Female Sex and Advanced Age Are Independent Predictors of Coronary Artery Tortuosity in Patients Without Coronary Artery Disease

Koroner Arter Hastalığı Olmayan Hastalarda Kadın Cinsiyet ve İleri Yaş Koroner Arter Tortuozitesi İçin Bir Göstergedir

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Objective: Coronary artery tortuosity (CAT) is frequently observed in invasive angiography, though its aetiology and clinical significance remain ambiguous. The aim of our study was to investigate the parameters affecting CAT in patients without coronary artery disease (CAD).

Materials and Methods: 110 patients with CAT without CAD and 140 patients without CAT and without CAD were evaluated retrospectively. CAT was defined by ≥3 bends with a change in vessel direction of ≥45° present in both systole and diastole along the main trunk of at the least one coronary artery. Demographic, biochemical, echocardiogrphic and angiographic parameters were compared between groups.

Results: Patients with CAT without CAD were older and more often female sex. 24 (21.8%) were males and 86 (78.2%) were females in patients with CAT. The mean age of the patients with CAT were 61.4±10.6 years and the patients without CAT and without CAD were 55.9±10.9 years. Among the patients with CAT, 62.7% had hypertension, 27.3% had diabetes mellitus and 30% were smokers. But, there was not significant difference between groups (p=0.469, p=0.446, p=0.242, respectively). Left anterior descending artery (LAD) was the most commonly affected tortuous coronary artery (86.4%). Multivariate analysis showed significant relationship between age (p=0.019), female sex (p<0.001) and CAT.

Conclusion: We found that female sex and advanced age were major predictors of in patients with CAT without CAD. Other traditional risk factors such as diabetes mellitus, hypertension and smoking were thought not to influence the development of CAT. LAD was the most commonly affected tortuous coronary artery. Further researches are required to understand the mechanisms underlying sex and age related changes in the arterial wall related with CAT.

Keywords: Coronary artery tortuosity, Aging, Gender

Amaç: Koroner arter tortuozitesi (KAT), invaziv koroner anjiyografide sıkça gözlenmekle birlikte etiyolojisi ve klinik önemi halen belirsizdir. Çalışmamızın amacı, koroner arter hastalığı (KAH) bulunmayan hastalarda KAT'ı etkileyen parametreleri incelemektir.

Gereç ve Yöntem: KAH'ı olmayan 110 KAT izlenen hasta ile KAH ve KAT'ı olmayan 140 hasta retrospektif olarak değerlendirildi. KAT, en az bir koroner arterin ana gövdesi boyunca hem sistol hem de diyastolde izlenen, damar yönünde ≥45° değişiklik gösteren ≥3 kıvrım olarak tanımlandı. Demografik, biyokimyasal, ekokardiyografik ve anjiyografik parametreler gruplar arasında karşılaştırıldı.

Bulgular: KAT'ı olan hastalar daha yaşlıydı ve çoğunlukla kadın cinsiyetteydi. KAT'lı hastaların 24'ü (%21.8) erkek, 86'sı (%78.2) kadındı. KAT'lı hastaların yaş ortalaması 61.4±10.6 yıl iken kontrol grubunun 55.9±10.9 yıl idi. KAT'lı hastaların %62.7'sinde hipertansiyon, %27.3'ünde diabetes mellitus ve %30'unda sigara kullanımı mevcuttu. Ancak gruplar arasında anlamlı bir fark yoktu (p=0.469, p=0.446, p=0.242, sırasıyla). KAT en sık izlenen koroner arter sol ön inen koroner arter (LAD) idi (%86.4). Çok değişkenli regreyon analizi yaş (p=0.019), kadın cinsiyet (p<0.001) ve KAT arasında anlamlı ilişki olduğunu gösterdi.

Sonuç: Kadın cinsiyet ve ileri yaşın, koroner arter hastalığı bulunmayan hastalarda KAT'ın ana öngörücüsü olduğunu saptadık. Çalışmamızda diabetes mellitus, hipertansiyon ve sigara kullanımı gibi geleneksel risk faktörleri ile KAT gelişimi arasında anlamlı bir ilişki yoktu. KAT en sık izlenen koroner arter LAD idi. KAT'a neden olabilecek damar duvarındaki cinsiyet ve yaşa bağlı değişikliklerin altında yatan mekanizmaları anlamak için daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Koroner arter tortuozitesi, Yaşlanma, Cinsiyet

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INTRODUCTION

Coronary artery tortuosity (CAT) is usually detected incidentally on coronary angiography and is not an uncommon finding (Chiha et al.,2016; Ozyasar et al., 2024). However CAT is not adequately reported in coronary angiography reports (Helisch et al., 1994). CAT may be considered an anatomic variant in which the affected coronary arteries exhibit consecutive curvatures or helical coils (Chiha et al., 2016). It is unknown whether CAT plays a role in angina pectoris, although there is some evidence that myocardial perfusion defects occur in individuals with severe CAT and normal coronary arteries (Gaibazzi et al., 2011) and some studies showed that CAT without coronary artery disease (CAD) may cause angina pectoris during exercise test or activity (Zegers et al., 2007). CAT causes changes in blood flow distal to the tortuous segment and a decrease in coronary artery pressure and may therefore lead to ischemia (Hassanin Hanboly et al., 2021).

There are insufficient studies in the literature regarding the clinical significance of CAT and its relationship with cardiac risk factors. Although most CAT studies include patients with CAD, we focused on determining the characteristics of CAT in patients without CAD.

MATERIALS AND METHODS

A total of 110 patients with CAT without CAD and 140 patients without CAT and without CAD detected by invasive coronary angiography were included in this study.

