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RESEARCH

Triglyceride-glucose index is associated with residual SYNTAX score in patients with ST-segment elevation myocardial infarction

Trigliserit-glikoz indeksi ST-segment yükselmeli miyokard enfarktüslü hastalarda rezidüel SYNTAX skoru ile ilişkilidir

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Abstract

Purpose: The triglyceride-glucose index (TyG) is an important parameter that reflects insulin resistance and its use has increased recently. Its relationship with cardiovascular diseases has been shown in previous studies. Our aim was to investigate the association of residual SYNTAX score (rSS) with TyG index in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention.

Materials and Methods: A total of 663 STEMI patients who underwent primary percutaneous coronary intervention were included in the study. The patients were divided into 2 groups according to the TyG index level as high and low. The cut-off value for the TyG index was determined as 9.61 by ROC analysis. Coronary artery disease severity was calculated for both groups besides baseline clinical and demographic variables.

Results: A total of 281 patients were evaluated in the high TyG index group and 386 patients in the low TyG index group. A rSS above 8 was considered high. The proportion of patients with high rSS in the increased TyG index group was found to be significantly higher than in the other group [114 (40.6) vs. 54 (14.0)]. In addition, higher TyG index is determined to be the independent predictor of higher rSS in logistic regression analysis.

Conclusion: High TyG index had a strong association with rSS and higher TyG index was an independent predictor of increased rSS in patients with STEMI.

Keywords: Triglyceride-glucose index, ST elevation myocardial infarction, residual SYNTAX score

Öz

Amaç: Trigliserit-glukoz indeksi (TyG) insülin direncini yansıtan önemli bir parametredir ve son yıllarda kullanımı artmıştır. Kardiyovasküler hastalıklarla ilişkisi daha önceki çalışmalarda gösterilmiştir. Amacımız, primer perkütan koroner girişim uygulanan ST segment yükselmeli miyokard enfarktüsü (STEMI) hastalarında rezidüel SYNTAX skorunun (rSS) TyG indeksi ile ilişkisini araştırmaktır.

Gereç ve Yöntem: Çalışmaya primer perkütan koroner girişim uygulanan toplam 663 STEMI hastası dahil edildi. Hastalar, TyG indeks düzeyine göre yüksek ve düşük olmak üzere iki gruba ayrıldı. TyG indeksi için cut-off değeri ROC analizi ile 9,61 olarak belirlendi. Başlangıç klinik ve demografik değişkenlerin yanı sıra koroner arter hastalığı şiddeti her iki grup için de hesaplandı.

Bulgular: Yüksek TyG indeksi grubunda 281 hasta ve düşük TyG indeksi grubunda 386 hasta değerlendirildi. 8'in üzerindeki rSS, yüksek olarak kabul edildi. Artmış TyG indeksi grubunda yüksek rSS olan hastaların oranı diğer gruba göre anlamlı derecede yüksek bulundu [114 (40.6) vs. 54 (14.0]. Ek olarak, lojistik regresyon analizinde daha yüksek TyG indeksi, daha yüksek rSS'nin bağımsız öngörücüsü olarak belirlenir.

Sonuç: Yüksek TyG indeksi, rSS ile güçlü bir ilişkiye sahiptir ve daha yüksek TyG indeksi, STEMI hastalarında artan rSS'nin bağımsız bir öngördürücüsüdür.

Anahtar kelimeler: Trigliserid- glukoz indeksi, St yükselmeli miyokart enfarktüsü, rezidüel SYNTAX skoru

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INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) remains the leading cause of morbidity and mortality worldwide. Percutaneous coronary intervention (PCI) to the culprit lesion is the cornerstone of treatment in patients with STEMI. Additional vascular lesions and multivessel disease are observed between 40% and 65% in STEMI patients[1,2]. Complete revascularization may be required in these patients and the prognosis may be poor in patients who do not undergo complete revascularization. The residual syntax score (rSS) shows the severity of atherosclerosis after PCI and was first described in the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) study. rSS values above 8, were associated with an increased 1-year mortality in patients with STEMI[3]. Therefore, determining the severity of atherosclerosis in patients with myocardial infarction is an important point in predicting prognosis.

