High Triglyceride-Glucose Index (TyG) is Associated With Adverse Cardiovascular Events in Patients With Type 2 Diabetes Mellitus (T2DM) and Chronic Total Occlusion (CTO) After Percutaneous Coronary Intervention (PCI)

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Research

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Abstract

Background: The triglyceride-glucose index (TyG index) is a reliable surrogate marker of insulin resistance, which is associated with cardiovascular disease morbidity and prognosis. However, the predictive value of the TyG index for cardiovascular events in patients with type 2 diabetes mellitus (T2DM) and chronic total occlusion (CTO) after percutaneous coronary intervention (PCI) has not been specifically studied.

Method: The study retrospectively enrolled 687 patients with T2DM and CTO after PCI in the final analysis. Patients were divided into three groups according to the TyG index tertiles. The TyG index was calculated as ln [fasting triglyceride (mg/dL) × fasting glucose (mg/dL)/2]. The primary observational endpoint was the composite of overall death, non-fatal stroke, non-fatal myocardial infarction (MI), or unplanned revascularization.

Results: During a median follow-up of 22.0 months, 159 patients (23.14%) experienced primary endpoint events. Multivariate Cox hazards regression analysis showed that the TyG index was significantly correlated with the primary endpoint [HR 2.827, 95% CI (1.877-4.529), P＜0.001]. Kaplan–Meier curves for the primary endpoint showed a significant difference between the lower and higher TyG index group was mainly driven by the increased incidence of unplanned revascularization (Log-rank P＜0.001).

Conclusion: The TyG index may be a remarkable predictor of adverse cardiovascular events, especially unplanned revascularization in patients with T2DM and CTO who are treated by PCI.

Introduction

Coronary artery disease (CAD) has one of the highest morbidity and mortality in the world. By 2030, according to data from the World Health Organization (WHO), the number of cardiovascular events in China will increase by about 73% [1]. AS we know, Type 2 diabetes mellitus (T2DM) is a traditional risk factor of cardiovascular disease [2], chronic total occlusion (CTO) in type 2 diabetes mellitus (T2DM) patients is very common. Previous studies showed that this proportion is up to 34-40% [3, 4]. CTO with T2DM patients have more diffuse, anatomically complex coronary artery lesions and was associated with poor clinical outcomes. In clinical practice, we found that the poor prognosis of CTO with T2DM patients was different from those of common coronary heart disease, it is mainly reflected in ischemic heart disease, which leads to the occurrence of heart failure. Even if CTO vessels are successfully opened and coronary stents are implanted, Adverse cardiovascular events will still occur. At present, which indicators can predict the occurrence of cardiovascular events in T2DM patients with CTO after PCI is unknown. Therefore, it is essential to find a reliable method to identify the high-risk occurrence of MACE patients to provide intensive treatment.

The progression of insulin resistance not only leads to cardiovascular disease in patients with or without diabetes but also correlates with cardiovascular outcomes in patients with cardiovascular disease (CVD) [5, 6]. TyG is a novel, convenient and inexpensive test to determine insulin resistance, which only needs to

detect fasting glucose and triglyceride. It has been proved to be a significant correlation with HOMR which is used as a clinically useful surrogate measure of insulin resistance [7].

Many studies have shown that the TyG index is associated with cardiovascular disease morbidity and prognosis [8–11]; However, the prognostic value of the TyG index for cardiovascular events in patients with T2DM and CTO after PCI has not been specifically studied. In this sense, we studied the relationship between baseline TyG and cardiovascular outcomes in patients with T2DM and CTO who underwent PCI.

Methods

Study population

The present study is a single-center, retrospective observational cohort study. From January 2018 to December 2019, 687 consecutive patients with T2DM who were diagnosed with CTO and treated with PCI at Beijing An Zhen hospital were enrolled. The exclusion criteria were as follows: (1) Missing clinical data or follow-up data; (2) A prior coronary artery bypass grafting (CABG); (3) Left ventricular ejection fraction (LVEF) < 30%; (4) Renal dysfunction with estimated glomerular filtration rate (eGFR) < 30ml/(min*1.7□) or kidney dialysis; (5) Extreme body mass index (BMI >45kg/□) and suspected familial hypertriglyceridemia [plasma TGs ≥ 500mg/dl (5.65mmol/L)]; (6) PCI failure or PCI-related complications; (7) Patients with a malignant tumor or other chronic diseases.

Data collection and definitions

Patients' data of demographic, clinical, and angiographic characteristics were collected from the medical information recording system of Beijing An Zhen Hospital.

The blood samples were collected after an overnight fast on admission and analyzed quickly after sampling. The routine hematology and biochemical parameters, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein-C (LDL-C), high-density lipoprotein-C (HDL-C), FBG, glycosylated serum albumin, serum uric acid, serum creatinine, estimated glomerular filtration rate, and other biomarkers, were determined by standard laboratory methods in the central lab of Beijing Anzhen Hospital. The TyG index was calculated as the ln (fasting TG level [mg/dL] × FBG level [mg/dL]/2) [12]. CTO was defined as a coronary arterial total occlusion with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 and the duration of occlusion ≥3 months [13]. Overall death was defined as cardiovascular or non-cardiovascular causes. Unplanned revascularization was defined as the revascularization of the target vessel or non-target vessel.

Follow-up details

All patients were followed up every 6 months after baseline PCI. The follow-up period of this study lasted December 2020. The information about adverse events was obtained by trained professionals contacting patients or their families by telephone, who did not understand the baseline characteristics and were determined by carefully reviewing the corresponding medical records.

Endpoints

The primary observational endpoint was the composite of overall death, non-fatal stroke, non-fatal myocardial infarction (MI), or unplanned revascularization.

