



The role of triglyceride glucose index in predicting in-hospital adverse cardiovascular outcomes in patients with acute coronary syndrome

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Abstract

Previous studies have shown the association of triglyceride glucose (TyG) index with metabolic syndrome (MetS), cardiovascular disease (CVD) and long-term adverse cardiovascular outcomes. However, to best our knowledge, the relation between the TyG index and in-hospital adverse cardiovascular outcomes in acute coronary syndrome (ACS) has not yet been reported. Hence, in this study, we aimed to evaluate the role of the TyG index in predicting in-hospital adverse cardiovascular outcomes in ACS and to compare its performance with the Global Acute Coronary Events Register (GRACE) risk score. 170 patients diagnosed with ACS and underwent coronary angiography were analyzed retrospectively. The TyG index was calculated using the following formula: $\ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting blood glucose (mg/dL)} / 2]$. Receiver operating characteristics (ROC) curve analysis was used to evaluate the performance of the TyG index and GRACE risk score in predicting in-hospital adverse cardiovascular outcomes. A binary logistic regression model was applied to determine the independent predictors for in-hospital adverse cardiovascular outcomes. At the initial analysis, patients with adverse cardiovascular outcomes had higher TyG index and GRACE risk score ($p=0.011$, $p<0.001$). In ROC curve analysis, the GRACE score performed better in predicting in-hospital adverse cardiovascular outcomes compared to TyG index (AUC:0.716, $p<0.001$; AUC:0.588, $p=0.054$ respectively). In binary logistic regression analysis, left ventricular ejection fraction (LVEF), multi-vessel disease and GRACE risk score were independent predictors for in-hospital adverse cardiovascular outcomes (OR: 0.840, 95% CI: 0.791-0.891, $p<0.001$; OR: 3.581, 95% CI:1.382-9.282, $p=0.009$; OR= 1.017, 95% CI: 1.001-1.034, $p=0.04$ respectively). Our study findings revealed that the TyG index was scant in predicting in-hospital adverse cardiovascular outcomes compared to GRACE risk score. The independent predictors for in-hospital adverse cardiovascular outcomes were LVEF, multivessel disease and GRACE risk score.

Keywords: acute coronary syndrome, cardiovascular outcomes, GRACE, triglyceride glucose index

1. Introduction

Cardiovascular disease (CVD) is still one of the leading causes of mortality and morbidity today. Despite favorable advances in treatment, the increase in dysmetabolic diseases such as hypertension, diabetes and hyperlipidemia cause a slower decrease in CVD-related deaths (1, 2). Insulin resistance (IR) associated with glycolipid disorders has become an important risk factor for CVD (3). In addition, there is constant evidence that IR may lead to atherosclerosis process and adverse cardiovascular events through inducing of proinflammatory cytokines, impairment of endothelial dysfunction, triggering of pro-coagulant factor expression and increased oxidative stress (4).

Recently, the triglyceride glucose (TyG) index derived from triglyceride and glucose has been preferred for IR evaluation due to not requiring special techniques and low cost (5). The studies have shown that TyG index may be associated with coronary artery calcification, arterial stiffness, carotid atherosclerosis, and coronary artery disease

(CAD) (6). In addition, some studies have revealed an association between the TyG index with adverse cardiovascular outcomes, both in the general population and in patient cohorts (7, 8). However, to the best of our knowledge, no study has been reported on the relation between the TyG index with in-hospital adverse cardiovascular outcomes and its comparison with The Global Registry of Acute Coronary Events (GRACE) risk score in acute coronary syndrome (ACS). Thus, in this study, we aimed to examine the relation between TyG index and in-hospital adverse cardiovascular outcomes in ACS and to compare its performance with the GRACE risk score.

2. Materials and methods

2.1. Study population

In this retrospective observational study, 198 consecutive patients who were hospitalized for ACS and underwent coronary angiography at our tertiary care center between January 2020 and September 2020 were included. Malignancy, acute infection, severe liver failure, kidney and thyroid dysfunction, pregnancy, being under fibrates

treatment and missing data were defined as exclusion criteria, and as a result of the final analysis, the study was conducted with a total of 170 patients.