In recent years, prognostic studies on diabetes and insulin resistance (IR), which are defined as the equivalent of cardiovascular disease, have been increasing[4–6]. IR is a syndrome defined as decreased insulin sensitivity in peripheral tissues due to disturbances in glucose uptake and oxidation, and its role in the development of diabetes and cardiovascular disease has been clearly demonstrated[7]. Although hyperinsulinemic-euglycemic clamp is the traditional method in the diagnosis of IR, in clinical practice there are some difficulties because it is a costly, time-consuming and invasive method[8]. Therefore, simple parameters are needed for the measurement of IR. The triglyceride-glucose index (TyG index), which was developed based on this idea, is a simple index calculated with fasting plasma glucose and triglyceride (TG) values. Previous studies have shown that the TyG index is significantly correlated with IR and is a reliable indicator of IR[9,10]. It is revealed that the TyG index is an independent risk factor for cardiovascular disease. Furthermore, this index has been shown to be associated with future cardiovascular events such as myocardial infarction, all cause mortality, and the necessity for coronary revascularization[11,12]. On the other hand, all these data are based on stable coronary artery patients and there is insufficient data on the association between the TyG index and the severity of atherosclerosis in patients with STEMI. Our aim is to investigate the relationship between rSS, which indicates the severity of atherosclerosis, and the TyG index in STEMI patients.

MATERIALS AND METHODS

Study population

In our study, STEMI patients who underwent primary percutaneous coronary intervention (PPCI) between December 2018 and December 2021 were evaluated retrospectively. Diagnosis of STEMI as defined in the Fourth Universal Definition of Myocardial Infarction by the European Society of Cardiology: typical chest pain for more than 20 minutes and ST-segment elevation in at least 2 contiguous leads with the following cutoff points: 0.2 mV in men 40 years old; 0.25 mV in men <40 years old or 0.15 mV in women in leads V2 to V3 and/or 0.1 mV in the other leads as well as posterior (V7-V9) and right derivations (V3R-V4R)[13]. Patients with history of previous PCI or coronary artery bypass grafting surgery, infectious or inflammatory disease, autoimmune disease, severe renal or liver disease, hematological disease, malignancy and patients with ongoing immunosuppressive treatment were excluded from the study. Patients who underwent intervention in a non-culprit lesion during the index procedure and patients using statins were also excluded from the study. Intervention was planned at least 1 month after the index procedure for another coronary artery stenosis requiring revascularization.

Ethical approval was obtained for the study by the Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Ethics Committee (Date: 01.06.2022, decision number: 2022-5.29) and written informed consent was obtained from each participant.

Laboratory tests

Blood samples were obtained from the antecubital vein of each patient after at least 12 hours of overnight fasting. Fasting plasma glucose concentrations were measured by the enzymatic hexokinase method. TGs, total cholesterol (TC), high-density lipoprotein–cholesterol (HDL-C), and low-density lipo-protein-cholesterol (LDL-C) were measured using an automatic biochemistry analyzer (Hitachi 7150, Japan) in an enzymatic assay. The TyG index was calculated using the formula: ln [fasting TGs (mg/dL) ×FPG(mg/dL)/2][14].

Percutaneous coronary intervention and rSS evaluation

PCI procedure; defined as balloon dilation or stent implantation into an infarct-related artery by an experienced cardiologist using standard techniques. The procedure was performed within 90 minutes after admission from femoral or radial access. All patients were given ticagrelor or prasugrel or clopidogrel in addition to aspirin, and the choice between these agents was left to the operator. Statins, beta blockers, and angiotensin converting enzyme inhibitors were used in all patients without contraindications.