Statistical analysis

Continuous variables were presented as the mean±standard deviation is consistent with a normal distribution, otherwise as to the median and interquartile range (IQR). Categorical variables were expressed as numbers and percentages. The ANOVA or Kruskal-Wallis tests were used to analyze differences in continuous variables. The Pearson chi-square test (Pearson X^2 test) or Fisher's exact test was used to analyze categorical variables. The correlation between the TyG index and traditional cardiovascular risk factors was evaluated by Pearson correlation analysis. Receiver-operating characteristic (ROC) curve analysis was used to predict the value of the TyG index for the primary endpoint. The Kaplan–Meier survival analyses were performed to evaluate the incidence rate of primary endpoint between groups according to the TyG index tertiles, and otherness between groups was evaluated by a log-rank test. Variables with a univariate P value <0.05 were selected for multivariate analysis. Multivariate cox proportional hazards regression analysis to estimate whether TyG is a predictor of adverse cardiovascular events and to identify other factors related to outcome in patients with T2DM and CTO who were treated by PCI. The predictive value of the TyG index for each component of the primary endpoint was also evaluated by univariate and multivariate Cox regression analysis. Since the TyG index was calculated according to FBG and TGs, these two variables were not taken into multivariate analysis. All statistical analysis results were two-tailed and a p-value <0.05 was regarded as statistically significant. Data were analyzed by IBM SPSS statistics 24.

Result

As shown in Figure.1, Six hundred and eighty-seven patients (mean age: 59.1 ± 9.8 years; 82.82% men) were enrolled in the final analysis. Throughout a median of 22.0 months follow-up, 20 patients (of the total population) were lost to follow-up. 159 (23.14%) patients intimate primary terminus events, as well as 10 (1.46%) overall cause death, 30 (4.41%) non-fatal MI, and 109 (15.87%) unplanned revascularization.

Baseline characteristics of patients

According to the TyG index tertiles, baseline characteristics of groups were presented in Table 1. As TyG index elevated, body mass index, TGs, TC, LDL-C, uric acid, FBG, Glycosylated serum protein (GA), and Insulin used significantly increased, while HDL-C levels and the number of LAD lesions were decreased. The ROC curves of the triglyceride-glucose index as a marker to predict the primary endpoint in CTO patients after PCI were presented in Figure.2. The AUC of the TyG index for forecasting the occurrence of the primary endpoint in CTO patients was 0.623 (95% CI 0.575–0.671; P□0.001). The baseline characteristics of the groups stratified by the primary endpoint are shown in Table 2. Compared

with the without events group, the Primary endpoint group had a higher proportion of males, smoking, drinking, Previous MI, Past PCI, Previous Stroke, and had higher Uric acid, FPG, TyG index, TC, TG, LDL, lower blood pressure. In these variables, Only FBG, TGs, TyG index, Uric acid were independently associated with the primary endpoint group. The other variables were no statistical significance.

The TyG index had a higher correlation with traditional cardiovascular risk factors

The result of the Pearson correlation analysis of the correlation between the TyG index and traditional cardiovascular risk factors is shown in Table 3. TyG index had a higher correlation with BMI, Glycosylated serum protein (GA), TGs, FBG, LDL-C, TC, uric acid, and negatively associated with Age, HDL-C, and LVEF (all $P < 0.05$).

The TyG index was significantly correlated with the primary endpoint

The univariate and multivariate Cox proportional hazard analysis for the primary endpoint is shown in Table 4. The univariate analysis showed that TyG index, Previous MI, TGs, FPG, oral P2Y12 inhibitors agent, uric acid, insulin injection were risk factors for adverse cardiovascular events in patients with T2DM and CTO after PCI (all P□0.05). To determine whether TyG is an independent risk factor for adverse cardiovascular events and to identify other factors related to outcome, We performed a multivariate analysis. After adjusting variables with a univariate P value□0.05, Multivariate analysis revealed that both the TyG index and oral P2Y12 inhibitors agent were significantly correlated with the primary endpoint (P□ 0.05). The incidence of the primary endpoint and each component according to the TyG index tertiles is shown in Table 5. Compared with the Q1 group, Both the primary endpoint and unplanned repeat revascularization increased significantly in Q2, Q3 group (chi-square $P < 0.001$), while the overall death, non-fatal stroke, non-fatal MI were without Statistical significance between the three groups. To further verify the reliability and stability of the results, we evaluated the predictive value of the TyG index as a nominal and continuous variable respectively for each component of the primary endpoint by univariate and multivariate Cox proportional hazard analysis. In univariate analysis, TyG index as a nominal and taking Q1 as the reference□the result showed that Q2, Q3 group were associated with the primary endpoint (Q2: HR 1.675, 95% CI 1.081-2.596, P= 0.021; Q3: HR 2.827, 95% CI 1.877-4.529, P□0.001;) and Q3 group was associated with unplanned revascularization (Q2: HR 1.535 95% CI 0.882-2.672, P= 0.129; Q3: HR 3.115, 95% CI 1.888-5.139, P□0.001;). However, the higher TyG index is unable to predict the overall death, non-fatal stroke, and non-fatal MI. After adjusting for age, gender, and other confounding factors, Multivariate analysis showed that the incidence of the primary endpoint (Q2: HR 1.778 95% CI 1.124-2.813, P= 0.014; Q3: HR 3.199, 95% CI 2.000-5.118, P□0.001;) and unplanned repeat revascularization (Q2: HR 1.610 95% CI 0.900-2.883, P= 0.109; Q3: HR 3.743, 95% CI 2.113-6.63, P□ 0.001;) were increased as the TyG increase, while the Q2 and Q3 group fail to predict the overall death, non-fatal stroke and non-fatal MI. When the TyG index was a continuous variable, either the univariate or multivariate analysis, the result was similar to the TyG index as a nominal variable (Table 5).

The higher TyG index group is significantly associated with the primary endpoint and unplanned revascularization.

