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Original Article

The predictive value of triglyceride to high density lipoprotein cholesterol ratio in patients with isolated coronary artery ectasia

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Abstract

Aim: The pathophysiology of coronary artery ectasia (CAE) has not been clear. Dyslipidemia is a serious cause for increasing the risk of coronary artery disease. The relationship between isolated CAE and dyslipidemia is unknown. We evaluated the triglyceride to high-density lipoprotein cholesterol ratio (Tg to HDLc) and dyslipidemia in patients with isolated CAE.

Material and Methods: We included 60 patients and 70 controls with normal coronary arteries with similar baseline risk factors. Total cholesterol (Tc), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (Tg) levels were measured and Tg to HDLc ratio was calculated. Factors predicting CAE were analyzed.

Results: When compared with the controls serum Tg level and Tg to HDLc ratio were significantly higher, HDLc level was significantly lower in the patients (p=0.001; p=0.004; p=0.001, an respectively). The multivariate logistic regression analysis revealed that Tg to HDLc ratio (OR:1.476, 95% CI 0.1199-1.817, p=0.001) was independent factor predicting isolated CAE. In the ROC curve analysis, Tg to HDLC ratio was found to be statistically significant with a cut-off point value of 4.2 was determined to predict isolated CAE [AUC=0.829, (95% CI, 0.752-0.906), p=0.001].

Conclusion: Tg to HDLc ratio, HDLc and triglycerides were found to be independent factors predicting isolated CAE. These lipid parameters and Tg to HDLc ratio may be a valuable, easily accessible, non-invasive way of predicting the presence of isolated CAE.

Keywords: Coronary artery disease; coronary artery ectasia; dyslipidemia; triglyceride

INTRODUCTION

Coronary artery ectasia is described as the enlargement of a coronary artery to one and a half times or more than that of the local or commonly normal coronary artery segment (1). Enlargements seen up to one and a half times of a coronary artery are described as ectasia and those over two-fold are called aneurysms (2). CAE is seen in the population with a frequency ranging between 0.3-4.9 % (3). It can be seen with coronary artery disease (CAD), but it can also be isolated. Isolated CAE without any stenotic lesions is rare among patients who undergo coronary angiography with a frequency of 0.1-0.79% (4,5). CAE may be congenital or acquired but most of the time it is associated with atherosclerosis (50%) (6), and congenital syndromes (20-30%) (7,9). The remaining 10-20% is thought to be related with connective tissue diseases such as scleroderma, polyarteritis nodosa, systemic lupus erythematosus (10). Inflammation plays an important role in the progression of atherosclerosis, coronary slow flow and also in CAE (11,12).

Dyslipidemia refers to a pathological condition that abnormal elevation of lipid parameters and lipoproteins in the blood and significantly increases the risk of CAD. Strong scientific evidence indicates that there is a significant association between incidence of cardiovascular disease (CVD) and dyslipidemia (13). Low HDLc, high Tg and high LDLc levels in the blood are the main determinants of CAD risk (14).Tg and also HDLc are considered important independent predictors that increase CAD severity (15). Therefore, Tg to HDLc ratio is accepted as an important predictor of atherosclerosis and coronary heart disease (CHD) (16).

Although the relationship between dyslipidemia and coronary artery disease is well known, there is little

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information about atherogenic dyslipidemia with isolated CAE. Therefore, We investigated the association between dyslipidemia and Tg to HDLc ratio in patients with isolated CAE.

MATERIAL and METHODS

A total of 10.320 coronary angiographies performed between June 2015 and August 2018 in our clinic were analyzed retrospectively. Among these, 60 patients with isolated CAE without stenotic lesions were identified and included in the study and in the control group, there were 70 participants with similar baseline risk factors and normal coronary arteries. Two independent interventional cardiologists unaware of the study results evaluated the coronary angiograms. CAE is described as the enlargement of a coronary artery to one and a half times or more than that of the local or commonly normal coronary artery segment in accordance with the angiographic description of Hartnell et al (1). Coronary angiography was performed in patients with myocardial ischemia and the presence of typical angina. Exclusion criterias were history of myocardial infarction, valvular heart disease, arrhythmia, left ventricular ejection fraction <50% (systolic heart failure), any cardiomyopathy, chronic renal failure, autoimmune diseases, malignancy and use of a cardiotoxic medication, or lipid-lowering therapy, and congenital heart disease. The patients with coronary artery stenosis over 30% were also excluded.