After the primary intervention, coronary angiographies were examined by two experienced cardiologists and the severity of coronary artery disease was evaluated. First, the SYNTAX I score was calculated, then rSS was calculated by evaluating coronary artery stenosis after PPCI. Coronary arteries were evaluated as 16 separate segments. Segments with 50% or more lumen stenosis and at least 1.5 mm in diameter were assessed[15]. The SYNTAX score calculator (www.syntaxscore.com) was used to calculate the SYNTAX I score and rSS. An rSS above 8 was considered high rSS. Finally, clinical variables such as age, gender, creatinine clearance, left ventricular ejection fraction (LVEF), peripheral artery disease (PAD), and chronic obstructive pulmonary disease were recorded for the calculation of the SYNTAX II score.

Statistical analysis

Statistical analysis of the study was performed with the SPSS Version 24.0 program (SPSS Inc., Chicago, Illinois, USA). Whether the variables showed normal distribution was evaluated using visual (histograms, probability curves) and analytical methods (Kolmogorov-Smirnov's or Shapiro-Wilk). Normally distributed numerical variables were expressed as mean±standard deviation (SD), non-normally distributed numerical variables were expressed as median (25th to 75th percentile), and categorical variables were expressed as percent (%). ROC (Receiver Operating Characteristic) curve and Youden index [max (Sensitivity + Selectivity -1)] were used to determine the TyG index predictive cut-off value for detecting high rSS. The area under the ROC curve above 0.5 was considered significant. Statistical analysis of numerical variables between groups was done with Student's t-test or Mann Whitney U test, and analysis of categorical variables with Chi-square or Fisher exact test. The correlation between the TyG index and other numerical variables was evaluated by Pearson or Spearman analysis. In order to identify independent predictors of high rSS, univariate logistic regression analysis was performed first, followed by multivariate logistic regression analysis using parameters that were significant in univariate analysis. P values less than 0.05 were considered significant in this study.

RESULTS

The mean age of 663 patients was 55.6 ± 11.2, and 536 (81.0%) of the patients were male and 127 (19.0%) were female. Mean TyG index value was 9.50±0.74, median SYNTAX score was 15.5 (10.0-22.5), and median rSS value was 3.0 (0.0-9.0). SYNTAX score >22 were considered as moderate-high SYNTAX score, and rSS >8 were considered as high rSS. Firstly, the ROC curve was created in order to determine the predictive cut-off value for the TyG index, which detects high rSS (Figure 1), and the cut-off value was determined as 9.61 using the Youden index (AUC: 0.694, 95% CI: 0.651-0.738, P<0.001). Then, the values >9.61 were accepted as high TyG index and the values ≤9.61 were accepted as low TyG index, and the patients were divided into two groups according to the TyG index.

The comparison of the groups in terms of baseline characteristics is shown in Table 1. As expected, patients in the group with high TyG index; had higher glucose and TG levels and higher rates of diabetes mellitus (DM). In addition, the high TyG index group had significantly higher total cholesterol, higher alanine aminotransferase (ALT) and lower HDL levels. There was no significant difference between the two groups in terms of other variables. In Table 2, the groups were compared in terms of variables related to LVEF and coronary anatomy. The median LVEF value was similar between the groups. Although the culprit lesion was proportionally more in RCA and less in LAD in the high TyG index group, it could not reach the significance level (P=0.051). Moreover, SYNTAX score, SYNTAX score II PCI, and rSS were higher in the high TyG index group (respectively; P<0.001, P=0.006, P<0.001). In parallel, higher TyG index values were found in patients with high rSS (P<0.001) (Figure 2).

