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The Triglyceride Glucose Index and Triglyceride/HDL Ratio as Predictors of Coronary Artery Disease

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ABSTRACT

Aim: Triglyceride to high density lipoprotein cholesterol (TG/HDL-C) ratio and triglyceride-glucose (TyG) index are simple, reliable screening methods. It has been shown that the TyG index predicts mortality in cardiovascular diseases, and the TG/HDL-C ratio predicts the severity of coronary artery disease (CAD). The aim of this study is to define the relationship between the SYNTAX score, which indicates the severity of CAD, and the TyG index and TG/HDL-C ratio.

Material and Methods: A total of 408 patients who underwent coronary angiography were evaluated in this study. TyG index, TG/HDL-C ratio and SYNTAX scores were calculated. Patients were grouped according to their diagnosis and SYNTAX scores. Relationships between TyG index, TG/HDL-C ratio and SYNTAX score were examined.

Results: There was a significant relationship between the TyG index and the presence of CAD (p<0.001). TyG index was significantly higher in patients with severe CAD than patients with mild CAD ((8.46 ± 0.54) vs.(8.98 ± 0.67), p=0.045). While there was a significant positive association between TG/HDL-C ratio and the presence of CAD (p<0.001), there was no significant relationship between severity of CAD (p=0.814). The TyG index values of those presenting with ST elevation myocardial infarction were higher than those presenting with stable angina pectoris (p=0.050).

Conclusion: The TyG index and TG/HDL-C ratio were predictors of the presence of CAD and the TyG index also provides guidance on the severity of CAD. Standard use may be considered in addition to risk scoring in the diagnosis of CAD and planning coronary angiography.

Keywords: Triglyceride-glucose index; triglyceride/high density lipoprotein ratio; SYNTAX score; coronary artery disease.

Koroner Arter Hastalığının Öngördürücüleri Olarak Trigliserid Glikoz İndeksi ve Trigliserid/HDL Oranı

ÖZ

Amaç: Trigliserid/yüksek yoğunluklu lipoprotein kolesterol oranı (TG/HDL-C) ve trigliserid-glikoz (TyG) indeksi basit, güvenilir tarama yöntemleridir. TyG indeksinin kardiyovasküler hastalıklarda mortaliteyi öngördüğü ve TG/HDL-C oranının koroner arter hastalığının (KAH) ciddiyetini öngördüğü gösterilmiştir. Bu çalışmanın amacı, KAH'ın şiddetini gösteren SYNTAX puanı ile TyG indeksi ve TG/HDL-C oranı arasındaki ilişkiyi belirlemektir.

Gereç ve Yöntemler: Bu çalışmada koroner anjiyografi yapılan toplam 408 hasta değerlendirildi. TyG indeksi, TG/HDL-C oranı ve SYNTAX skorları hesaplandı. Hastalar tanılarına ve SYNTAX puanlarına göre gruplandırıldı. TyG indeksi, TG/HDL-C oranı ve SYNTAX skor arası ilişki incelendi.

Bulgular: TyG indeksi ile KAH varlığı arasında anlamlı bir ilişki vardı (p <0,001). TyG indeksi, şiddetli KAH olan hastalarda hafif KAH olan hastalarda bafif KAH olan hastalarda göre anlamlı olarak daha yüksekti ((8.46 ± 0.54) ve (8.98 ± 0.67), p=0.045). TG / HDL-K oranı ile KAH varlığı arasında anlamlı pozitif ilişki varken (p <0,001), KAH şiddeti arasında anlamlı bir ilişki yoktu (p=0,814). ST yükselmeli miyokard infarktüsü ile başvuranların TyG indeksi değerleri stabil anjina pektoris ile başvuranlara göre daha yüksekti (p=0,050).

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Sonuç: TyG indeksi ve TG / HDL-C oranı, KAH varlığının öngörücüleridir ve TyG indeksi, KAH'ın ciddiyeti hakkında da yol gösterir. KAH tanısında ve koroner anjiyografi planlamasında risk skorlamalarına ek olarak standart kullanımı düşünülebilir.

Anahtar Kelimeler: Trigliserid-glikoz indeksi; trigliserit/yüksek yoğunluklu lipoprotein oranı; SYNTAX skoru; koroner arter hastalığı.

