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İzole Koroner Arter Ektazili Hastalarda Aterojenik Dislipideminin Araştırılması

Investigation of Atherogenic Dyslipidemia in Patients with İsolated Coronary Artery Ectasia

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ÖZ

GİRİŞ ve AMAÇ: *Koroner arter ektazisinin (KAE) patofizyolojisi açıkça tanımlanamamıştır. Dislipidemi, kardiyovasküler hastalık (KVH) için bağımsız bir risk faktörü olarak kabul edilir. Her ne kadar aterojenik dislipidemi ile KVH arasındaki ilişki iyi bilinse de, izole KAE ile aterojenik dislipidemi hakkında bilgi yoktur. Bu çalışmanın amacı, izole KAE'li hastalarda aterojenik dislipidemiyi değerlendirmektir.*

YÖNTEM ve GEREÇLER: *Hasta grubunda izole KAE olan 91 hasta vardı ve kontrol grubu normal koroner anjiyogramları olan 90 ardışık kişiden oluşuyordu. Serum total kolesterol (TK), trigliserit (TG), düşük yoğunluklu lipoprotein kolesterol (LDL-K), yüksek yoğunluklu lipoprotein kolesterol (HDL-K) ve aterojenik endeksler (aterojenik dislipidemi indeksi, HDL-K olmayan, aterojenik katsayısı, kardiyak risk oranları 1 ve 2) analiz edildi.*

BULGULAR: *Aterojenik dislipidemi indeksi, HDL-K olmayan, aterojenik katsayısı ve kardiyak risk oranları 1 ve 2 izole KAE hastalarında kontrollerden anlamlı olarak daha yüksekti (p <0.001; p = 0.001; p = 0.001; p = 0.001; p <0,001, sırasıyla). Çok değişkenli lojistik regresyon modelleri, aterojenik dislipidemi endeksinin izole KAE'yi öngören bağımsız faktör olduğunu ortaya koymuştur (p <0.001, Odds oranı (OR) = 1.329,% 95 Güven aralığı (C.I.) = 1.110-1.591).*

TARTIŞMA ve SONUÇ: *Bu çalışma, aterojenik dislipidemi ile izole KAE arasındaki ilişkiyi değerlendiren ilk çalışmadır. Bulgularımız, artmış aterojenik endekslerin (aterojenik dislipidemi indeksi, HDL-K olmayan, aterojenik katsayısı, kardiyak risk oranları 1 ve 2) izole KAE'nin erken dönem patogenezinde rol oynayabileceğini göstermektedir.*

Anahtar Kelimeler: *aterojenik dislipidemi, koroner arter hastalığı, izole koroner arter ektazisi*

ABSTRACT

INTRODUCTION: *The pathophysiology of coronary artery ectasia (CAE) has not been clearly identified. Dyslipidemia is considered an independent risk factor for cardiovascular disease (CVD). Although the relationship between atherogenic dyslipidemia and CVD is well known, there is no information about atherogenic dyslipidemia with isolated CAE. The aim of the present study was to evaluate the atherogenic dyslipidemia in patients with isolated CAE.*

METHODS: *The patient group included 91 patients with isolated CAE and the control group consisted of 90 consecutive subjects who proved to have normal coronary angiograms. Serum levels of total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and atherogenic indices (atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, cardiac risk ratios 1 and 2) were analyzed.*

RESULTS: *The atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, and cardiac risk ratios 1 and 2 were significantly greater in the isolated CAE patients than in the controls (p < 0.001; p = 0.001; p = 0.001; p = 0.001; p < 0.001, respectively). The multivariate logistic regression models revealed that atherogenic dyslipidemia index was found to be independent factor predicting isolated CAE (p < 0.001, Odds ratio (OR) = 1.329, 95% Confidence interval (C.I.) = 1.110–1.591).*

DISCUSSION and CONCLUSION: *This is the first study that evaluates the relationship between the atherogenic dyslipidemia and isolated CAE. Our findings suggest that increased atherogenic indices (atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, cardiac risk ratios 1 and 2) may be involved in the early pathogenesis of the isolated CAE.*

Keywords: *atherogenic dyslipidemia, coronary artery disease, isolated coronary artery ectasia*