Kaplan–Meier curves for the incidence of primary endpoint and each component of it according to the TyG index tertiles were shown in Figure.3. Kaplan–Meier curves showed that the Q3 group had a higher risk for the primary endpoint (Fig.3a, Log-rank P < 0.001) and unplanned revascularization (Fig.3d, Log-rank P < 0.001). However, there is no statistical significance for overall-cause death (Fig. 3b, Log-rank P =0.88), non-fatal myocardial infarction (Fig.3c, Log-rank P =0.27), and non-fatal stroke (Fig. 3e, Log-rank P =0.73) between the three groups.

Discussion

The presence of CTO lesions is the strongest independent predictor of incomplete revascularization among patients treated with PCI [14]. Patients with T2DM and incomplete revascularization have an increased risk of long-term cardiovascular events including death, MI, stroke, and repeat revascularization [15]. Although CTO vessels are successfully opened, Diabetic patients remain at increased risk for adverse cardiovascular events following PCI, driven by higher rates of target lesion revascularization (TLR) [16]. Our study sought a novel method to identify the high-risk occurrence of MACE in T2DM patients with CTO undergoing PCI.

Our main findings include: (1) TyG is significantly associated with the primary endpoint, which was composed of non-fatal myocardial infarction, non-fatal stroke, overall death, and unplanned revascularization in T2DM patients with CTO after PCI. (2) TyG is correlated with multiple cardiovascular disease risk factors. (3) The predictive effect of the TyG index on the compound primary endpoint was mainly reflected in the unplanned revascularization.

Diabetes is a major risk factor for cardiovascular disease, which is common in patients with CTO. But Only 35% of the additional cardiovascular risk caused by T2DM is mediated by traditional cardiovascular risk factors. The most enormous mediating effect is insulin resistance [17]. Insulin resistance is a major component of metabolic syndrome, type 2 diabetes, and cardiovascular disease (CVD) [18]. The gold standard for measuring insulin resistance is the hyperinsulinemic-euglycemic glucose clamp technique which is mainly used in clinical research to limit its clinical application. Homoeostasis model assessment (HOMA) and QUICKI were widely used as clinically useful surrogate insulin resistance measures [18]. However, it costs a lot of money, takes a long time to test, and insulin level is not a routine clinical test, which can’t be used in a wide range of clinical applications. Therefore, convenient and inexpensive tests are needed to determine insulin resistance. TyG is a novel surrogate marker of insulin resistance, which only detects fasting glucose and triglyceride. It has been proved to be a significant correlation with HOMR [21], but it is faster, more convenient, and less expensive than HOMR.

The mechanism of cardiovascular disease caused by insulin resistance can be summarized into three aspects. (i) Insulin signaling is key to the activation of nitric oxide, an effective vasodilator dose, and anti-atherosclerosis [22, 23], Insulin resistance leads to impaired insulin signaling, which leads to high blood pressure and atherosclerosis. (ii) Insulin resistance causes compensatory hyperinsulinemia, Hyperinsulinemia can stimulate the synthesis and secretion of very-low-density lipoprotein (LDL) [24],

stimulate vascular smooth muscle cell proliferation [25], promote the release of inflammatory factors [26], and enhance LDL cholesterol transport to arterial smooth muscle cells [27]. (iii) Insulin resistance is associated with Metabolic syndrome, Each component of the Metabolic syndrome is an independent risk factor for ASCVD [28].

Many studies have shown that the TyG index is associated with cardiovascular disease morbidity and prognosis. Da, S.A. et al. evaluated the correlation between the TyG index and coronary artery disease, as well as cardiovascular risk factors, showed that the TyG index was positively correlated with a higher prevalence of symptomatic CAD, which could be used as a marker for atherosclerosis [8]. The study from Luo et al. enrolled 1092 STEMI patients after PCI to assess the role of the TyG index as a predictor of prognosis in STEMI patients after PCI. According to the TyG index, The patients were divided into 4 quartiles. The results suggested that the TyG index might be an effective predictor of clinical outcomes in STEMI patients undergoing PCI (HR 1.529 95% CI 1.001-2.061; P = 0.003) [9]. Another observational study from Mao et al. showed that TyG index was not only an independent predictor of coronary artery severity and cardiovascular disease prognosis in patients with acute non-ST-segment elevation myocardial infarction but also had strongly independently associated with SYNTAX score (OR 6.055, 95% CI 2.915-12.579, $P < 0.001$) [10]. A recent study from Ma, X., et al. included 776 patients with T2DM and ACS who underwent PCI to research the prognostic usefulness of the TyG index in patients with T2DM and ACS after PCI. The result suggested that TyG may be a valuable predictor of adverse cardiovascular outcomes after PCI in patients with T2DM and ACS [11]. Previous research had also shown that the TyG index was a significant correlation with subclinical CAD in healthy individuals [29], the progression of coronary artery calcification [30–32], the macro-and microvascular damage [33], the arterial stiffness [34], hypertension [35], the number and the severity of artery stenoses [36]. However, the effects of the TyG index on cardiovascular prognosis in T2DM patients with CTO after PCI are still unclear.

Our study showed that the major MACE rates among T2DM patients with CTO after PCI were caused by unplanned revascularization, which is consistent with the Sohrabi et al. study[37], and the higher TyG is a significant correlation with unplanned revascularization. We found that the TyG index was a positive correlation with BMI, GA, LDL-C, TC, uric acid, and was negatively associated with HDL-C. Furthermore, these variables were significantly higher in patients in the Q3 group than Q1, Q2 group. These factors are traditional risk factors for cardiovascular disease, which partly explains why TyG can predict cardiovascular disease outcome events.

Limitation

This study had several limitations. First, this study was a single-center, retrospective study, which may have a selection bias or potential confounding factors. Meanwhile, the small sample size of this study may weaken the conviction of the results. Second, the experimental parameters were only measured at admission, and the dynamic changes of TyG were not monitored during the follow-up period, which may result in measurement bias. Third, Some patients have used lipid-lowering and hypoglycemic drugs before admission, which may affect the results of triglyceride and fasting blood glucose. Fourth, We did

not routinely calculate the SYNTAX score, so we did not evaluate the correlation between the TYG index and syntax score.