INTRODUCTION

Coronary artery disease is one of the most important causes of the cardiovascular deaths. The main risk factors in the development of CAD are male gender, hypertension, diabetes, smoking, family history, and hyperlipidemia (1). In clinical practice, CAD may present as stable angina pectoris (SAP), unstable angina pectoris (USAP), non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI). Some scoring systems have been developed to determine the severity of CAD according to coronary angiography findings. The SYNTAX score is one of the scoring systems used in evaluating the severity of CAD (2).

High triglyceride and fasting blood sugar levels are also components of the metabolic syndrome (3). The combination of both indicators, the TyG index, is calculated as Ln (fasting triglyceride (mg / dl) × fasting glucose (mg / dl) / 2). Especially in diabetic patients, the relationship between TyG index and CAD has been demonstrated (4). However, the role of the TyG index in predicting the severity of coronary artery disease in patients diagnosed with coronary artery disease, regardless of diabetes diagnosis, has not been comprehensively evaluated.

The relationship between total cholesterol, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) and CAD is known (5). There is evidence that serum triglyceride value may be an independent risk factor for cardiovascular diseases (6,7). High TG and low HDL-C are the main features of the metabolic syndrome, which is strongly associated with CAD (3). TG / HDL-C ratio may be a good predictor of CAD (8,9).

The aim of this study is to evaluate the relationship between the TyG index and TG / HDL-C ratio, which are composed of metabolic syndrome components and have been supported CAD relations by previous studies, and the SYNTAX score.

MATERIAL AND METHODS Study design

A total of 1200 patients who underwent coronary angiography at our institution between the August 2019 and March 2020 were retrospectively screened. Those who have previously undergone percutaneous or surgical revascularization, those who are receiving hyperlipidemia treatment, those whose triglyceride and glucose values are not recorded, patients with chronic renal failure, chronic liver disease, malignancy, severe heart valve disease and severe heart failure, patients with type 1 diabetes and patients on insulin therapy were excluded from the study. Finally, data of 408 patients who underwent coronary angiography were recorded. The study was approved by the Ethics Committee of Ankara City Hospital (09.12.2020, E1-20-1360).

Laboratory Measurements

Serum fasting glucose, blood urea nitrogen (BUN), serum creatinine, total cholesterol, triglyceride, LDL-C, HDL-C, hemoglobin, and platelet levels were recorded from the available hospital data on the first day of hospitalization. The TyG index was calculated as Ln (fasting triglycerides mg/dL \times fasting glucose mg/dL /2) (4). The TG / HDL-C ratio was calculated by dividing the serum triglyceride level to the HDL-C level (10).

SYNTAX Score

The SYNTAX score, which consists of 12 basic questions, is prepared by using angiographic features such as the number of lesions, plaque structure, thrombus content, functional significance, and the location of the lesion, and enables the severity of coronary artery disease to be determined. It is also an important guide in identifying patients who will undergo percutaneous or surgical revascularization. In our study, angiographic data were obtained from cardiac catheterization laboratory records. SYNTAX score was obtained by calculating separately for each lesion and summing up all lesion scores. SYNTAX score $\leq 1-22$ low, 23-32 medium, 33 and above, was considered high (11).

Statistical analysis

Data analysis was performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was determined by the Kolmogorov Smirnov test. Identifying statistics of parametric numeric data were calculated as average ± standard deviation, non parametric ones were calculated as median (minimum-maximum); categorical data were given as percentage (%). Comparison of categorical measurements between the groups were done with the Chi Square Test. For the comparison of numeric measurements between the groups, T test was used in Independent Groups if the assumptions were ensured, and the Mann Whitney U test if the assumptions were not ensured. While the differences in normally distributed variables among more than two independent groups were analyzed by One-Way ANOVA, otherwise, not normally distrubuted data were compared with the Kruskal Wallis test. It was evaluated degrees of relation between variables with pearson correlation or spearman correlation analysis. Continuous variables were compared with an one way anova test or the Kruskal wallis test. LSD or Conover-Inman test were performed for the binary comparisons among the groups. It was accepted p-value < 0.05 as significant level on all sctatistical analysis.