This study was in compliance with the Helsinki Declaration of Human Rights and was approved by the local institutional ethical committee (Pamukkale University Faculty of Medicine Hospital, Denizli, Turkey; 22.12.2020/24, protocol no: 60116787-020). Informed consent was obtained from each patient before participating in the study.

2.2. Data collection and definition

Demographic and clinical data including age, gender, smoking, medical history, standard laboratory parameters and, angiographic images were analyzed retrospectively. The TyG index was calculated using the following formula: $\ln [\text{fasting TG (mg/dL)} \times \text{fasting blood glucose (mg/dL)} / 2]$ (9). GRACE risk score consisting of age, systolic blood pressure, heart rate, presence of cardiac arrest, Killip class, ST segment deviation, serum creatinine, and positive cardiac markers was calculated for each patient using data from the registry system (10). ACS was defined as a collection of clinical syndromes, including unstable angina (UA), non-ST-elevation myocardial infarction (STEMI), and ST-elevation myocardial infarction (STEMI). Hypertension was defined as blood pressure $\geq 140/90$ mmHg or currently taking antihypertensive treatment. Diabetes was defined as plasma glucose ≥ 200 mg/dL at any time or fasting blood glucose ≥ 126 mg/dL or under treatment. In-hospital adverse cardiovascular outcomes included cardiac death, cardiogenic shock, significant arrhythmia, recurrent revascularization and heart failure. The experience of any of these was defined as an in-hospital adverse cardiovascular outcome.

2.3. Statistical analysis

The data were analyzed using SPSS v.21.0 Windows (SPSS, Inc., Chicago, Ill., USA) programme package. Continuous variables were expressed as mean \pm SD or median, and categorical variables were presented as frequency and percentage. Kolmogorov-Smirnov test was used to determine the normal distribution and the comparisons based on normality distribution were done with Student's t-test or Mann-Whitney U test. Categorical variables were compared using χ^2 test. Pearson's or Spearman correlation analysis was used to evaluate the relationship between the continuous variables. A binary logistic regression analysis was used to determine whether the TyG index was an independent predictor for in-hospital adverse cardiovascular outcomes. The performance of the TyG index and GRACE scores were compared using the receiver operating characteristics (ROC) curve analysis in predicting in-hospital adverse cardiovascular outcomes, and $p < 0.05$ was considered statistically significant.

3. Results

Patients without in-hospital adverse cardiovascular outcomes were assigned as group 1 (n=103) and those with in-hospital adverse cardiovascular outcomes were assigned as group 2 (n=67). The demographic and clinical characteristics of the groups are presented in Table 1. There were no significant differences in mean age, male gender, smoking, hypertension, previous MI or revascularization history between the groups. However, diabetes incidence was significantly higher in group 2 ($p=0.044$). 27%, 47%, 26% of the patients were diagnosed with UA, NSTEMI and STEMI, respectively in group 1. In group 2, 9%, 31% and 59% of patients had UA, NSTEMI and STEMI respectively. While the percentages of single and two-vessel disease were higher in group 1, multi-vessel disease was more common in group 2. There were significant differences in LVEF, glucose, HbA1c, creatinine, WBC between the groups. However, lipid parameters, hemogram, TG/HDL-C, LDL-C/HDL-C were similar. When the groups were compared in terms of TyG index and GRACE risk score, TyG index and GRACE risk score of group 2 increased significantly (9.00 ± 0.70 vs 9.30 ± 0.82 , $p=0.011$; 114.42 ± 25.68 vs 138.76 ± 33.16 , $p < 0.001$ respectively).

A comparison of in-hospital adverse cardiovascular outcomes based on the median TyG index of the study population is shown in Table 2. There were no significant differences in incidence of cardiogenic shock, heart failure, cardiac death and significant arrhythmia in patients with low and high TyG index. However, the incidence of recurrent ischemia increased in patients with high TyG index compared to those with low TyG index ($p=0.02$). There was no difference between the groups in terms of single- or two-vessel disease, however multi-vessel disease was more common in patients with high TyG index ($p=0.042$) (Table 3).