Diabetes mellitus was diagnosed according to the 'American Diabetes Association 2010 Guidelines' criteria (17). Hypertension (HT) was defined according to the presence of systolic/diastolic blood pressure ≥140/90 mm Hg during the hospital admission or previous diagnosis. After a twelve hour fasting, venous blood samples were taken for the following: serum glucose level, glycated HbA1c, lipid parameters, creatinine and complete blood count. LDLc was measured directly at triglyceride values above 400 mg/dL.

All ethical procedures in studies with human participants were performed and approval for the study was obtained from the Medical Ethics Committee of University of Health Sciences, Sisli Hamidiye Etfal Education and Research Hospital. Informed consent was not need. We used medical records only.

Statistical analysis

The data for continuous variables were reported as the mean ± standard deviation Categorical variables were reported as numbers and percentages. Data distribution was assessed with Kolmogorov-Smirnov test. Because of the sample size, non-normal distribution of variables was assumed and non-parametric tests were used for between group comparisons. A univariate comparison was performed with x^2-analysis for categorical data. To determine isolated CAE predictors, logistic regression model was used including all variables at 95% confidence level and for a p <0.05. The Tg to HDLc ratio to predict the presence of isolated CAE was evaluated with receiver operator characteristic curves. Statistical significance was described as a p <0.05. All the statistical analyses were performed using SPSS 20 software (SPSS Inc., Chicago, Illinois).

RESULTS

A total of 130 participants, 60 patients and 70 controls were included in the study. Of all patients, 59 (45.4%) were current smokers, 70 (53.8%) had HT and 20 (15.4%) had DM. The mean age of the patients was 58±9 years, and 63 (48.5%) were female. The baseline characteristics of the participants are presented in Table 1.

Table 1. Basal clinical and laboratory characteristics of patients

Clinical features	(n=130)
Age	58±9
Female (%)	63 (48.5)
Smoking (%)	59 (45.4)
BMI (kg/m2)	25.8±3.5
Hypertension (%)	70 (53.8)
Diabetes mellitus (%)	20 (15.4)
LVEF (%)	54±9
Coronary artery ectasia (%)	60 (46)
Hemoglobin (g/dL)	13.6±1.9
WBC count (K/μL)	8681±3048
Lymphocyte (K/μL)	2505±824
Neutrophil (K/μL)	5331±2885
Monocytes(K/μL)	630±205
Platelet (10^9/L)	241±63
Total cholesterol (mg/)	189±45
HDLc (mg/dL)	44±12
LDLc (mg/dL)	117±39
Triglyceride (mg/dL)	169±79
Tg to HDLc ratio	3.7±3.3
Creatinine (mg/dL)	0.9±0.7
Glucose (mg/dL)	118±56

BMI:Body mass index , LVEF: Left ventricular ejection fraction, WBC:White blood cell, HDLc: high-density lipoprotein cholesterol, LDLc: low-density lipoprotein cholesterol

Patients and controls were similar according to age, hypertension, body mass index, diabetes mellitus, smoking, total cholesterol, LDLc, glucose, LVEF and blood counts excluding hemoglobin. The number of female was higher in the control group (p=0.005). Hemoglobin and creatinine levels were significantly higher in the isolated CAE than the controls (p=0.003, p=0.002; respectively). Similarly, Tg to HDLc ratio and triglycerides levels were significantly higher, serum HDLc was

significantly lower in the isolated CAE than the controls (p=0.001; p=0.004 ; p=0.001, respectively). The baseline characteristics of the participants are presented in Table 2.