RESULTS

A total of 408 patients who underwent coronary angiography were evaluated. The patients were divided into 4 groups according to their admission diagnosis as 144 patients with stable angina pectoris (35.3%), 71 patients with USAP (17.4%), 113 patients with NSTEMI (27.7%) and 80 patients with STEMI (19.6%). While normal coronary arteries were detected in 110 patients (26.9%) in coronary angiography, more than 50% of stenosis was present in at least one major epicardial

vessel of the 298 patients (73.1%). According to SYNTAX scores of the 298 patients, of them 115 (38.6%) had mild, of them 94 had moderate (31.5%) and of them 89 had severe (29.9%) CAD.

The TyG index (p <0.001) and TG / HDL-C ratio (p <0.001) were statistically significantly higher in the group with CAD compared to the group with normal coronary arteries. In the group with CAD, male gender (p<0.001), smoking (p=0.003), presence of HT (p=0.019), presence of DM (p<0.001), BUN level

(p=0.008), fasting blood glucose (p=0.001) and triglyceride (p<0.001) values were higher than the non-CAD group. HDL-C value was significantly lower in the group with CAD (p <0.001). Mean age, mean BMI, hemoglobin, creatinine, total cholesterol and LDL cholesterol values were similar for the two groups. The demographic, clinical and laboratory data of the patients according to the presence of CAD are summarized in Table 1.

Table 1. Demographic variables and basic clinical characteristics in CAD and non-CAD groups.

	CAD group (n=298) mean±SD or n(%)	Non-CAD group (n=110)	P value
Age, year	60.47 ± 10.48	58.66±9.61	0.115
Gender, male	208 (71.2%)	46(39.7%)	<0.001
BMI (kg/m ²)	26.06 ± 2.59	25.92±3.12	0.136
НТ	197 (67.50%)	63(54.30%)	0.019
DM	131 (43.95%)	29(26.36%)	<0.001
Smoking	176(59.06%)	35(31.81%)	0.003
LVEF(%)	49.86±11.28	61.62±4.68	0.001
TyG index	8.75 ± 0.61	8.16±0.54	<0.001
TG/HDL-C	4.66±2.86	3.21±1.59	<0.001
Hemoglobin (g/dl)	13.82 ± 1.90	13.83±1.60	0.950
Fasting Glucose	132.60±55.28	112.57±39.70	0.001
BUN	39.38±18.73	33.83±17.99	0.008
Creatinine (mg/dl)	1.08 ± 0.57	0.99±0.62	0.168
Total cholesterol (mg/dl)	205.96± 41.48	202.08 ± 48.72	0.458
HDL (mg/dl)	43.44 ± 11.53	49.36±14.11	<0.001
LDL (mg/dl)	121.36 ± 40.10	126.60±34.67	0.226
Triglyceride (mg/dl)	189.06 ± 98.89	150.19±64.42	<0.001

HT; Hypertension; DM, diabetes mellitus; BMI, body mass index; HDL, high-density lipoprotein; LDL, low- density lipoprotein; BUN, blood urine nitrogene; LVEF, left ventricular ejection fraction; TyG index, triglyceride-glucose index; TG/HDL-C, triglyceride-HDL cholesterol ratio; CAD, coronary artery disease; SD, standart deviation.



Figure 1. The TyG index rates by CAD severity categorized by SYNTAX score. TyG index, triglyceride-glucose index;. a: Mild vs Modarate, b: Mild vs Severe, c: Modarate vs Severe, d: Non-CAD vs CAD



Figure 2. The TG / HDL-C ratios by CAD severity categorized by the SYNTAX score. TG/HDL-C, Triglyceride / high density lipoprotein cholesterol ratio; CAD, coronary artery disease, a: Mild vs Modarate, b: Mild vs Severe, c: Modarate vs Severe, d: Non-CAD vs CAD

A significant relationship was found between mild, moderate and severe CAD in terms of mean age (p=0.001), fasting blood glucose (p <0.001), BUN (p=0.001), and presence of DM (p=0.001). There was no statistically significant difference in terms of gender, smoking, BMI, presence of HT, creatinine, total cholesterol, LDL-C, HDL-C and triglyceride values. The relationship of CAD severity and cardiovascular risk factors, TyG index and TG / HDL-C are summarized in Table 2.