In correlation analysis, the TyG index showed a significant association with hypertension, diabetes, NSTEMI, LVEF, HbA1c, lipid parameters, creatinine, WBC, and multi-vessel disease (Table 4). However, the performance of the TyG index in predicting in-hospital adverse cardiovascular outcomes was not at expected level in the ROC curve analysis (95% CI=0.501-0.674, AUC=0.588, 94% sensitivity, 25% specificity, $p=0.054$). The GRACE risk score predicted in-hospital adverse cardiovascular outcomes with 58% sensitivity and 81% specificity at a cut-off value of 135.50 (95% CI=0.633-0.799, AUC=0.716, $p < 0.001$) and its performance was better compared to the TyG index (Fig. 1). In binary logistic regression analysis, the parameters associated with in-hospital adverse cardiovascular outcomes were LVEF, multi-vessel disease and GRACE risk score, regardless of all causes, as presented in Table 5.

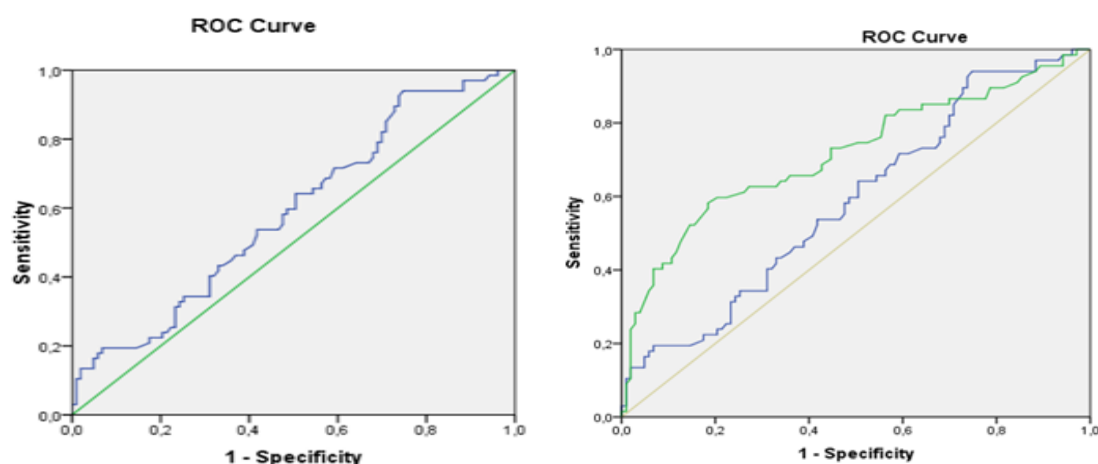


Fig. 1. Receiver operating characteristic (ROC) curves in predicting in-hospital adverse cardiovascular outcomes

Table 1. Baseline characteristics and clinical data of study population

Variables	Group I (n=103)	Group II (n=67)	p- value
Mean age (years)	65.01±11.28	67.78±15.29	0.177
Male gender, n (%)	65 (63)	40 (60)	0.412
Hypertension, n (%)	57 (55)	31 (46)	0.159
Diabetes, n (%)	33 (32)	31(46)	0.044
Current smoking, n (%)	34 (33)	25 (37)	0.339
Previous MI, n (%)	9 (9)	7 (10)	0.709
PCI history, n (%)	6 (6)	4 (6)	0.969
CABG history, n (%)	7 (7)	6 (9)	0.605
UA, n (%)	28 (27)	6 (9)	0.004
NSTEMI, n (%)	48 (47)	21(31)	0.034
STEMI, n (%)	27 (26)	40 (59)	<0.001
LVEF %, (median)	55.00	35.00	<0.001
Blood glucose, mg/dL (median)	120.00	174.00	<0.001
HbA1c %, (median)	7.60	8.80	0.047
Creatinine, mg/dL (median)	0.86	0.96	0.004
Tchol, mg/dL	173.99±39.19	171.37±41.45	0.678
LDL-C,mg/dL	104.14±34.86	106.12±34.70	0.717
HDL-C, mg/dL (median)	39.00	40.00	0.952
TG, mg/dL (median)	118.00	130.00	0.275
Hemoglobin, g/dL (median)	13.20	12.80	0.288
WBC, cells/ μ L (median)	9.08	10.70	<0.001
TyG index	9.00±0.70	9.30±0.82	0.011
LDL-C/HDL-C	2.7±1.16	2.8±1.19	0.548
TG/HDL-C	3.27	3.35	0.557
Single-vessel disease, n (%)	39 (38)	12 (18)	0.006
Two-vessel disease, n (%)	35 (34)	10 (15)	0.006
Multi-vessel disease, n (%)	29 (28)	45 (67)	<0.001
GRACE risk score	114.42±25.68	138.76±33.16	<0.001