Table 2. Demographic and biochemical characteristics of the controls and the patients with isolated coronary artery ectasia

	Controls (n=70)	İsolated coronary artery ectasia (n=60)	P value
Age (year)	57±8	59±10	0.209
Sex (male/female)	28/42	39/21	0.005
BMI (kg/m^2)	26.6±3.7	25.9±5.7	0.432
Smoking (%)	30 (42.9)	29 (49.2)	0.597
Hypertension (%)	40 (57.1)	30 (50)	0.481
Diabetes mellitus	11 (15.7)	9 (15.0)	0.554
T.Cholesterol (mg/dL)	184±47	195±44	0.226
Triglyceride (mg/dL)	130±66	214±70	0.001
HDLc (mg/dL)	47±15	41±6.3	0.004
LDLc (mg/dL)	110±39	124±38	0.069
Tg to HDLc ratio	3.3±2.8	5.3±2.1	0.001
Creatinine (mg/dL)	0.8±0.3	1.1±0.9	0.002
Hemoglobin (g/dL)	13.0±1.7	13.9±2.0	0.003
WBC count (K/µL)	8408±3281	8999±2744	0.130
Lymphocyte (K/µL)	2411±740	2615±908	0.212
Monocytes (K/µL)	602±186	663±223	0.189
Neutrophil (K/µL)	5138±2941	5556±2825	0.186
Platelet (10^9/L)	249±63	232±61	0.080
Glucose (mg/dL)	115±58	121±55	0.933
LVEF %	53±9	55±9	0.075

BMI:Body mass index , LVEF: Left ventricular ejection fraction, WBC:White blood cell, HDLc: high-density lipoprotein cholesterol, LDLc: low-density lipoprotein cholesterol

Tg to HDLc ratio (OR:1.476, 95% CI 0.1199-1.817, p=0.001) was an independent factor predicting isolated CAE (Table 3). In the ROC curve analysis, the area under the curve (AUC) was found to be statistically significant (AUC=0.829, 95% CI, 0.752-0.906; p=0.001). As an optimal cut-off point, a high-risk Tg to HDLc ratio value of 4.2 was determined to predict isolated CAE, with an 85% sensitivity and an 78.6% specificity. (Figure 1).

Table 3. The independent predictors of isolated CAE in multivariate logistic regression analysis

Variables	Multivariate OR (95% CI)	P value
Smoking	1.007 (457-2.221)	0.986
Hypertension	0.755 (0.338-1.686)	0.493
Diabetes mellitus	0.981 (0.324-2.972)	0.973
LDLc (mg/dL)	1.025 (0.993-1.058)	0.121
Total cholesterol (mg/dl)	0.984 (0.958-1.010)	0.235
Tg to HDLc ratio	1.476 (1.199-1.817)	0.001

CEA: Coronary artery ectasia; OR: Odds ratio; CI: confidence interval

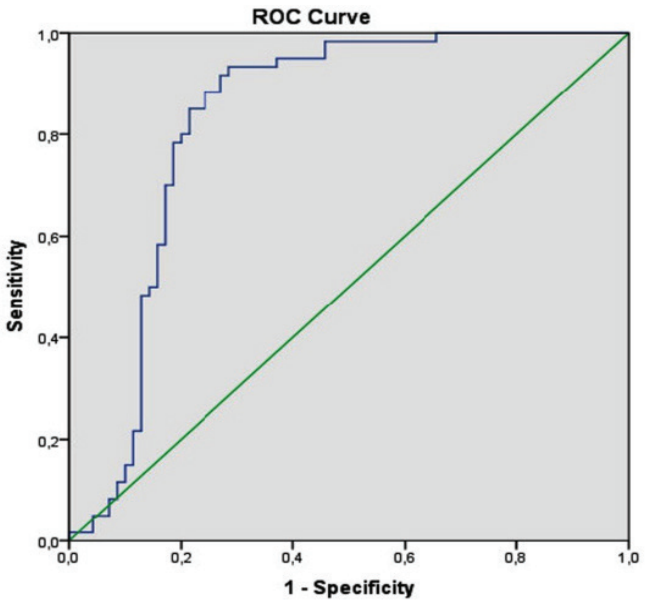

Figure 1. ROC curve analysis demonstrating the sensitivities and specificities of Tg to HDLc ratio to predict isolated CAE (AUC:0.829, %95 CI 0.752-0.906, p=0.001)

DISCUSSION

In this study, we investigated the relationship between dyslipidemia especially Tg to HDLc ratio with isolated CAE. The most important findings of this study were increased Tg to HDLc ratio and serum Tg level in patients with isolated CAE compared to controls. As far as we know, this is the first study to demonstrate the predictive value of the Tg to HDLc ratio in patients with isolated CAE.