Conclusion

The TyG index, which is a novel, simple and reliable surrogate marker of insulin resistance, maybe a remarkable predictor of adverse cardiovascular events, especially revascularization in type 2 diabetic patients after CTO PCI. Further prospective, large, multicenter studies are needed to confirm our findings.

Abbreviations

Type 2 Diabetes Mellitus, T2DM; Chronic Total Occlusion, CTO; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TGs, triglycerides; FBG, fasting blood glucose; GA, glycated albumin; TyG, triglyceride glucose; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, Calcium Channel Blockers; LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery LVEF, left ventricular ejection fraction; HR, hazard ratio; CI, confidence interval.

Declarations

Ethics approval and consent to participate

The present study was performed by the Helsinki Declaration of Human Rights and approved by the Clinical Research Ethics Committee of Beijing An Zhen Hospital, Capital Medical University. Given the retrospective nature of this study, and written informed consent was obtained from all patients.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests:

The authors declare no potential conflict of interest.

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Authors' contributions:

XLL takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. QF, XLL takes responsibility for research design. HXS, JYZ, FQ, take responsibility for data collection. DHZ QM JHL takes responsibility for the data review. All authors read and approved the final manuscript.

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Tables

Table 1 Baseline clinical characteristics of patients according to the TyG index tertiles

Note:Values are presented as the mean±SD, median (IQR) or number (%).

The groups were stratified by tthe TyG index tertiles

Abbreviation:BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CKD,chronic kidney disease; LVEF, left ventricular ejection fraction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TGs, triglycerides; FBG, fasting blood glucose; GA, glycated albumin; TyG, triglyceride glucose; eGFR, estimated glomerular filtration rate; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, Calcium Channel Blockers; LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 2 Baseline clinical characteristics of patients stratified by the primary ednpoint

Table 2 (continues)

Note:Values are presented as the mean±SD, median (IQR) or number (%).

Abbreviation:BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CKD,chronic kidney disease; LVEF, left ventricular ejection fraction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TGs, triglycerides; FBG, fasting blood glucose; GA, glycated albumin; TyG, triglyceride glucose; eGFR, estimated glomerular filtration rate; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, Calcium Channel Blockers; LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 3 Correlations between the TyG index and traditional cardiovascular risk factors

Abbreviation:BMI, body mass index; FBG, fasting blood glucose; GA, glycated albumin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; TGs, triglycerides;

Table 4 Relationship between the incidence of the primary endpoint and the TyG index

Abbreviation:BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; CKD,chronic kidney disease; LVEF, left ventricular ejection fraction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TGs, triglycerides; FBG, fasting blood glucose; GA, glycated albumin; TyG,

	Q1 (n=229)	Q2 (n=229)	Q3 (n=229)	P value
Demographics				
Age,years	60.25±9.59	58.70±10.07	58.41±9.72	0.097
Male Sex,n□%□	191 (83.4)	194 (84.7)	184 (80.3)	0.446
BMI,kg/m²	25.37±3.15	26.82±3.13	27.18±3.15	<0.001
Medical measurements				
SBP,mmHg	128±16	128±16	128±15	0.930
DBP,mmHg	76±11	76±10	77±10	0.506
Risk factors				
Smoking,n(%)	0.52 (0.50)	0.53 (0.50)	0.54 (0.50)	0.895
drinkers,n(%)	67 (29.3)	62 (27.1)	58 (25.3)	0.639
Hypertension,n(%)	154 (67.2)	152 (66.4)	164 (71.6)	0.434
Dyslipidaemia,n(%)	165 (72.1)	160 (69.9)	154 (67.2)	0.534
Previous MI,n(%)	64 (27.9)	56 (24.5)	73 (31.9)	0.209
Past PCI,n(%)	77 (33.6)	74 (32.3)	87 (38.0)	0.409
Previous Stroke,n(%)	24 (10.5)	17 (7.4)	24 (10.5)	0.435
CKD,n(%)	3 (1.3)	6 (2.6)	8 (3.5)	0.318
LVEF(%)	61±8	59±9	59±8	0.010
Laboratory findings				
TC (mg/dL)	138.79±35.81	147.82±40.68	158.72±39.77	<0.001
LDL-C (mg/dL)	81.14±32.68	88.13±36.06	89.00±32.44	0.024
HDL-C (mg/dL)	38.22±13.81	38.21±14.04	36.62±11.94	0.332
Triglycerides (mg/dL)	88.0(67.0,104.0)	143.0(121.0,163.0)	212.0(160.0,282.0)	<0.001
FPG (mg/dL)	98.0(91.0,111.0)	112.0(98.0,134.0)	155.0(123.0,201.0)	<0.001
GA, %	15.0(13.0,17.0)	16.0(14.0,18.0)	18.0(15.0,22.0)	<0.001
TyG index	8.0(8.0,9.0)	9.0(9.0, 9.0)	10.0(9.0,10.0□	<0.001
eGFR, mL/min	94.92±16.63	93.52±15.62	95.09±15.93	0.516
Uric acid,umol/L	346.21±82.30	372.78±96.68	371.91±91.90	0.002