Table 1. Baseline demographic and clinical variables of the study population

Variable	All patients (N = 663)	Low TyG index n= 386	High TyG index n= 281	P
Age (years)	55.6±11.2	55.1±11.5	56.3±10.9	0.182
Gender (female), n (%)	127 (19.0)	72 (18.6)	55 (19.6)	0.753
Smoking, n (%)	312 (46.7)	187 (48.3)	125 (44.5)	0.327
Hypertension, n (%)	217 (32.5)	114 (29.5)	103 (36.7)	0.050
Diabetes mellitus, n (%)	131 (19.6)	49 (12.7)	82 (29.2)	<0.001
Peripheral arterial disease, n (%)	23 (3.4)	12 (3.1)	11 (3.9)	0.569
COPD, n (%)	24 (3.6)	12 (3.1)	12 (4.3)	0.423
Medication usage, n (%)				
β-blocker	11 (1.6)	6 (1.6)	5 (1.8)	1.0
ACEI	81 (12.1)	42 (10.9)	39 (13.9)	0.237
ARB	31 (4.6)	15 (3.9)	16 (5.7)	0.270
CCB	34 (5.1)	19 (4.9)	15 (5.3)	0.804
Total cholesterol (mg/dL)	199±43	192±42	209±42	<0.001
LDL-C (mg/dL)	121±37	120±38	121±37	0.680
HDL-C (mg/dL)	40 (34-47)	42 (35-47)	37 (32-45)	<0.001
Triglycerides (mg/dL)	178 (121-260)	132 (101-174)	271 (212-380)	<0.001
Creatinine (mg/dL)	0.85 (0.73-1.02)	0.84 (0.74-1.00)	0.85 (0.73-1.03)	0.462
Glucose (mg/dL)	135 (109-184)	119 (102-141)	178 (135-273)	<0.001
ALT (U/L)	21 (15-30)	20 (15-29)	22 (16-32)	0.030
C-reactive protein (mg/L)	4.0 (1.9-9.3)	4.0 (1.9-9.3)	3.8 (1.8-9.2)	0.923
Hemoglobin (g/dL)	14.7 (13.2-15.7)	14.6 (13.2-15.5)	14.7 (13.2-15.8)	0.553
Leukocytes x 103/mm3	12.0 (9.6-14.3)	11.9 (9.2-14.3)	12.2 (10.0-14.6)	0.097
Lymphocyte (109/L)	2.5 (1.7-3.7)	2.5 (1.7-3.7)	2.6 (1.7-3.7)	0.746
Neutrophils (109/L)	7.6 (5.6-10.3)	7.3 (5.4-10.4)	7.7 (6.0-10.3)	0.156
Platelets x 103/mm3	261 (223-317)	260 (223-317)	262 (224-319)	0.926

ACEI, angiotensin-converting enzyme inhibitor; ALT, alanine aminotransferase; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride-glucose.

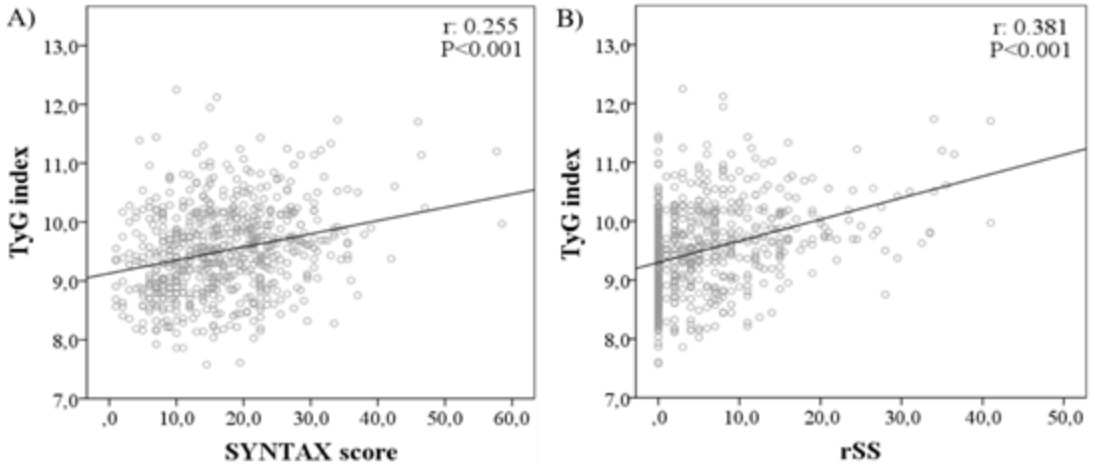

Figure 1A. TyG index and SYNTAX score correlation graph. 1B. TyG index and rSS correlation graph.