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; UA, unstable angina; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; LVEF, left ventricular ejection fraction; Tchol; total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; WBC, white blood cells; TyG index, triglyceride glucose index

Table 2. The comparison of in-hospital adverse cardiovascular outcomes between the groups based on median TyG index

Variables	Low (<9.04)(n=84)	High (>9.04)(n=86)	p
Cardiogenic shock	-	2 (2)	0.160
Heart failure	29 (35)	32 (37)	0.715
Significant arrhythmia	7 (8)	14 (16)	0.115
Recurrent ischemia	-	9 (11)	0.002
Cardiac death	4 (5)	11 (13)	0.065

TyG index, triglyceride glucose index

Table 3. The number of diseased vessels according to median TyG index

Variables	Low (<9.04) n=84	High (>9.04) n=86	p
Single-vessel disease, n (%)	26 (31)	25 (29)	0.789
Two-vessel disease, n (%)	28 (33)	17 (20)	0.154
Multi-vessel disease, n (%)	30 (36)	44 (51)	0.042

TyG index, triglyceride glucose index

Table 4. The correlation analysis of TyG index

Variables	r	p
Age	-0.105	0.173
Hipertension	0.201	0.008
Diabetes	0.477	<0.001
NSTEMI	0.292	0.012
LVEF	-0.217	0.005
HbA1c	0.516	<0.001
Creatinine	0.228	0.003
Tchol	0.248	<0.001
LDL-C	0.189	0.013
HDL-C	-0.300	<0.001
WBC	0.282	0.018
Multi-vessel disease	0.346	0.027
GRACE risk score	0.046	0.549

NSTEMI, non- ST- elevation myocardial infarction; LVEF, left ventricular ejection fraction; Tchol; total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; WBC, white blood cells; TyG index, triglyceride glucose index

Table 5. Binary logistic regression analysis for in-hospital adverse cardiovascular outcomes

Variables	OR	95% CI		p
		Lower bound	Upper bound	
LVEF	0.840	0.791	0.891	<0.001
WBC	1.098	0.968	1.246	0.146
Multi-vessel disease	3.581	1.382	9.282	0.009
GRACE risk score	1.017	1.001	1.034	0.040
TyG index	1.158	0.602	2.227	0.660

LVEF, left ventricular ejection fraction; WBC, white blood cells; TyG index, triglyceride glucose index

4. Discussion

In the current study, we investigated the impact of TyG index on in-hospital adverse cardiovascular outcomes in patients diagnosed with ACS at the first time and our main findings were as follows: (1) TyG index and GRACE risk score were higher in patients with in-hospital adverse cardiovascular outcomes; (2) There were no significant differences in in-hospital adverse outcomes including heart failure, cardiac death, cardiogenic shock, and heart failure between patients with high and low TyG index. However, recurrent ischemia

was more common in patients with high TyG index. In addition, TyG index was significantly correlated with dysmetabolic conditions such as hypertension, diabetes, dyslipidemia, and multi-vessel disease; (3) GRACE risk score performed better in predicting in-hospital adverse outcomes compared to TyG index; (4) LVEF, multivessel disease and GRACE risk score were independent predictors for in-hospital adverse cardiovascular outcomes.

Many studies have shown that IR is associated with CVD and cardiovascular outcomes, in both short-term and long-term prognosis (11). However, the pathophysiological mechanisms by which IR plays a role in CVD have not been clearly determined. Inflammation, oxidative stress, lipid metabolism disorders, disruption of endothelial dysfunction through decreased NO release and inducing of the coagulation cascade are blamed mechanisms (4).