Medications at discharge				
Aspirin, n (%)	228 (99.6)	225 (98.3)	229 (100.0)	0.073
P2Y12 inhibitors, n (%)	145 (63.3)	153 (66.8)	162 (70.7)	0.240
Statin,n(%)	177 (77.3)	179 (78.2)	191 (83.4)	0.214
ACEI/ARBs, n (%)	75 (32.8)	71 (31.0)	82 (35.8)	0.543
β-blockers, n (%)	113 (49.3)	116 (50.7)	137 (59.8)	0.050
Insulin, n (%)	13 (5.7)	19 (8.3)	35 (15.3)	0.002
CCB,n(%)	32 (14.0)	23 (10.0)	31 (13.5)	0.379
Angiographic findings				
One-vessel disease,n(%)	51 (22.3)	42 (18.3)	41 (17.9)	0.430
Two-vessel disease,n(%)	64 (27.9)	54 (23.6)	62 (27.1)	0.531
three-vessel disease,n(%)	114 (49.8)	130 (56.8)	125 (54.6)	0.308
Target vessel territory				
LAD, n (%)	104 (45.4)	87 (38.0)	77 (33.6)	0.033
LCX, n (%)	41 (17.9)	51 (22.3)	47 (20.5)	0.504
RCA, n (%)	120 (52.4)	133(58.1)	134 (58.5)	0.339

triglyceride glucose; eGFR, estimated glomerular filtration rate; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, Calcium Channel Blockers; LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 5 Incidence of primary endpoint and each compenents according to the TyG index tertiles

Note: The groups were stratified by the TyG index tertiles

Abbreviation: TyG triglyceride glucose, MI myocardial infarction

Table 6 Univariable and Multivariable Cox regression analysis of Primary endpoint

	Without events (n=528)	Primary endpoint (n=159)	P value
Demographics			
Age,years	59.02±9.49	59.44±10.84	0.640
Male Sex,n□%□	434 (82.2)	135 (84.9)	0.500
BMI,kg/m²	26.42±3.28	26.59±3.10	0.552
Medical measurements			
SBP,mmHg	128.08±16.14	127.70±14.31	0.793
DBP,mmHg	76.48±10.71	75.01±9.60	0.613
Risk factors			
Smoking,n(%)	273 (51.7)	91 (57.2)	0.257
drinkers,n(%)	141 (26.7)	46 (28.9)	0.652
Hypertension,n(%)	363 (68.8)	107 (67.3)	0.804
Dyslipidaemia,n(%)	362 (68.6)	117 (73.6)	0.267
Previous MI,n(%)	137 (25.9)	56 (35.2)	0.029
Past PCI,n(%)	181 (34.3)	57 (35.8)	0.788
Previous Stroke,n(%)	47 (8.9)	18 (11.3)	0.448
CKD,n(%)	13 (2.5)	4 (2.5)	0.970
LVEF(%)	60±8.0	59±10.0	0.100
Laboratory findings			
TC (mg/dL)	147.70±39.47	150.91±40.06	0.372
LDL-C (mg/dL)	85.78±33.87	87.11±34.1	0.667
HDL-C (mg/dL)	37.71±13.01	37.59±14.24	0.923
Triglycerides (mg/dL)	132.0 (91.0,178.0)	147.0 (121.0,203.0)	<0.001
FPG (mg/dL)	111.0 (96.0,143.3)	127.0 (99.5,166.0)	<0.001
GA, %	16.0 (14.0,19.0)	16.0 (14.0,19.0)	0.517
TyG index	8.96±0.65	9.25±0.63	<0.001
eGFR, mL/min	94.75±15.70	93.71±17.22	0.476
Uric acid,umol/L	358.65±88.12	380.19±99.25	0.009
Medications at discharge			

Aspirin, n (%)	524 (99.2)	158 (99.4)	0.867
P2Y12 inhibitors, n (%)	347 (65.7)	113 (71.1)	0.246
Statin,n(%)	424 (80.3)	123 (77.4)	0.487
ACEI/ARBs, n (%)	175 (33.1)	53 (33.3)	0.965
β-blockers, n (%)	278 (52.7)	88 (55.3)	0.613
Insulin, n (%)	47 (8.9)	20 (12.6)	0.223
CCB,n(%)	64 (12.1)	22 (13.8)	0.663
Angiographic findings			
One-vessel disease,n(%)	98 (18.6)	36 (22.6)	0.306
Two-vessel disease,n(%)	144 (27.3)	36 (22.6)	0.289
three-vessel disease,n(%)	284 (53.8)	85 (53.5)	0.942
Target vessel territory			
LAD, n (%)	198 (37.5)	70 (44.0)	0.166
LCX, n (%)	110 (20.8)	29 (18.2)	0.548

	Without events (n=528)	Primary endpoint (n=159)	P value
RCA, n (%)	302 (57.2)	85 (53.5)	0.458

	Correlation coefficient	P value
Age	-1.06	0.006
BMI	0.268	<0.001
FBG	0.633	<0.001
GA	0.260	<0.001
TG	0.820	<0.001
TC	0.233	<0.001
LDL-C	0.097	0.011
HDL-C	-0.072	0.058
Uric acid	0.143	<0.001
eGFR	-0.005	0.892
LVEF	-0.080	0.036

	Univariate analsis HR (95% CI)	P value	Multivariate analsis HR (95% CI)	P value
TyG index tertiles				
Q1	Reference		Reference	
Q2	1.675 (1.081-2.596)	0.021	1.601 (1.031-2.486)	0.036
Q3	2.827 (1.877-4.259)	<0.001	2.560 (1.684-3.892)	< 0.001
Age,years	1.007 (0.991-1.023)	0.423		
Male Sex	1.181 (0.765-1.823)	0.453		
BMI,kg/m²	1.022 (0.974-1.073)	0.370		
SBP,mmHg	0.999 (0.989-1.009)	0.824		
DBP,mmHg	0.995 (0.981-1.010)	0.532		
Smoking,n(%)	1.167 (0.853-1.598)	0.334		
drinkers,n(%)	1.057 (0.750-1.490)	0.751		
Hypertension,n(%)	0.945 (0.678-1.316)	0.738		
Dyslipidaemia,n(%)	1.403 (0.986-1.998)	0.060		
Previous MI,n(%)	1.421 (1.026-1.967)	0.034	1.346 (0.968-1.870)	0.077
Past PCI,n(%)	1.180 (0.853-1.632)	0.318		
Previous Stroke,n(%)	1.283 (0.786-2.096)	0.319		
CKD,n(%)	0.890 (0.329-2.402)	0.817		
LVEF(%)	0.984 (0.967-1.000)	0.050		
TC (mg/dL)	1.000 (0.997-1.004)	0.856		
LDL-C (mg/dL)	0.999 (0.995-1.004)	0.701		
HDL-C (mg/dL)	1.000 (0.988-1.011)	0.969		
GA, %	1.001 (0.973-1.029)	0.947		
eGFR, mL/min	0.995 (0.986-1.004)	0.289		
Uric acid,umol/L	1.002 (1.000-1.003)	0.024	1.001(0.999-1.003)	0.230
Aspirin, n (%)	1.053 (0.147-7.522)	0.959		
P2Y12 inhibitors, n (%)	1.681 (1.189-2.376)	0.003	1.584 (1.119-2.244)	0.010
Statin,n(%)	1.085 (0.747-1.576)	0.670		