Table 2. Angiographic variables and cardiac functions of patients

Variable	All patients (N = 613)	Low TyG index n= 268	High TyG index n= 345	P
LVEF (%)	50 (40-55)	50 (40-55)	48 (40-55)	0.569
Culprit vessel, n (%)				
LAD	337 (50.4)	209 (54.0)	128 (45.6)	0.051
CXA	101 (15.1)	59 (15.2)	42 (14.9)	
RCA	230 (34.4)	119 (30.7)	111 (39.5)	
SYNTAX score	15.5 (10.0-22.5)	14.5 (9.0-21.0)	19.0 (13.0-25.0)	<0.001
SYNTAX score group, n (%)				
Low (≤22)	494 (74.0)	309 (79.8)	185 (65.8)	<0.001
Moderate to high (>22)	174 (26.0)	78 (20.2)	96 (34.2)	
SYNTAX score II PCI	25.7 (19.4-33.6)	24.7 (18.6-32.0)	27.2 (20.5-35.6)	0.006
Residual SYNTAX score	3.0 (0.0-9.0)	1.0 (0.0-5.0)	7.0 (2.0-13.0)	<0.001
Residual SYNTAX group, n (%)				
Low (≤8)	500 (74.9)	333 (86.0)	167 (59.4)	<0.001
High (>8)	168 (25.1)	54 (14.0)	114 (40.6)	

CXA, circumflex artery; LAD, left anterior descending; LVEF, left ventricle ejection fraction; PCI, percutaneous coronary intervention; RCA, right coronary artery; TyG, triglyceride-glucose.

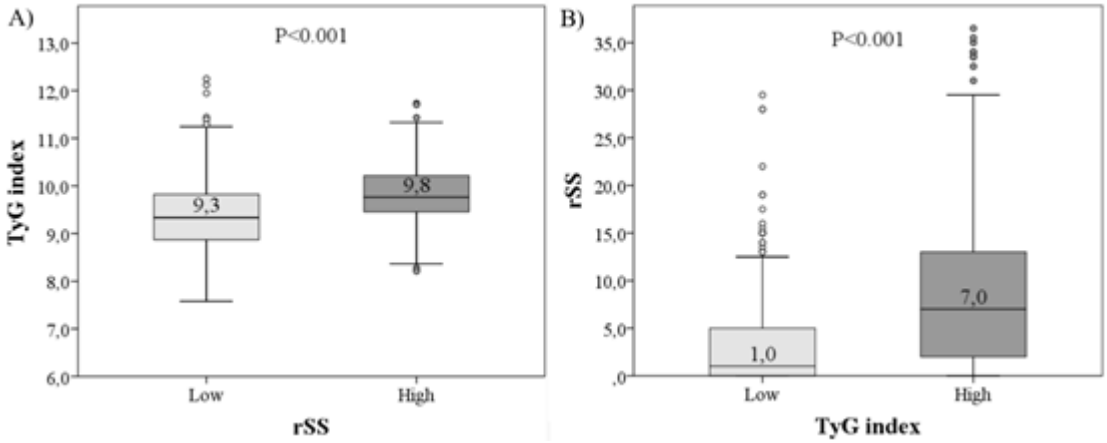

Figure 2A. TyG index box plot graph according to low and high rSS. 2B. rSS box plot graph according to low and high TyG index.

Table 3. Correlation between TyG index and clinical variables

Variable	Correlation coefficient	P
Age	0.044	0.257
LVEF	-0.028	0.473
SYNTAX score	0.255	<0.001
SYNTAX score II	0.151	<0.001
rSS	0.381	<0.001

LVEF, left ventricle ejection fraction; NLR, neutrophil to lymphocyte ratio; rSS, residual SYNTAX score.