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INTRODUCTION

Coronary artery ectasia (CAE) has been characterized as a localized or diffuse non-obstructive lesion of the epicardial coronary arteries with a luminal dilation exceeding 1.5-fold the normal adjacent segment or vessel diameter (1). In several studies, the incidence of CAE has been reported to be 1.2-4.9 % (2). Almost 20–30% of cases of coronary ectasia are congenital and the rest are acquired. Of the acquired cases, 50% are associated with atherosclerosis while 10%–20% are associated with inflammatory and connective tissue diseases, syphilis, and bacterial infections (3-6). The inflammation plays an important role in terms of progression of atherosclerosis and acute and chronic forms of artery disease, and also in CAE and coronary slow flow (7,8). Despite the intense interest in etiology, prognosis and treatment of patients with ectasia, this issue remains unknown. In the absence of coronary artery disease (CAD), the presence of isolated CAE is mentioned. Isolated CAE, which excludes atherosclerosis, connective tissue disorders, and other cardiac defects, is very rare with an angiographic frequency of 0.1–0.32% (9).

Strong scientific evidence indicates that there is a significant association between incidence of cardiovascular disease (CVD) and high level of LDL-C and also low level of HDL-C (10,11); therefore the LDL-C/HDL-C ratio is often calculated to estimate cardiovascular risk (12). On the other hand, high level of TG has been related with an increased LDL-C particles and increased cardiovascular risk (13). Many clinical studies make effort to introduce a better marker of atherogenic dyslipidemia that can predict the risk of CVD to be useful for evaluating response to treatment instead of the classical ratio. In recent years, researchers have focused on a new comprehensive lipid index, atherogenic dyslipidemia index, which might comprehensively reflect the balance between atherogenic and anti-atherogenic factors. It has been shown that atherogenic dyslipidemia index (or atherogenic index of plasma) [TG/HDL-C] is a strong marker to predict the risk of atherosclerosis and coronary heart disease (CHD) (14-19).

Atherogenic dyslipidemia and atherogenic indices (atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, cardiac risk ratios 1 and 2) in coronary artery diseases (such as CAE) other than atherosclerotic cardiovascular diseases have not been adequately investigated. Although the relationship between atherogenic dyslipidemia and CVD is well known, there is no information about atherogenic dyslipidemia with isolated CAE. The aim of this study is to evaluate the atherogenic dyslipidemia in patients with isolated CAE.

METHODS

Study population

One hundred eighty-one consecutive patients between 18 and 80 years old were enrolled into the study between January 2016 and October 2018 in Karaman State Hospital. The patient group included 91 patients with isolated CAE who had irregularities with ectatic coronaries without any stenotic lesions. The control group consisted of 90 age- and gender-matched subjects who were selected in a consecutive manner from the catheterized patients during the same study period and who proved to have normal coronary angiograms. The indication for coronary angiography was either the presence of typical angina or positive or equivocal results of noninvasive screening tests for myocardial ischemia in both of the groups. Exclusion criteria were history of myocardial infarction, percutaneous coronary intervention, and coronary bypass grafting, valvular heart diseases, arrhythmia, cardiac pacemaker, heart failure, cardiomyopathy, left ventricular ejection fraction (LVEF) < 55%, chronic renal failure (glomerular filtration rate < 60 ml/min/1.73 m2), malignancy and use of cardiotoxic medication, receiving lipid-lowering therapy, and congenital heart disease. The patients who had coronary stenotic lesions of > 20% were also excluded from the study. The study was approved by the local ethics committee. Informed consent was obtained from all of the patients included in the study.

Demographic and clinical evaluation of patients

Hypertension (HT) was defined by a previous diagnosis of HT or the presence of systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg. Diabetes Mellitus (DM) was defined as fasting plasma glucose ≥126mg/dl or plasma glucose level ≥ 200 mg/dl 2 hours after the 75

mg oral glucose tolerance test or glycated hemoglobin ≥6.5% or patients using antidiabetic medications. Hyperlipidemia (HLP) was defined as total cholesterol >190 mg/dl. Patients who self-reported as having smoked during the previous six months were classified as smokers.

Blood sampling

Blood samples were taken from all participants after 12-14 hours fasting to determine the lipid profile and atherogenic indices. All samples were checked in central laboratory of state health center.