ACEI/ARBs, n (%)	1.104 (0.793-1.536)	0.558		
β-blockers, n (%)	1.122 (0.821-1.534)	0.470		
Insulin, n (%)	1.789 (1.118-2.864)	0.015	1.371 (0.849-2.216)	0.197
CCB,n(%)	1.330 (0.847-2.088)	0.215		
Angiographic findings				
One-vessel disease,n(%)	1.229 (0.848-1.782)	0.277		
Two-vessel disease,n(%)	0.787 (0.543-1.141)	0.206		
three-vessel disease,n(%)	1.016 (0.744-1.388)	0.919		
Target vessel territory				
LAD, n (%)	1.229 (0.899-1.682)	0.196		
LCX, n (%)	0.901 (0.602-1.347)	0.610		
RCA, n (%)	0.867 (0.635-1.184)	0.370		

	Q1 (n=229)	Q2 (n=229)	Q3 (n=229)	P value
Primary endpoint, n (%)	33 (14.4)	51(22.3)	75 (32.8)	<0.001
Overall death, n (%)	3 (1.3)	3 (1.3)	4 (1.7)	0.904
Non-fatal stroke, n (%)	4 (1.7)	6 (2.6)	5 (2.2)	0.815
Non-fatal MI, n (%)	7 (3.1)	10 (4.4)	13 (5.7)	0.390
Unplanned revascularization, n (%)	21 (9.2)	31 (13.5)	57 (24.9)	<0.001

	Univariable analysis		Multivariable analysis[c]	
	HR (95%CI)	P value	HR (95%CI)	P value
TyG index as a nominal variable[a]				
Primary endpoint				
Q1	Reference	-/-	Reference	-/-
Q2	1.675 (1.081-2.596)	0.021	1.778 (1.124-2.813)	0.014
Q3	2.827 (1.877-4.529)	<0.001	3.199 (2.000-5.118)	<0.001
Overall death				
Q1	Reference	-/-	Reference	-/-
Q2	1.022 (0.206-5.062)	0.979	0.478 (0.032-7.032)	0.590
Q3	1.392 (0.12-6.221)	0.665	0.293 (0.013-6.727)	0.442
Non-fatal stroke				
Q1	Reference	-/-	Reference	-/-
Q2	1.735 (0.487-6.179)	0.295	1.501 (0.340-6.627)	0.592
Q3	1.363 (0.365-5.084)	0.645	0.958 (0.193-4.752)	0.959
Unplanted repeat revascularization				
Q1	Reference	-/-	Reference	-/-
Q2	1.535 (0.882-2.672)	0.129	1.610 (0.900-2.883)	0.109
Q3	3.115 (1.888-5.139)	<0.001	3.743 (2.113-6.630)	<0.001
Non-fatal MI				
Q1	Reference	-/-	Reference	-/-
Q2	1.507 (0.573-3.959)	0.406	1.668 (0.588-4.729)	0.336
Q3	2.090 (0.834-5.238)	0.116	1.970 (0.676-5.741)	0.214

TyG index as a continuous variable[b]				
Primary endpoint	1.833 (1.466-2.293)	<0.001	2.168 (1.599-2.940)	<0.001
Overall death	1.698 (0.694-4.152)	0.246	0.783 (0.115-5.349)	0.803
Non-fatal stroke	1.153 (0.545-2.437)	0.710	0.920 (0.315-2.688)	0.879
Unplanned revascularization	1.919 (1.467-2.511)	<0.001	2.320 (1.609-3.346)	<0.001
Non-fatal MI	1.671 (0.992-2.816)	0.054	1.935 (0.944-3.967)	0.072

TyG triglyceride glucose, MI myocardial infarction, HR hazard ratio, CI confidence interval

a The HR was examined regarding Q1 group as reference (stratified by the TyG index tertiles)

b The HR was examined by per 1-unit increase of TyG index

c The multivariate analysis was adjusted for age, male, BMI, SBP, DBP, smoking, drinkers, Hypertension, dyslipidemia, previous MI, past PCI, previous stroke, CKD, LVEF, TC, LDL-C, HDL-C, eGFR, Uric acid, GA, Aspirin, P2Y12 inhibitors, Statin, ACEI/ARBs, β-blockers, Insulin, CCB, One-vessel disease, Two-vessel disease, three-vessel disease, LAD treatment, LCX treatment, RCA treatment.