TyG index was significantly higher in patients with severe CAD than patients with mild CAD ((8.46±0.54)

vs.(8.98±0.67), p=0.045). Moderate CAD patients had higher TyG index values than patients with mild CAD ((8.46±0.54) vs. (8.79±0.61), p=0.078). There was no significant association between patients with moderate and severe CAD in terms of the TyG index (p=0.168). Figure 1 shows the TyG index rates by CAD severity categorized by SYNTAX score.

No significant relationship was found between the SYNTAX score and TG / HDL-C ratio in terms of mild-moderate and severe CAD (p=0.814). Figure 2 shows the TG / HDL-C ratios by CAD severity categorized by the SYNTAX score.

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	SYNTAX ≤1-22 (n=115) mean±SD or n(%)	SYNTAX 23-32 (n=94) mean±SD or n(%)	SYNTAX ≥33 (n=89) mean±SD or n(%)	p value
Age, year	58.91±10.18	59.40±10.20	63.60±10.55	0.001 ^{b,c}
Gender, male	76 (66.1%)	68 (72.3%)	65 (73.0%)	0.478
BMI (kg/m ²)	27.17±3.06	27.01±2.49	27.07±2.02	0.686
НТ	72(62.6%)	60(63.8%)	68(76.4%)	0.083
DM	34(29.6%)	45(47.9%)	52(58.4%)	0.001 ^b
Smoking	71(61.7%)	63(67.0%)	55(61.8%)	0.732
LVEF(%)	55.50±8.16	50.02±9.39	43.10±12.71	<0.001
TyG index	8.46±0.54	8.79±0.61	8.98±0.67	0.045 ^b
TG/HDL-C	4.60±2.40	4.71±3.57	4.47±2.55	0.814
Hemoglobin (g/dl)	14.05±1.73	14.01±1.60	13.31±2.95	0.076
Fasting Glucose	117.42±45.48	138.45±53.96	141.03±63.54	<0.001 ^{a,b}
BUN	35.26±13.77	38.05±16.73	44.10±23.54	0.001 ^b
Creatinine (mg/dl)	0.97±0.30	1.10±0.69	1.20±0.66	0.062
Total cholesterol (mg/dl)	203.93±48.30	200.44±44.47	201.40±53.78	0.983
HDL (mg/dl)	43.87±9.51	43.23±12.28	42.10±13.09	0.379
LDL (mg/dl)	122.31±41.07	120.15±38.55	121.41±40.86	0.997
Triglyceride (mg/dl)	193.22±99.95	192.34±100.97	180.23±95.81	0.092

HT; Hypertension; DM, diabetes mellitus; BMI, body mass index; HDL, high-density lipoprotein; LDL, low- density lipoprotein; BUN, blood urine nitrogene; LVEF, left ventricular ejection fraction; TyG index, triglyceride-glucose index; TG/HDL-C, triglyceride-HDL cholesterol ratio; CAD, coronary artery disease; SAP, stable angina pectoris USAP, unstable angina pectoris; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction, SD, standart deviation. Continuous variables are expressed as the mean ± standard deviation (SD). Continuous variables were compared with an one way anova test or the Kruskal wallis test. LSD or Conover-Inman test were performed for the binary comparisons among the groups and the p value was set at 0.05. Significant differences were found between; a: Mild vs Modarate, b: Mild vs Severe, c: Modarate vs Severe

When patients with no CAD were excluded from the evaluation and analyzed in terms of their admission diagnoses and the relation of TyG index, TG / HDL-C ratios. There was no statistically significant relationship between indexes and admission diagnoses. There was a borderline significant relationship between SAP and STEMI patients only for the TyG index (p=0.050).

There was a mildly significant relationship between the TyG index and the presence of CAD in diabetic patients ((8.99 \pm 0.60), (8.73 \pm 0.54) p=0.049). TG / HDL-C ratio was significantly higher in patients with CAD ((4.75 \pm 2.80), (3.14 \pm 1.25) p=0.005).

DISCUSSION

In our study, the role of the TyG index and TG / HDL-C ratio in evaluating the presence and severity of CAD, and their relationship with admission diagnoses were

examined. While the TyG index and TG / HDL-C ratio were predictive for the presence of coronary artery disease, a significant relationship was found between the TyG index and mild-severe CAD in patients with coronary artery disease. It was found that TG / HDL-C ratio did not have a predictive value in terms of mildmoderate-severe CAD.