Determination of lipid profile and atherogenic indices

The serum levels of TC, TG, LDL-C, HDL-C, and the atherogenic indices of all the subjects were analyzed. TC, TG, and HDL-C concentrations were measured by biochemical analyses using commercial kits. LDL-C was determined using the Friedewald et al. equation (20). The atherogenic dyslipidemia index (TG/HDL-C), non HDL-C (TC-HDL-C), atherogenic coefficient (non HDL-C/HDL-C), cardiac risk ratio 1 (TC/HDL-C) and cardiac risk ratio 2 (LDL-C/HDL-C) were determined using the Ikewuchi equation (21-23).

Assessment of coronary artery ectasia

Coronary angiography was performed by the Judkins technique without the use of nitroglycerin, adenosine, or a calcium channel blocker using 6-French right and left heart catheters. Angiograms were analyzed by two blinded interventional cardiologists without knowledge of the clinical status or laboratory measurements. Coronary diameter was measured as the maximum diameter of the ectatic segment using a computerized quantitative coronary angiographic analysis system. CAE was defined as dilation of the coronary artery >1.5-fold the diameter of the adjacent normal coronary vessels according to Falsetti and Carroll (24). Markis classified CAE in four types: type 1 includes diffuse ectasia involving two or three vessels, type 2 includes diffuse ectasia in one vessel and discrete ectasia in another vessel, type 3 includes diffuse ectasia in only one vessel, and type 4 includes localized or segmental ectasia in only one vessel (25).

Statistical analysis

SPSS 25.0 (IBM Corp., Armonk, NY, USA) program was used for variable analysis. Normally distributed continuous data were expressed as mean ± standard deviation (minimum–maximum). Continuous variables that are not normally distributed were expressed as median (minimum–maximum), and categorical variables were expressed as n and percentages. The normal distribution of the data was evaluated by Lilliefors-corrected Kolmogorov-Smirnov test and Shapiro-Wilk test and the variance homogeneity was evaluated by the Levene test. The Independent-Samples T test was used with the Bootstrap results when comparing two independent groups with one according to the quantitative data, and the Mann- Whitney U test was used together with the Monte Carlo results. To compare categorical variables, Pearson chi-square and Fisher Exact tests were tested using exact results. One-way Anova test was used for the comparison of ectasia subgroups by quantitative variables. Multivariate logistic regression test was used with Forward Stepwise (Wald) method in order to determine the relationship between the explanatory variables which were significant in other analyses. Receiver operator characteristic curves (ROCs) were used to analyze the sensitivities of uric acid, atherogenic dyslipidemia index, and MPV to predict the presence of isolated CAE. Variables were examined at 95% confidence level. A p-value < 0.05 was considered as statistically significant.

RESULTS

The right coronary artery was the most affected artery by ectasia both alone and in combination with other arteries (76%) (Table 1).

Table 1. Distribution of ectatic arteries

Ectatic Coronary Artery	N: 91 n (%)
RCA	36 (39.56)
Cx	9 (9.89)
LAD	5 (5.49)
RCA + Cx	20 (21.97)
RCA + LAD	11 (12.08)
LAD + Cx	7 (7.69)
RCA + Cx + LAD	3 (3.29)

RCA: right coronary artery, Cx: circumflex artery, LAD: left anterior descending coronary artery

The mean age of the patients was 61.75 ± 10.02 years, and 71.8% were male. Of all patients, 73.5% had HT, 32% had DM, and 48.6% were current smokers. HLP was more frequent in the isolated CAE group than in the control group (69.2 % vs. 31.1 %) (p<0.001) (Table 2). There were not any significant differences between groups for age, gender, history of HT, DM, body mass index, and smoking (Table 2).