The correlation of TyG index with other variables was shown in Table 3. TyG index was not correlated with age and LVEF. A significant correlation was observed between the TyG index and the SYNTAX

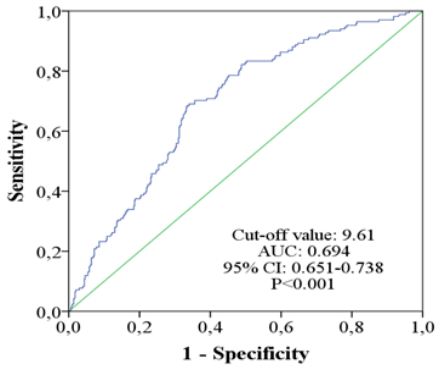

Figure 3. TyG index ROC curve for high rSS presence.

score, SYNTAX II score PCI and rSS values. The highest correlation coefficient was obtained with rSS (r=0.381, P<0.001) (Figure 3).

Univariable logistic regression analysis was performed to identify independent predictors of high rSS in patients undergoing primary percutaneous intervention. Age, HT, PAD, hemoglobin level, lymphocyte level, neutrophil level, high TyG index, LVEF and the artery with the culprit lesion were found to be associated with high rSS. In the multivariable analysis created with these variables, age (P=0.002), LVEF (P=0.012), the artery with the culprit lesion (P=0.003) and high TyG index (OR: 4.057, 95% CI: 2.737-6.013, P<0.001)) were determined as independent predictors of high rSS (Table 4).

Table 4. Univariable and multivariable logistic regression analysis giving information about independent predictors of high residual SYNTAX score

Variable	Univariable analysis			Multivariable analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.042	1.025-1.059	<0.001	1.031	1.011-1.051	0.002
Hypertension	1.715	1.194-2.464	0.003	1.194	0.788-1.809	0.403
Peripheral arterial disease	2.849	1.233-685	0.014	2.266	0.864-5.943	0.096
Hemoglobin	0.877	0.799-0.962	0.006	0.955	0.856-1.066	0.414
Lymphocyte	0.851	0.756-0.959	0.008	0.901	0.792-1.026	0.115
Neutrophils	1.048	1.005-1.092	0.028	1.042	0.994-1.093	0.090
High TyG index	4.210	2.898-6.115	<0.001	4.057	2.737-6.013	<0.001
LVEF	0.982	0.965-0.999	0.040	0.972	0.950-0.994	0.012
Culprit vessel			0.001			0.003
LAD*	0.504	0.342-0.744	0.001	0.456	0.282-0.739	0.001
CXA*	0.952	0.574-1.580	0.850	0.944	0.541-1.646	0.838

Abbreviations: CXA, circumflex artery; LAD, left anterior descending; LVEF, left ventricle ejection fraction; TyG, triglyceride-glucose
*Compared to right coronary artery

DISCUSSION

In this study, we aimed to reveal the relationship between rSS, which indicates the severity of atherosclerosis, and the TyG index in STEMI patients who underwent primary percutaneous coronary intervention. The main findings from this study; a) Patients with a higher TyG index had a higher SYNTAX score and higher rSS, b) Age, artery with the culprit lesion, low LVEF and higher TyG index were determined as independent risk factors for high rSS. To the best of our knowledge, this is the first study which represents this relationship in the current literature.

TyG index, considered as a marker of DM, hyperlipidemia and even metabolic syndrome, is a relatively new risk score. This index has been applied to different patient subgroups so far. Firstly, Selvi et al reported that TyG index has a strong relationship with HbA1c and IR, which may lead us to use TyG index as a follow-up marker in daily practice[16]. In addition, the TyG index has been associated with increased arterial stiffness and renal microvascular damage. Zhao et al. reported that the TyG index was associated with pulse wave velocity (PWV) even in non-diabetic patients[17]. However, these research data showed that the TyG index was not associated with carotid or lower extremity artery disease[17]. On the other hand, cardiovascular complications such as lower extremity arterial stenosis tend to be more common in hospitalized diabetic patients with a