In previous studies, the relationship between atherosclerosis and TyG index was investigated. It has been stated that the TyG index is positively associated with the prevalence of symptomatic CAD and can be used as a marker for atherosclerosis (12). It was also found that the TyG index was independently associated with arterial stiffness (13).

The study investigating the role of the TyG index in demonstrating the severity of CAD belongs to an isolated group of the patients with NSTEMI (14). In this study, it

was determined that the TyG index may be an independent predictor for CAD severity and cardiovascular outcomes in NSTEMI. It has been shown that high TyG index in STEMI patients is associated with an increased risk of major cardiac and cerebrovascular events (15).

In previous studies, increased TG / HDL-C ratio was associated with LDL particle size and this ratio was defined as an atherogenic marker (16). It has been found that the TG / HDL ratio is a strong predictor of myocardial infarction (17). In postmenopausal women, a high triglyceride / HDL-C ratio has been associated with an increased likelihood of carotid plaques (18). In female patients, it has been shown that the TG / HDL-C ratio is independently associated with major cardiovascular events in patients presenting with revascularized STelevation myocardial infarction (10). It has been shown that the TG / HDL-C ratio may be an important predictor for acute coronary syndrome in the young adult population (19). In addition, after a successful revascularization for acute coronary syndrome, TG / HDL-C ratio was determined to be a risk factor for revascularization (20).

In a study, the relationship between TG / HDL ratio and Gensini score was investigated, and it was found that the TG / HDL ratio was predictive for CAD (21). In our study, no significant relationship was found between TG / HDL-C and the severity of CAD determined by the SYNTAX score. In the study of Yunke et al., the fact that patients who had previously undergone percutaneous and surgical revascularization and those who received hyperlipidemia treatment were not excluded from the study. Due to the presence of cholesterol data in the indexes used, patients who were revascularized before and received hyperlipidemia treatment were not included in our study.

In our study, one of the reasons that the TG / HDL-C ratio was not related to the severity of CAD is that triglyceride and HDL levels did not change significantly as the SYNTAX score increased. SYNTAX score and lipid parameters were evaluated in previous studies. In the group including NSTEMI patients, the relationship between SYNTAX score and HDL value was significant (22), while no relationship was found between low and high SYNTAX score and dyslipidemia in stable CAD (23). Another reason is that the nutritional deficiency that develops on the basis of chronic disease in the presence of severe CAD may have caused the difference to decrease in the advanced stage and the results to be insignificant. These results once again emphasize the importance of detecting and treating hyperlipidemia before the diagnosis of CAD. In our study, patients who received hyperlipidemia treatment were not evaluated in terms of affecting the validity of the indices used. However, in order to determine the results in diabetic patients, type 2 DM patients whose blood glucose was regulated with an oral antidiabetic were included in the study. The rate of diabetes was significantly higher in patients with CAD, and the presence of diabetes was positively associated with the severity of CAD. While the TyG index was significantly lower in predicting CAD in diabetic patients, the TG / HDL-C ratio was significantly higher in those with diabetes and CAD.

The relationship between insulin resistance and the severity of coronary atherosclerosis in diabetic and nondiabetic patients have been shown in previous studies (24,25). TyG index is a marker associated with insulin resistance (26) and metabolic syndrome (27). The relationship between the TyG index and the presence and severity of CAD was supported by our study.

Limitation

In our study, the patients could not be evaluated in terms of short and long-term adverse cardiovascular events due to insufficient follow-up data. The prognostic value of the TyG index and TG / HDL-C ratio could not be examined. Diabetic patients were not excluded from the study, but type 1 DM patients with uncontrolled diabetes and patients using insulin were not included in the study. In our study, the high rate of normal coronary artery was associated with the exclusion of patients who had a previous diagnosis of CAD and had undergone percutaneous and surgical revascularization.

CONCLUSION

TyG index and TG/HDL-C ratio are valuable applicable markers to predict the presence of coronary artery disease. The TyG index can be useful in estimating the severity of CAD. The TyG index and TG/HDL-C ratio may play a key role in predicting cardiovascular specific risk. These results remind once again the importance of a healthy and cholesterol-restricted diet, hyperlipidemia treatment and blood glucose regulation in terms of CAD.

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