Table 2. Patient characteristics and biochemical values

	Control (n = 90)	Isolated CAE (n = 91)	Total (n = 181)	p-Value
Age [1]	59.68 ± 8.47	63.11 ± 9.08	61.75 ± 10.02	0.213 [a]
Height (cm) [1]	166.82 ± 7.44	166.02 ± 7.31	166.42 ± 7.37	0.450 [a]
Weight (kg) [1]	80.34 ± 13.71	79.44 ± 10.62	79.89 ± 12.23	0.599 [a]
BMI (kg/m^2) [1]	28.97 ± 4.83	28.85 ± 3.95	28.91 ± 4.40	0.848 [a]
Male gender [2]	64 (71.1)	66 (72.5)	130 (71.8)	0.870 [b]
Hypertension [2]	66 (73.3)	67 (73.6)	133 (73.5)	0.999 [b]
Diabetes Mellitus [2]	28 (31.1)	30 (33)	58 (32)	0.874 [b]
Hyperlipidemia [2]	28 (31.1)	63 (69.2)	91 (50.3)	< 0.001 [b]
Smoking [2]	42 (46.6)	46 (50.5)	88 (48.6)	0.216 [b]
Fasting Glucose (mg/dl) [3]	97.5 (74 / 160)	99 (76 / 323)	98 (74 / 323)	0.100 [c]
Creatinine (mg/dl) [3]	0.88 (0.56/ 1.14)	0.94 (0.78 / 1.3)	0.92 (0.56 / 1.3)	0.314 [c]
Uric acid (mg/dl) [3]	5 (3.2 / 8.1)	7.5 (3.3 / 10.2)	5.6 (3.2 / 10.2)	< 0.001 [c]
Na (mmol/L) [3]	140 (137 / 146)	138 (134 / 145)	139 (134 / 146)	0.426 [c]
K (mmol/L) [3]	4.4 (3.8 / 5)	4.3 (3.2 / 5.1)	4.4 (3.2 / 5.1)	0.499 [c]
Ca (mg/dl) [3]	9.5 (9 / 10.4)	9.4 (8.7 / 10.3)	9.45 (8.7 / 10.4)	0.744 [c]
Mg (mg/dl) [3]	2.04 (1.78 / 2.2)	2.01 (1.6 / 2.72)	2.04 (1.6 / 2.72)	0.918 [c]
AST (U/L) [3]	26 (12 / 180)	25 (11 / 283)	26 (11 / 283)	0.518 [c]
ALT (U/L) [3]	20 (5 / 60)	24 (8 / 68)	21 (5 / 68)	0.872 [c]
T.Bilirubin (mg/dl) [3]	0.615 (0.28/ 1.3)	0.62 (0.28/ 1.78)	0.62 (0.28/ 1.78)	0.623 [c]
D.Bilirubin (mg/dl) [3]	0.13 (0.03/ 0.43)	0.13 (0.03/ 0.43)	0.13 (0.03/ 0.43)	0.879 [c]
I.Bilirubin (mg/dl) [3]	0.47 (0.22/ 1.06)	0.5 (0.22 / 1.53)	0.49 (0.22/ 1.53)	0.441 [c]

[1]Data are expressed as mean ± standart deviation, [2]Data are expressed as n (%),[3]Data are expressed as median (minimum-maximum), [a] Independent Samples T Test (Bootstrap), [b] Pearson chi-square test (Exact), [c] Mann Whitney U Test (Monte Carlo), CAE: coronary artery ectasia , BMI: body mass index

Uric acid level was significantly higher in the isolated CAE group than in the control group (p < 0.001) (Table 2).

TC, TG, and LDL-C were significantly higher in the isolated CAE group than in the control group (p = 0.001; p < 0.001; p < 0.001, respectively); and HDL-C was significantly lower in the isolated CAE group than in the control group (p = 0.01) (Table 3).

The atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, and cardiac risk ratios 1 and 2 were significantly greater in isolated CAE patients than in the controls (p < 0.001; p = 0.001; p = 0.001; p = 0.001; p <0.001, respectively) (Table 3).