higher TyG index. Thus, this point has not been clarified yet[18]. Okamura et al. stated that the TyG index is a safe and easy marker that can be used to screen healthy individuals for chronic kidney disease[19]. Among 11712 patients without any medication were screened in terms of chronic kidney disease and it was reported that the TyG index could be a predictor of chronic kidney disease[19]. In another study, Srinivasan et al. reported that retinopathy and nephropathy are more common in diabetic patients with a high TyG index, and that the TyG index could be used to screen for these microvascular complications in the course of DM[20].

rSS system is a relatively new score and has been driven from original Syntax Score. It indicates the severity of remaining obstructive coronary artery disease after treatment with PCI. Older age, medically treated DM, low LVEF, reduced creatinine clearance and rSS values higher than 8 were associated with increased 5-year mortality[15]. In recent studies, advanced age, low LVEF and responsible vascular lesion have been shown as independent risk factors[21]. Neutrophil Lymphocyte Ratio, which is considered as an inflammatory marker, was found to be higher in STEMI patients with higher rSS[22]. Coronary lesion burden, which is an important reflection of the atherosclerotic process, is directly related to inflammation and the prediction of inflammatory markers in this regard has been proven[23,24]. As a matter of fact, IR and DM, another clinical condition associated with the inflammatory process, are not only causes of atherosclerosis, but are also considered equivalent to coronary artery disease. Patients with DM have a 2- to 4-fold increased risk of coronary artery disease[25]. In addition, DM is associated with increased severity of coronary artery disease. The coronary atherosclerotic burden is higher in diabetic patients than in non-diabetic patients. The TyG index has proven to be a good predictor of IR. Also IR is a marker of oxidative stress and inflammation[26]. Therefore, the TyG index could be a useful marker for detecting atherosclerotic burden and inflammatory status. Although there are several studies which have illustrated the relationship with poor prognosis in both ST-elevated or non-ST-elevated myocardial infarction[26,27], the relationship with rSS and higher TyG index values have not been shown yet. In this study, we showed that there is a significant relationship between high TyG index and rSS in STEMI, which is a mortal consequence of atherosclerosis. Our study revealed TyG index was an independent predictor of the rSS.

Advanced age is closely associated with coronary artery disease, and problems such as calcification, multivessel disease and tortiosity increase the SYNTAX score[28]. In addition, comorbid conditions such as HT, hyperlipidemia and PAD are more common in elderly patients[29]. The relationship of advanced age with both SYNTAX Score and rSS has been demonstrated by previous studies[30]. Consistent with the literature, our study showed that advanced age was associated with the rSS, and even an independent predictor of rSS.

Our study has some limitations. Firstly, the number of patients included in this retrospective study is relatively small. Therefore, our findings should be supported by prospective studies involving large patient groups. The absence of a control group is the second limitation. In addition, not evaluating the effect of increased TyG index on cardiovascular events in the short and long term is another limitation.

In conclusion, high TyG index is associated with higher rSS in STEMI patients. The TyG index is also an independent indicator of increased coronary artery disease severity after PCI. In addition, the TyG index correlates with rSS and it is a cheap and rapid scoring system for estimating atherosclerotic burden in STEMI patients. In order for the current index to be used in the clinic practice; prospective, randomized controlled studies with a larger number of patients are needed.

Yazar Katkıları: Çalışma konsepti/Tasarımı: YA, SK, ARD; Veri toplama: YA, GD, EA, AEU; Veri analizi ve yorumlama: YA, ARD, BU; Yazı taslağı: YA, TA, AG, ME; İçeriğin eleştirel incelenmesi: ME; Son onay ve sorumluluk: YA, ARD, AG, TA, SK, BU, GD, EA, AEU, ME; Teknik ve malzeme desteği: -; Süpervizyon: YA, AG, TA; Fon sağlama (mevcut ise): yok.
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