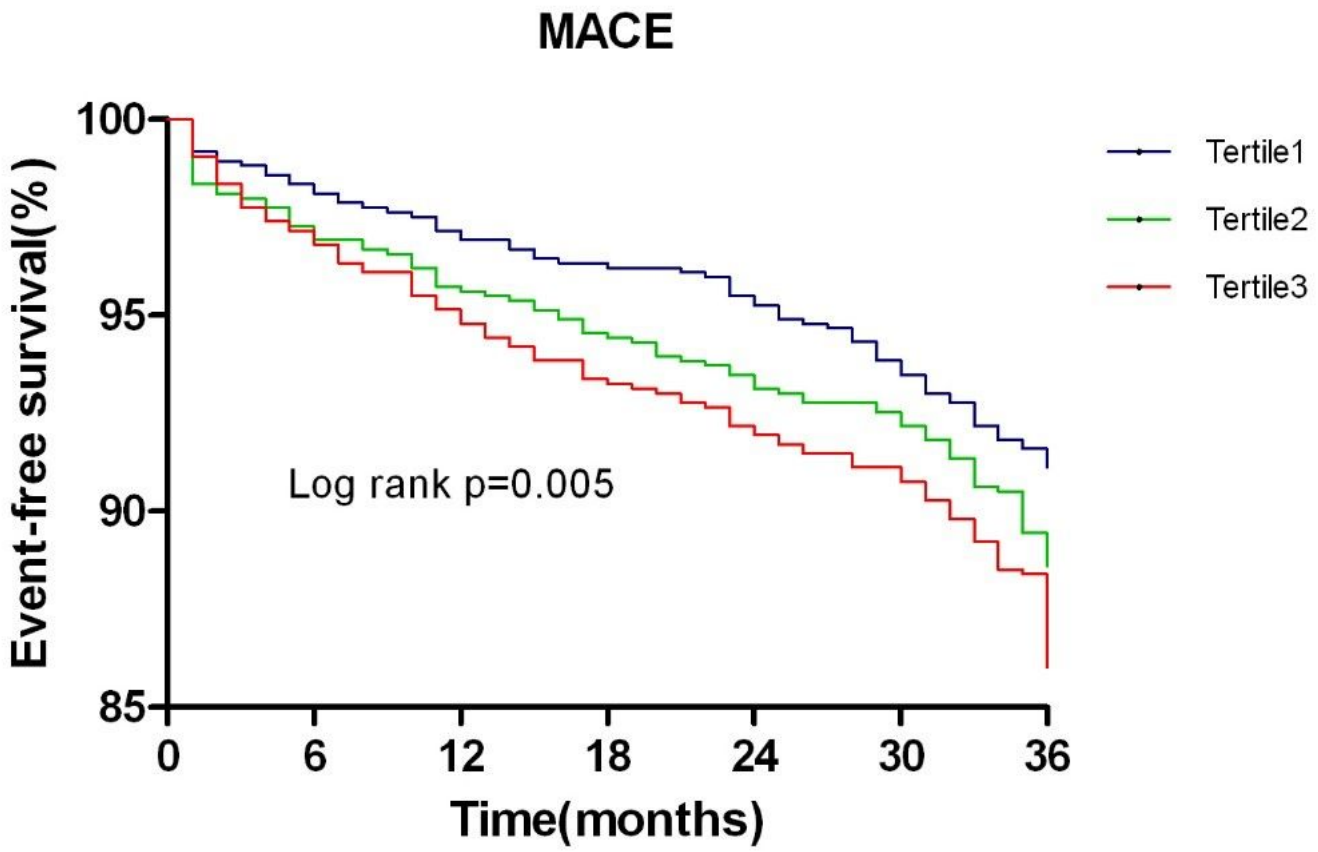

Figure 1

Kaplan-Meier survival curve for MACE（major adverse cardiovascular events） across TyG index tertiles.