Table 3. Dyslipidemic profile and hematological values

	Control (n = 90)	Isolated CAE (n = 91)	Total (n = 181)	p-Value
TC (mg/dl)	202.64 ± 42.22	245.78 ± 59.48	224.33 ± 55.84	0.001 [a]
TG (mg/dl)	146.74 ± 86.52	292.69 ± 126.65	183.24 ± 102.58	< 0.001 [a]
LDL-C (mg/dl)	95.5 ± 42.88	155.26 ± 58.95	129.43 ± 51.76	< 0.001 [a]
HDL-C (mg/dl)	42.52 ± 6.85	39.23 ± 5.46	41.54 ± 8.32	0.01 [a]
Atherogenic Dyslipidemia Index (TG/HDL-C)	3.18 ± 2.76	7.64 ± 5.49	4.39 ± 3.21	< 0.001 [a]
Non HDL-C (TC - HDL-C) (mg/dl)	158.31 ± 43.75	204.80 ± 64.09	181.69 ± 59.53	0.001 [a]
Atherogenic Coefficient (Non HDL-C/HDL-C)	3.78 ± 1.41	5.42 ± 2.35	4.60 ± 2.10	0.001 [a]
Cardiac Risk Ratio 1 (TC/HDL-C)	4.78 ± 1.41	6.42 ± 2.35	5.60 ± 2.10	0.001 [a]
Cardiac Risk Ratio 2 (LDL/HDL-C)	2.33 ± 1.76	4.03 ± 3.47	3.07 ± 2.85	< 0.001 [a]
WBC (K/uL)	8702.53 ± 2353.64	8810.35 ± 2590.92	8756.74 ± 2469.49	0.780 [a]
Neutrophil (K/uL)	5357.50 ± 2085.12	5413.27 ± 2127.06	5385.54 ± 2100.64	0.869 [a]
Lymphocyte (K/uL)	2407.88 ± 819.21	2403.90 ± 858.57	2405.88 ± 836.90	0.976 [a]
Hemoglobin (g/dL)	14.65 ± 2.77	14.52 ± 3.15	14.58 ± 2.96	0.561 [a]
Hematocrit (%)	43.45 ± 16.22	43.2 ± 20.1	43.4 ± 18.56	0.861 [a]
Platelet (K/uL)	257000 ± 155000	236000 ± 132000	246000 ± 138000	0.746 [a]
Monocytes (K/uL)	640 ± 240	620 ± 288	630 ± 264	0.813 [a]
RDW (fL)	42.7 ± 8.4	43 ± 8.8	42.8 ± 8.5	0.941 [a]
PDW (K/uL)	12.65 ± 4.48	12.6 ± 6.25	12.6 ± 5.12	0.918 [a]
MPV (fL)	9.22 ± 1.08	10.68 ± 1.11	9.96 ± 1.31	0.001 [a]

Data are expressed as mean ± standard deviation, [a] Independent Samples T Test (Bootstrap) , TC: total cholesterol , TG: triglyceride, LDL-C: low density lipoprotein cholesterol , HDL-C: high density lipoprotein cholesterol, WBC: white blood cell, RDW: red cell distribution width , PDW: platelet distribution width , MPV: mean platelet volume, CAE: coronary artery ectasia

Mean platelet volume (MPV) was significantly higher in the isolated CAE group than in the control group (p = 0.001) (Table 3).

No significant differences were found between the ectasia subgroups (Type 1, 2, 3, and 4 CAE) in terms of biochemical, dyslipidemic, and hematological data (Table 4).

The multivariate logistic regression models revealed that uric acid level (p = 0.002, Odds ratio (OR) =1.648, 95% Confidence interval (C.I.) = 1.208–2.248), atherogenic dyslipidemia index (p < 0.001, OR = 1.329, 95% C.I. = 1.110–1.591), and MPV (p < 0.001, OR = 3.134, 95% C.I. = 2.046–4.802) were found to be independent factors predicting isolated CAE (Table 5).

ROC analyses were performed to find out ideal uric acid, atherogenic dyslipiemia index, and MPV cut off values to predict the presence of isolated CAE. An uric acid value of > 6.3 has 64.8 % sensitivity, 87.8 % specificity; an atherogenic dyslipidemia index value of > 7.25 has 58.2 % sensitivity, 92.2 % specificity; and a MPV value of > 9.75 has 84.6 % sensitivity, 66.7 % specificity to detect the presence of isolated CAE [AUC 0.795, (p < 0.001); AUC 0.773, (p < 0.001); and AUC 0.824, (p < 0.001), respectively] (Figure 1, Table 6).