Figures

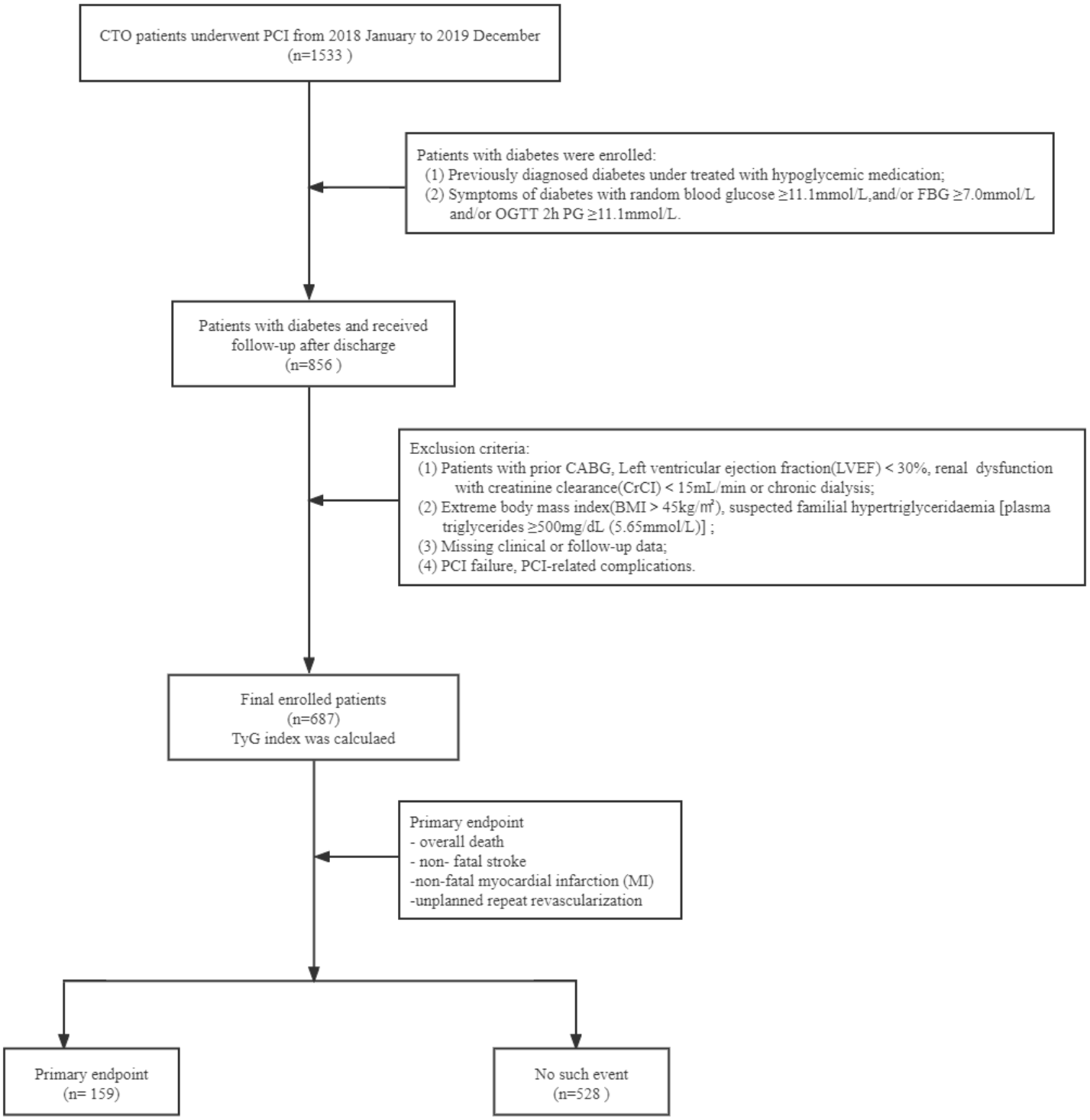

Figure 1

The flow chart of study population enrollment. CTO□chronic total occlusion; PCI percutaneous coronary intervention; FBG, fasting blood glucose; OGTT, Oral glucose tolerance test; CABG coronary artery bypass grafting, TGs triglycerides; BMI: body mass index, TyG triglyceride glucose.

