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The clinical importance of triglyceride/glucose ratio in the primary prevention of cardiovascular diseases: A retrospective cohort study

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Abstract

Background/Aim: Atherosclerosis plays a significant role in cardiovascular diseases. Dyslipidemia, inflammation, genetics, and environmental factors greatly impact the development and progression of atherosclerosis. This study aimed to investigate the importance of triglyceride-glucose ratio in primary cardiovascular event prevention.
Methods: Our retrospective cohort study included 56 patients (39 males, 17 females). Coronary computed tomography angiography (CCTA) images of the individuals were examined, and calcium score was calculated using the Agatston score. Those with a score of zero and those with scores>0 were included in Groups 1 and 2, respectively. Triglyceride/glucose (TyG) ratio and atherosclerotic cardiovascular disease (ASCVD) risk were calculated for all individuals.
Results: Among all patients, 69.6% had coronary artery calcium scores (CACs) of greater than zero. The TyG ratios were 0.92 (0.33) and 1.77 (0.83) in Groups 1 and 2, respectively ($P<0.001$). The ASCVD risk was 4.17 (4.92) in Group 1, and 16.24 (10.66) in Group 2 ($P<0.001$). The TyG ratio was positively correlated with calcium score and ASCVD risk (r=0.717, $P<0.001$ and r=0.456, $P<0.001$, respectively). TyG ratio (OR=33.132, 95% CI=4.404-249.254, $P=0.001$) predicted CACs in CTBA in the univariate logistic analysis. The cut-off level for the TyG ratio in the prediction of coronary atherosclerosis was 1.04, with a sensitivity of 74%, and a specificity of 88% (AUC=0.84, $P<0.001$).
Conclusion: The present study showed that the TyG ratio could assist the current risk assessment scores used for primary prevention in cardiovascular diseases.

Keywords: Cardiovascular diseases, Coronary calcium score, Prevention

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Ethics Committee Approval
Çanakkale Onsekiz Mart University clinical research ethics committee (11.11.2020/ 2011-KAEK-27/2020-E.2000141331)
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Introduction

Cardiovascular diseases (CVD) are among the chronic non-communicable diseases, which cause the highest mortality and morbidity in developed countries, despite rapid technological developments and improvements in risk factors in recent years [1]. The high incidence of CVD increased the routine use of noninvasive imaging methods in addition to invasive imaging methods such as coronary artery angiography (CAG) for diagnosis and treatment [2]. Coronary computed tomography angiography (CCTA) provides excellent diagnosis and is the preferred anatomical test for patients with an ASCVD score of 5-7.5 indicating moderate CV risk [3].

CCTA, which is a non-invasive method, has high sensitivity in predicting coronary artery disease (CAD). The coronary artery calcium score (CACs), obtained by performing CBTA, gives valuable information on the prediction and prognosis of patients [4]. Several studies showed that CACs is correlated with the percentage of stenosis in coronary arteries and the plaque burden causing stenosis. When CACs is zero, atherosclerotic activity is very likely to be excluded [5].

Various scoring systems are used in the risk assessment of CVD. Age, hypertension, smoking, and total cholesterol values are used in the current risk scoring systems [6]. Fasting blood glucose and plasma triglyceride levels are not included in most scoring systems; however, certain studies emphasized the importance of including the two values in risk classifications [7].

Triglyceride glucose (TyG) index, which can be calculated logarithmically, is a new marker proven for its relationship with carotid atherosclerosis and insulin resistance [8].

This study aimed to investigate the relationship of TyG ratio to CACs with a simpler calculation, and its usability in primary protection against CVD.

Materials and methods

Study population

This retrospective cohort study examined the coronary computed tomography angiography images obtained between January 2018 and September 2020 of 56 individuals with low and medium risk for coronary artery disease, who presented to the cardiology outpatient clinic. The medical history and laboratory values of the patients, whose calcium scores were calculated through the images, were also examined. The population of the study was divided into two groups as Group 1, including the individuals with CACs values equal to zero, and Group 2, consisting of patients with CACs values greater than zero.