Table 4. Biochemical, dyslipidemic, and hematological data in ectasia subgroups

	Type 1 CAE (n = 23)	Type 2 CAE (n = 19)	Type 3 CAE (n = 21)	Type 4 CAE (n = 28)	p-Value
TC (mg/dl)	254.13 ± 58.95	252.00 ± 78.43	247.81 ± 60.63	243.18 ± 43.39	0.622 [a]
TG (mg/dl)	295.69 ± 112.45	319.2 ± 120.52	289.76 ± 108.65	257.58 ± 121.15	0.278 [a]
LDL-C (mg/dl)	159.36 ± 55.76	162.14 ± 48.76	158.94 ± 52.24	156.75 ± 50.86	0.842 [a]
HDL-C (mg/dl)	36.44 ± 8.22	42.35 ± 7.84	39.5 ± 8.18	39.59 ± 7.42	0.343 [a]
Atherogenic Dyslipidemia Index (TG/HDL-C)	8.5 ± 4.15	7.39 ± 3.68	7.52 ± 2.98	7.12 ± 3.74	0.151 [a]
Non HDL-C (TC - HDL-C) (mg/dl)	215.52 ± 66.58	208.95 ± 80.54	207.10 ± 64.68	191.46 ± 48.56	0.613 [a]
Atherogenic Coefficient (Non HDL-C/HDL-C)	5.87 ± 3.95	5.45 ± 3.38	4.98 ± 4.22	5.12 ± 2.46	0.822 [a]
Cardiac Risk Ratio 1 (TC/HDL-C)	7.26 ± 2.79	6.00 ± 2.16	6.36 ± 2.12	6.06 ± 2.18	0.239 [a]
Cardiac Risk Ratio 2 (LDL/HDL-C)	4.53 ± 2.95	3.97 ± 3.46	4.15 ± 1.88	3.87 ± 2.74	0.286 [a]
Uric acid (mg/dl)	7.36 ± 2.88	6.55 ± 3.24	7.92 ± 3.79	7.85 ± 2.67	0.387 [a]
MPV (fL)	10.12 ± 1.28	9.86 ± 1.35	9.98 ± 1.24	10.18 ± 1.16	0.448 [a]

Data are expressed as mean ± standard deviation, a one-way ANOVA (Robuts Statistic:Brown-Forsythe), TC: total cholesterol , TG: triglyceride, LDL-C: low density lipoprotein cholesterol , HDL-C: high density lipoprotein cholesterol , MPV: mean platelet volume , CAE: coronary artery ectasia

Table 5. The independent predictors of isolated CAE in multivariate logistic regression analysis

Variable	p-Value	Odss Ratio (95% C.I.)
Uric acid	0.002	1.648 (1.208-2.248)
Atherogenic dyslipidemia index	< 0.001	1.329 (1.110-1.591)
MPV	< 0.001	3.134.046-4.802)

Multivariate logistic regression (method = Forward Stepwise (Wald)), CAE: coronary artery ectasia, MPV: mean platelet volume, C.I.: confidence interval

Table 6. Sensitivity and specificity

	Cut-Off Value	AUC	Sensitivity (%)	Specificity (%)	p-Value
Uric acid	6.3	0.795	64.8	87.8	< 0.001
Atherogenic dyslipidemia index	7.25	0.773	58.2	92.2	< 0.001
MPV	9.75	0.824	84.6	66.7	< 0.001

ROC (Receiver Operating Curve) analysis (Youden index J - Honley&Mc Nell), AUC: Area under the ROC curve, MPV: mean platelet volume

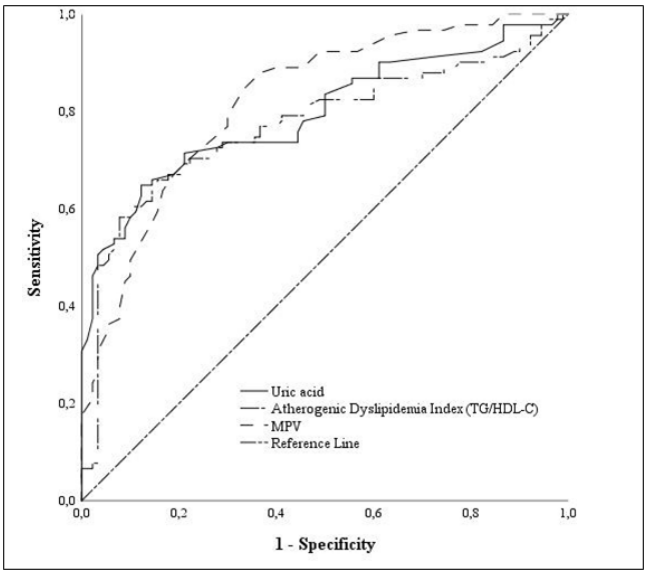

Figure 1. ROC curve analysis demonstrating the sensitivities and specificities of uric acid, atherogenic dyslipidemia index, and MPV to predict isolated CAE

DISCUSSION

In the present study we investigated the relationship between the atherogenic dyslipidemia and isolated CAE. The most relevant findings of this study were significant increases in serum levels of TC, TG, LDL-C, and atherogenic indices (atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, cardiac risk ratios 1 and 2) in the isolated CAE group than in the control group. To the best of our knowledge, the present study is the first to focus on the relationship between atherogenic dyslipidemia and isolated CAE.