In many studies, the relationship between high cholesterol levels and CAD has been demonstrated (18). Recent studies have shown that patients with CAD had significantly increased serum Tc, LDLc and Tg levels compared to healthy people (19). High Tg and low HDLc

levels are indicative of atherogenic LDLc. Therefore, Tg to HDLc ratio may be a powerful indicator for predicting and detecting the severity of coronary artery disease (20). However, we don't know the clinical significance of Tg to HDLc ratio in patients with isolated CAE.

Atherosclerosis is well known to cause CAE. Pathological examination of CAE specimens revealed cholesterol crystals, calcification, fibrosis, destruction in both the intima/media and lipid accumulation and these histological changes were found to be the same as atherosclerotic process. Ectasia occurs as a result of the atherosclerotic process causing widespread destruction of the muscular structure in the media layer leading to thinning of the vessel wall (1). It has been reported that the prevalence of CAE is higher in the familial hypercholesterolemia than in other coronary atherosclerosis patients and dyslipidemia may play a major role in the etiology of CAE (21). In our study, atherogenic lipid parameters were higher in isolated CAE patients and these findings support the previous assertions.

Many studies have demonstrated the correlation between coronary artery disease and the Tg to HDLc ratio. Amin MR. et al. reported that triglyceride level increased severity of CAD and high Tg to HDLc ratio level was an important indicator for development of atherogenic plaque and CAD. In the same study, high Tg to HDLc ratio was found to be the strongest predictor of coronary artery disease among other lipid parameters (22). A study conducted by Conkbayir C and Da Luz et al. (23, 24) demonstrated that the Tg to HDLc ratio was correlated with the severity of coronary lesions. In our study, atherogenic lipid parameters were increased in study patients than controls.

Hypertension is responsible for 35% of all atherosclerotic cardiovascular events and increases the risk of developing acute coronary syndrome by 2-3 times both in men and women (25). Markis et al. (26) reported that HT was more frequent in patients with ectasia and suggested that HT may be involved in the pathogenesis of coronary artery ectasia by accelerating the destruction of the media layer. Another study found that 55% of patients with CAE had HT (27). In our study, hypertension was not more frequent in the patients with isolated CAE.

There is much evidence showing that smoking initiates endothelial dysfunction and the inflammatory process in the endothelium. The deleterious effects of cigarette smoking such as disruption in vascular endothelial integrity, enhanced platelet activation and acceleration in the entry of leukocytes into atherosclerotic lesions have been shown in studies (28). In one recent study, Yılmaz et al. found any difference in smoking rate between patients with normal coronary arteries and with CAE (29). However, in our study the number of smokers was similar in the controls and patients.

LIMITATIONS

This study, we had a few limitations. First, it had a relatively small sample volume with single center design. Second, diagnosis of normal coronary arteries was solely based on conventionally angiograms which obviously cannot assess plaque burden. The use of intravascular techniques, such as ultrasound, would provide better information on the presence and extent of atherosclerotic plaque burden.

CONCLUSION

In conclusion, this is the first study that evaluated the relationship between Tg to HDLc ratio in isolated CAE. Our findings suggest that increased Tg and decreased HDLc may play a role in the early pathogenesis of CAE and high Tg to HDLc ratio may be a predictor of isolated CAE. Considering the above facts that, lipid parameters and Tg to HDL-C ratio could be a valuable, easily accessible, non-invasive way of predicting the presence of isolated CAE.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards and approval for the study was obtained from the Medical Ethics Committee of University of Health Sciences, Sisli Hamidiye Etfal Education and Research Hospital.

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