According to the SCORE risk table, patients older than 40 years and younger than 65 years were deemed eligible. Calculation of cardiovascular risk in individuals aged between 40-65 years was made using the SCORE risk table as recommended in the guidelines, and individuals under 40 and over 65 years of age were excluded because the risk table calculates the scores of patients in a certain age range [9]. Cardiovascular risk calculation was performed in patients who presented with chest pain and had a pre-diagnosis of coronary artery disease in the outpatient clinic, and patients with low and medium risk who underwent CCTA examination were included. Patients with chronic renal failure, acute coronary syndrome, active infection, malignant disease, cerebrovascular disease, coronary artery bypass, and stent history, patients who were scheduled for serious valve surgery and prosthetic valves, those with low-density lipoprotein (LDL) cholesterol values over 190 mg/dl, those with lipid metabolism disorders, hypertension or diabetes were not included. No patient was taking cholesterol-lowering medication. According to the CCTA report, less than 50% of all patients had nonsignificant stenosis in their coronary arteries.

Blood samples obtained from the antecubital veins after 12 hours of fasting were analyzed on the Beckman Coulter LH-780 device (Beckman Coulter Ireland Inc. Mervue, Galway, Ireland). The results of complete blood count, lipid panel, and kidney function tests were obtained. Blood samples were studied before CCTA.

The Score risk chart published on the https://www.heartscore.org website was used for the calculation of 10-year fatal CVD risks (ASCVD) [10]. A post-hoc power analysis was performed with G*Power (software version 3.1.9.6). An effect size of 0.75, alpha error of 0.05, and 17 patients in group 1 and 39 patients in group 2 yielded a power of 0.8167938 for the independent samples t-test.

Prior to the study, the approval of the Çanakkale Onsekiz Mart University Clinical Research Committee was obtained (Date: 11.11.2020 and Decision no: 2020-13/2011-KAEK-27/2020-E.2000141331). Our study was conducted in accordance with the Helsinki Declaration.

Calcium score of coronary arteries

Calcium scoring was performed using a 64-slice CT device (Acquilion 64 Toshiba, Japan, and Sensation 64 Siemens, Germany). The imaging was performed per the technique recommended in the literature, and the amount of calcification was calculated with Agatston scoring. An Agatston score of zero indicates that there is no calcification in the atherosclerotic plaque. An increase in the score indicates that the individual is at risk for cardiovascular disease [11].

The triglyceride/glucose (TyG) ratio was obtained by dividing the fasting triglyceride (mg/dl) value by the serum glucose (mg/dl) value.

Statistical analysis

SPSS 21.0 (SPSS Inc, Chicago, IL, USA) software was used for statistical analysis. Whether the variables conformed to the normal distribution was evaluated using the Shapiro-Wilk test. While the mean ± standard deviation was used in the presentation of continuous variables, percentage and number were used for categorical variables and the data were presented as median (minimum-maximum) for non-normally distributed continuous variables. Student's test analysis was performed for the normally distributed parametric values between groups, and the Chi-square test was used to compare the differences between categorical variables. Pearson's correlation analysis was used to determine the relationship between the TyG ratio, calcium score, and ASCVD risk. Univariate logistic regression analysis was performed to determine CACs in CTBA. The ROC curve analysis was performed to determine the accuracy of the ASCVD risk and TyG ratio values in predicting coronary atherosclerosis. A *P*-value of <0.05 was considered statistically significant.

Results

The basic clinical and laboratory values of the groups are presented in Table 1.