The studies have shown that TC, TG, LDL-C, and LDL/HDL ratios are significantly greater in CHD patients than in healthy people (26) and also shown that atherogenic indices, atherogenic coefficient, and cardiac risk ratios are major risk factors for atherosclerotic vascular disease and its complications (27,28). However, there is no information about atherogenic dyslipidemia in isolated CAE patients.

The studies point to the possibility that both ectasia and stenosis are formed from the same basic pathophysiology. Typically, ectasia shows diffuse hyalinization, lipid deposition, destruction of intima and media, and regional calcification. Fibrosis, cholesterol crystals and intramural bleeding are seen. These histological changes are similar to those seen in atherosclerosis, where invasion of the media results in the destruction of musculoelastic elements and thinning of the arterial wall (29,30). Sudhir et al. showed that CAE is more prevalent in patients with familial hypercholesterolemia than in other patients with coronary atherosclerosis. This suggests that disordered lipoprotein metabolism in familial hypercholesterolemia may predispose patients to aneurysmal coronary artery disease (31). As shown in the present study, the presence of atherogenic dyslipidemia in isolated CAE supports this pathophysiology.

It has been reported that there are significant relationships between serum uric acid levels and various inflammatory markers, oxidative stress, and endothelial dysfunction (32,33). In many studies, serum uric acid (SUA) level has been shown to be an important and independent risk factor for the development of CVD (34,35). Sen et al. demonstrated that SUA levels increased significantly in patients with isolated CAE (36). Similarly, in our study, SUA level was significantly higher in the isolated CAE group than in the control.

MPV, an indicator of platelet activation, has an independent effect on the pathophysiology of atherosclerosis in the presence of other risk factors. It has been shown that MPV is increased in acute coronary syndrome and congestive heart failure (37,38). Demir et al. showed that patients with CAE and CAD have higher MPV values than the subjects with normal coronary angiograms (39). Bitigen et al. reported that MPV values of patients with isolated CAE were significantly higher than in the control, and pointed out that increased MPV may indicate the altered platelet reactivity and aggregation and thereby may be associated with ischemic events, observed in patients with isolated CAE (40). In the present study, similarly, MPV values were significantly higher in the isolated CAE group than in the control group.

Bilirubin is an important and potent endogen antioxidant and anti-inflammatory agent. Several previously published studies have demonstrated the relationship between serum bilirubin levels and CVD such as CAD and atrial fibrillation (41,42). Demir et al. showed that total, direct, and indirect serum bilirubin levels were significantly lower among patients with CAE than in the control group (43). However, there was no significant difference between the isolated CAE group and the control

group in terms of serum total, direct, and indirect bilirubin levels in the present study (p = 0.623, p = 0.879, p = 0.441, respectively).

CONCLUSION

In conclusion, to the best of our knowledge, this is the first study that evaluates the relationship between the atherogenic dyslipidemia and isolated CAE. Our findings suggest that decreased HDL-C and increased TC, TG, LDL-C, and atherogenic indices (atherogenic dyslipidemia index, non HDL-C, atherogenic coefficient, cardiac risk ratios 1 and 2) may be involved in the early pathogenesis of CAE. The multivariate logistic regression models revealed that uric acid level, atherogenic dyslipidemia index, and MPV were found to be independent factors predicting isolated CAE. Further studies are needed to demonstrate the pathophysiology of CAE.

STUDY LIMITATIONS

The main limitation of our study is the limited number of patients. In the present study, there was no obstructive CAD group. The another limitation was that angiographic diagnosis of normal coronary arteries was based on axial contrast angiograms of the vessel lumen. Moreover, angiography cannot assess plaque burden, patients without evidence of luminal stenosis by angiography may also have plaque burden in the wall of the coronary arteries. It would be better to examine with intravascular techniques such as ultrasound whether the patients with isolated CAE had evidence of atherosclerotic plaque.

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