TyG index, a new method for evaluating IR, is associated with dysmetabolic conditions and CVD. Recently, the data reported that patients with increased TyG index have a higher risk of hypertension and diabetes. Moreover, the studies have found that the subclinical CAD may be more prevalent during screening with coronary CT angiography in patients with a high TyG index (12-14). Similar to these studies, there was a significant association between TyG index with hypertension, diabetes and impaired lipid parameters in our study. We also found a significant correlation between multi-vessel disease with TyG index and Mao et al.'s study supported our study by showing an increased incidence of multi-vessel disease in NSTEMI patients with a high TyG index (8). Recently, the relationship of the TyG index with cardiovascular outcomes has been investigated and in one study conducted with stable CAD patients; a high TyG index was associated with primary endpoints including all-cause death, non-fatal MI, recurrent revascularization and stroke (7). In another study, the TyG index showed successful performance in predicting cardiovascular events in patients with ACS, regardless of all causes (15). Additionally, the increased TyG index indicated the adverse cardiovascular outcomes in diabetic patients diagnosed with ACS undergoing PCI in one study (16). In this study, to the best of our knowledge, we investigated the role of the TyG index on in-hospital adverse outcomes in ACS patients at the first time. Patients with in-hospital adverse cardiovascular outcomes at baseline showed a higher TyG index. However, the TyG index failed to predict adverse in-hospital cardiovascular outcomes compared to the GRACE risk score. Also, TyG index was not an independent predictor for in-hospital adverse cardiovascular outcomes after adjusting for confounding factors. In all above studies, it was aimed to determine the long-term prognostic significance of the TyG index in CAD patients, not in-hospital adverse cardiovascular outcomes. However, adverse cardiovascular events observed during hospitalization after ACS were reported in our study. in-hospital adverse

cardiovascular outcomes may be more affected by hemodynamic status at admission, late hospitalization due to atypical angina, presence of previous CAD, late referrals from rural areas, and inclusion of patients with unsuccessful revascularization from an external center, rather than TyG index. However, the TyG index was significantly correlated with in-hospital recurrent ischemia in our study. This may be due to the TyG index's association with dysmetabolic conditions such as hypertension, diabetes, hyperglycemia, and lipid metabolism disorders, which predispose to atherosclerosis.

Another finding of our study was that the GRACE risk score, a clinical scoring, performed better in predicting in-hospital adverse cardiovascular outcomes compared to the TyG index and was an independent predictor for in-hospital adverse cardiovascular outcomes. Indeed, clinical evaluation may be better than laboratory parameters in predicting in-hospital adverse cardiovascular outcomes that may occur immediately after ACS. As a matter of fact, the GRACE risk score, developed from multinational prospective patient registries, has been accepted as a strong predictor of short-term prognosis in patients with ACS, and its use has been recommended by ESC guidelines. (17). The other independent predictors for in-hospital adverse cardiovascular outcomes were LVEF and multi-vessel disease in our study. In a study with 8983 ACS patients, LVEF at admission was an independent predictor of death and adverse cardiovascular outcomes (18). Also, low LVEF may have led to clinical instability in patients with in-hospital adverse cardiovascular outcomes in our study. In another study, multivessel disease was a more important predictor of in-hospital adverse cardiovascular outcomes in patients with ACS compared to TIMI and age (19), and the findings of this study were consistent with our study.

Our study had some limitations. First, our study was retrospective and the study sample was relatively small. Second, the study was conducted in a Turkish population, and the study findings may vary by ethnicity. Third, patients using antidiabetic agents were not excluded. Therefore, we cannot ignore the effects of antidiabetic drugs. Fourth, due to retrospective design, we had missing data such as body mass index, exercise status, dietary habits, and energy intake, which could affect patients' TyG index.

As a result, the TyG index was higher in patients with in-hospital adverse cardiovascular outcomes. The performance of the GRACE risk score in predicting in-hospital adverse cardiovascular outcomes was better compared to the TyG index. Thus, the TyG index may not be a useful marker to predict in-hospital prognosis in patients diagnosed with ACS. According to the findings of our study, the independent predictors of in-hospital adverse cardiovascular outcomes were LVEF, multivessel disease, and GRACE risk score. However, a larger sample size, longer follow-up time, and

multicenter studies are needed to confirm our findings.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

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