Table 1: Demographic, clinical and laboratory features of the patients

Variables	Group 1(n=17) (CACs =0)	Group 2 (n=39) (CACs >0)	*P*-value
Age (years), mean (SD)	46.2 (6.5)	56.8 (7.4)	<0.001
Female (n, %)	8(47.1)	9(23.1)	0.078
HT (n, %)	0(0)	22(56.4)	<0.001
DM (n, %)	2(11.8)	11(28.2)	0.160
Current smoker (n, %)	7(41.2)	23(59)	0.219
Serum glucose (mg/dL), mean (SD)	100.90 (19.73)	118.45 (34.95)	0.058
Creatinine (mg/dL), mean (SD)	0.76 (0.12)	0.87 (0.20)	0.013
TSH (mU/L), mean (SD)	0.76 (0.38)	0.76 (0.43)	0.992
LDL-C (mg/dL), mean (SD)	111.77 (25.61)	126.16 (39.50)	0.301
Triglyceride (mg/dL), mean (SD)	90.82 (26.41)	200.11 (79.72)	<0.001
HDL-C (mg/dL), mean (SD)	50.04 (11.94)	50.61 (10.82)	0.860
Total cholesterol (mg/dL), mean (SD)	175.52 (14.62)	206.61 (41.64)	0.004
WBC count, ($x10^3$ µL), mean (SD)	8.33 (1.60)	7.86 (1.93)	0.465
Hemoglobin (g/dL), mean (SD)	13.91 (1.58)	14.33 (1.26)	0.331
TyG ratio, mean (SD)	0.92 (0.33)	1.77 (0.83)	<0.001
ASCVD risk, mean (SD)	4.17 (4.92)	16.24 (10.66)	<0.001

DM: Diabetes mellitus, HT: Hypertension, TSH: Thyroid Stimulating Hormone, LDL-C: Low-density lipoprotein, HDL-C: High-density lipoprotein, WBC: White blood cell, TyG: Triglyceride-glucose, ASCVD: Atherosclerotic cardiovascular disease, CACs: Coronary artery calcium scores

The mean age of all individuals was 56 (8.6) years. Of the 56 individuals, 39 were male and 17 were female. Individuals with a calcium score greater than zero were older than the others. Group 2 had significantly higher total cholesterol and creatine values compared to Group 1 (*P*<0.05 for both parameters). In the group with a calcium score greater than zero, the TyG ratio and the risk of ASCVD were significantly higher (*P*<0.001 for both parameters). In the correlation analysis, the TyG ratio was positively correlated with the ASCVD risk and the calcium score (r=0.456, *P*<0.001 and r=0.717, *P*<0.001, respectively) (Table 2). Ty (*P*=0.027), total cholesterol (*P*=0.039), ASCVD risk (*P*=0.011) and TyG ratio (*P*=0.001) were predictors of CACs in CTBA in the univariate logistic regression (Table 3).

Table 2: Correlation coefficients for TyG

Variable	r	*P*-value
ASCVD risk	0.456	<0.001
CACs	0.717	<0.001

ASCVD: Atherosclerotic cardiovascular disease, TyG: Triglyceride-glucose, CACs: Coronary artery calcium scores

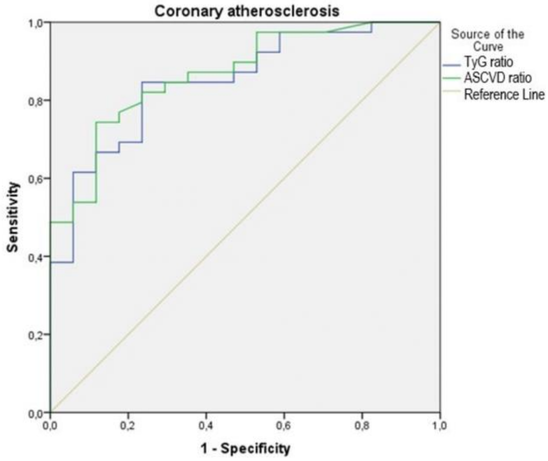
Table 3: Univariate regression analysis to determine CACs in CCTA

Variables	B	OR	*P*-value
Female gender	-1.086	0.338	0.078
HT	21.264	1.716	0.998
DM	1.081	2.946	0.194
Current smoker	0.720	2.054	0.223
LDL-C	0.012	1.012	0.141
Triglyceride	0.015	1.016	0.027
HDL-C	0.005	1.005	0.857
Total cholesterol	0.016	1.016	0.039
ASCVD risk	1.060	2.887	0.011
TyG ratio	3.500	33.132	0.001