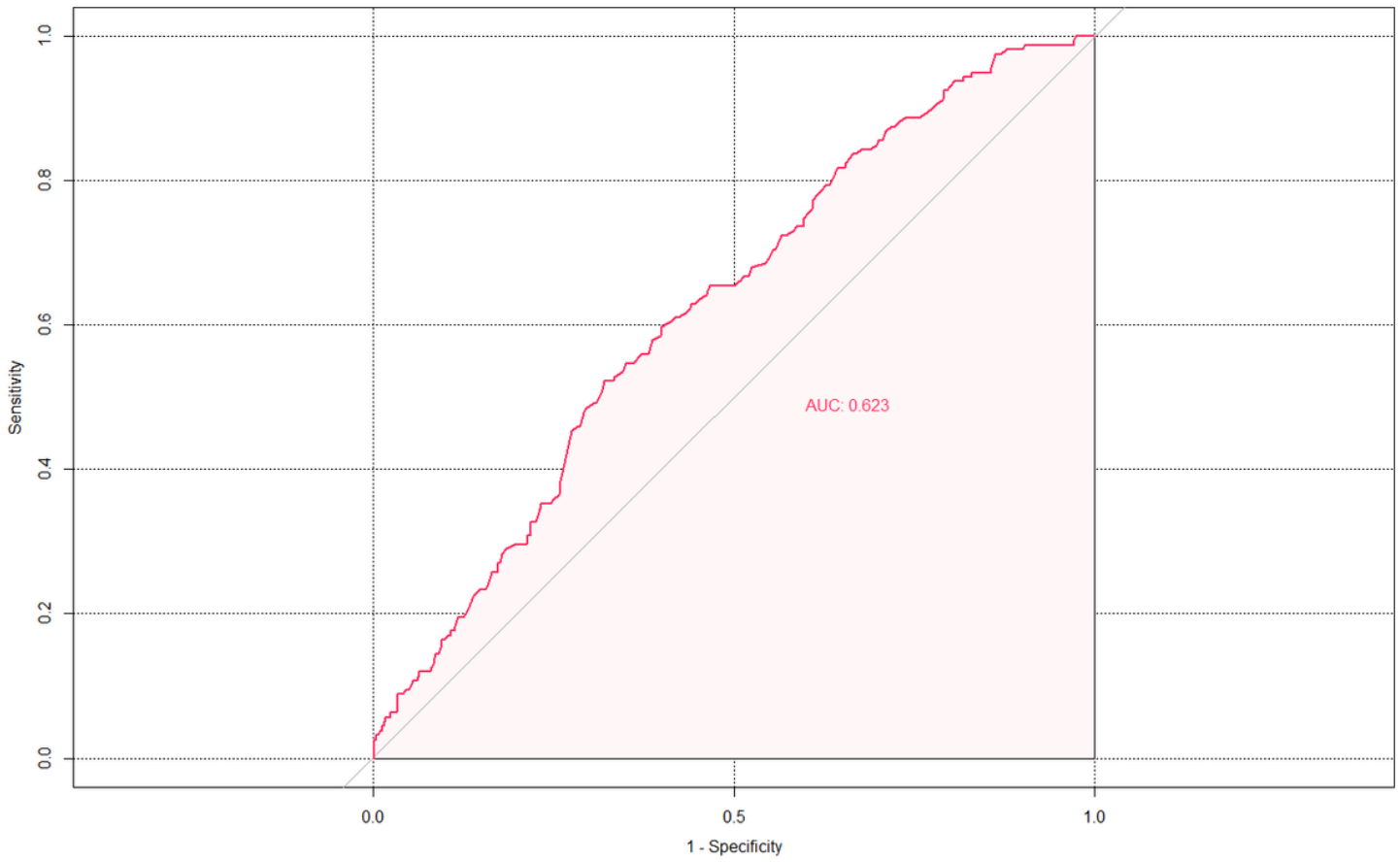

Figure 2

The receiver operating characteristic (ROC) curves of the triglyceride-glucose index as a marker to predict the primary endpoint in CTO patients after PCI. The area under ROC curves（AUCs）of the triglyceride-glucose index for predicting the occurrence of the primary endpoint in CTO patients within a median follow-up of 22.0 months after PCI was 0.623 (95% CI 0.575-0.671; P＜0.001).

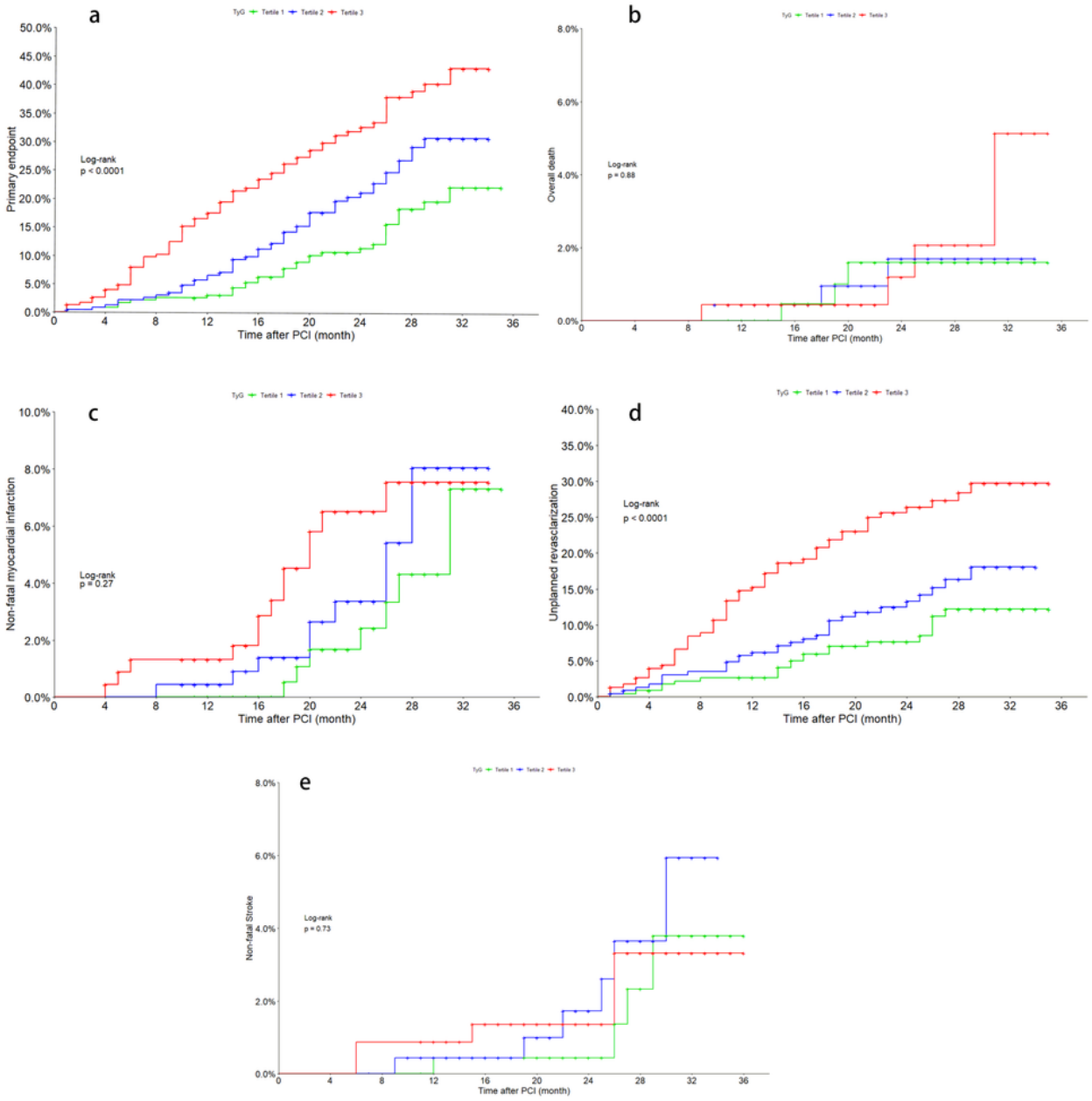

Figure 3

Kaplan–Meier curves for the primary endpoint (a), overall death (b), non-fatal MI (c), unplanned revascularization (d), non-fatal stroke (e); The groups were stratified by the TyG index tertiles. TyG triglyceride glucose; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.