SE: Standard error, OR: Odds ratio

The ROC analysis, which was performed to determine the accuracy of the ASCVD risk and TyG ratio values in predicting coronary atherosclerosis, is presented in Figure 1. The area under the curve (AUC) value of the ASCVD risk was 0.86 (95% confidence interval (CI): 0.74-0.95, *P*<0.001), and the AUC value of TyG ratio was 0.84 (95% CI: 0.74-0.95, *P*<0.001).

Figure 1: Receiver operating characteristic (ROC) curves for ASCVD ratio and TyG raito in the prediction of coronary atherosclerosis



Discussion

To the best of our knowledge, this is the first study to reveal the usability of the TyG ratio for primary prevention as well as its relationship with the ASCVD risk and coronary calcium scores of the individuals. Important results were obtained by statistical analysis. First, it was noticed that the TyG ratio could be used to prevent cardiovascular diseases, such as the ASCVD risk. Second, a positive correlation was detected between the coronary calcium score, which provides important insights into the detection of atherosclerotic activity, and the TyG ratio.

Atherosclerosis starts early in life and can cause various clinical pictures in the advanced decades. Pre-identification of CVD and the measures that can be taken by identifying reversible risk factors would reduce the clinical poor outcomes such as stroke and myocardial infarction (MI). Previous studies proved that the coronary calcium burden provides prognostic information in addition to the classic risk factors, and it should be considered when calculating the risk factors [12]. CVD can be excluded when CACs equals zero [13].

In their classification of the atherosclerotic CVD risk, Yader et al. reported that the CACs provided significant information in the long-term prediction of the ASCVD risk [14]. In our study, we demonstrated a significant correlation between ASCVD risk, CACs and TyG ratios. Since this relationship is particularly affected by nutritional habits, individual decisions should be made in clinical use. Triglycerides are fats carried in the blood. Most butter and oils consumed are in the form of triglycerides and the excess calories are converted into triglycerides and stored in fat cells in the body [15].

In their studies on dyslipidemia, Kim and Lee et al. reported that the logarithmically calculated TyG index was associated with arterial stiffness and coronary artery calcification in Korean adults. In another study, the TyG index was an independent predictor of the severity of coronary and peripheral artery diseases. The TyG index was associated with adverse cardiovascular outcomes in the follow-up of diabetes patients with stents diagnosed with acute coronary syndrome [16–18].

In most studies, the TyG index was associated with arterial diseases. We know that the CACs value increases due to the increase in the atherosclerotic activity, and the atherosclerotic activity increases due to the increase in the ASCVD risk [19].

We demonstrated that the TyG ratio, a simpler and practical calculation method, was positively correlated with coronary artery calcification, which is an indicator of atherosclerotic activity. Previous studies reported that dyslipidemia was associated with atherosclerosis, and each cardio-protective condition was had an important role in preventing atherosclerosis [20]. As a result of the correlation and the ROC analysis we performed in our study, we demonstrated that the TyG ratio can be used in primary protection, such as the ASCVD risk, which is associated with the atherosclerotic burden.

Limitation

Its retrospective and single-center design was the main limitation of our study. Another limitation was the small number of individuals included and the lack of follow-up data due to the type of study.

Conclusion

There are various risk factors in the formation of CVD, and it is not possible to include all risk factors in a single scoring system. Considering the literature, although there are various algorithms that can be used to calculate the cardiovascular disease risk of patients, their use in all individuals is limited. Hence, the identification of individual risk factors and their elimination, if possible, are of great importance in primary prevention. Multi-centered prospective studies are needed to elucidate the effects of the TyG ratio on mortality and morbidity in primary prevention, since no long-term follow-up results were available. The ASCVD risk can be obtained from the Score graph recommended in the literature.

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