Demographic characteristics, echocardiographic, biochemical, haematological and angiographic parameters were evaluated in Balikesir University Medical Faculty, Department of Cardiology retrospectively. All patients were over 18 years of age and underwent coronary angiography for various clinical indications. Exclusion criteria were myocardial infarction, cardiogenic shock, congenital heart disease, sepsis, pregnancy and end stage renal or liver disease.

Hypertension (HT) was defined as systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg or the use of antihypertensive medication (Williams et al., 2018). Diabetes mellitus (DM) was defined as fasting blood glucose ≥126 mg/dL, HbA1c ≥6.5%, 2 hour postprandial blood glucose ≥200 mg/dL or use of oral antidiabetic drug or insulin (American Diabetes Association., 2010). Smoking was defined as active tobacco using within the past 6 months (Yang et al., 2010). CAD was defined as stenosis ≥20% in at least one coronary artery (Tosu et al., 2014).

All coronary angiographies were performed using conventional techniques with the radial or femoral artery approach. CAT was defined by ≥3 bends with a change in vessel direction of ≥45° present in both systole and diastole along the main trunk of at least one artery (Zaacks et al., 1998; Turgut et al., 2007).

Statistical analysis and ethical aspects

Data were analyzed using SPSS 13.0 statistical software package. Shapiro–Wilk test was used to assess the data normality. All categorical data were reported as percentages. Continuous variable expressed as mean ± standard deviation and nonnormally distributed variables were presented as median and 25th-75th percentiles. Independent samples T test was used for normally distributed continuous variables and Mann Whitney U test was used for nonnormally distributed variables for comparing the groups. Categorical variables were compared with Chi Square test. Univariate and multivariate logistic regression analyses were used to evaluate the related parameters of CAT in patients without CAD. The variables with P <0.1 in the univariate analysis were included into the multivariate regression analysis. In this analysis, male gender was used as the reference group. Age and gender were found to be significant in univariate logistic regression analyses. Age and female sex were determined associated with CAT in patients without CAD in multivariate regression analysis. A p value of <0.05 was considered statistically significant.

This retrospective study was approved by the Balıkesir University Clinical Research Ethics Committee according to the Declaration of Helsinki (Decision no: 2025/2; Date: 07.01.2025).

RESULTS

A total of 110 patients with CAT without CAD and 140 patients without CAT and without CAD detected by invasive coronary angiography were included in this study.

The age was 61.1±10.8 years in patient with CAT and 55.9±10.9 years in patients without CAT and without CAD. Age was significantly higher in patients with CAT (p< 0.001). 24 (21.8%) were males and 86 (78.2%) were females in patients with CAT. 71 (50.7%) were males and 69 (49.3%) were females in patients without CAT and without CAD. Female sex was significantly higher in patients with CAT (p< 0.001). Among the patients with CAT, 62.7% had HT, 27.3% had DM and 30% were smokers. In the patients without CAT and without CAD; 61.4% had HT, 35.7% had DM and 35% were smokers. There were not any significant differences in the presence of traditional cardiovascular risk factors such as HT, DM and smoking (p=0.469; p=0.446; p=0.242, respectively) (Table 1).

Left anterior descending artery (LAD) was the most commonly affected tortuous coronary artery. Among patients with CAT, the prevalence of affected coronary artery was 86.4% for LAD, 71.8% for Circumflex Coronary Artery (Cx), 46.4% for Right Coronary Artery (RCA), 34.5% for LAD-Cx, 10% for LAD-RCA and 27.3% for triple vessel (Table 1).

Hematological and biochemical parameters were compared between groups. Hemoglobin (p=0.001) and hematocrit (p=0.002) levels were lower in patients with CAT than the patients without CAT and without CAD (12.9±1.7 g/dl vs 13.6±1.6 g/dl; 38.5±4.8 vs 40.3±4.4, respectively). There was not statistically significant differences in other biochemical and hematological parameters between groups (Table 2).

To determine the parameters associated with CAT in patients without CAD, we used univariate and multivariate logistic regression analyses. In univariate analysis, female sex [p<0.001, OR (95% CI) 0.271 (0.155–0.475)], age [p<0.001, OR (95% CI) 0.271 (0.155–0.475)] were found to be significant. Those that were significant were included in the multivariate analyses. In this model, age [p=0.019, OR (95% CI) 1.031 (1.005-1.057)] and female sex [p<0.001, OR (95% CI) 0.330 (0.184–0.591)] were associated with CAT in patients without CAD (Table 3).

Table 1. Baseline characteristics, echocardiographic and angiographic parameters of the groups

	Patients with Coronary Artery Tortuosity without Coronary Artery Disease (n=110)	Patients without Coronary Artery Tortuosity and without Coronary Artery Disease (n=140)	P
Age (years)	61.1±10.8	55.9±10.9	<0.001
Gender (Male/Female)	24/86 (21.8%-78.2%)	71/69 (50.7%-49.3%)	<0.001
Body mass index (kg/m^2)	28.8±2.95	28.09±3.2	0.083
Hypertension	69 (62.7%)	86 (61.4%)	0.469
Diabetes mellitus	30 (27.3%)	36 (25.7%)	0.446
Current Smoker	33 (30%)	49 (35%)	0.242
Ejection fraction (%)	60 (60-65)	60 (60-65)	0.840
Distribution of coronary artery tortuosity according to coronary arteries			
LAD	95 (86.4%)		
Cx	79 (71.8%)		
RCA	51 (46.4%)		
LAD-Cx	38 (34.5%)		
LAD-RCA	11(10%)		
Cx-RCA	0 (0%)		
LAD-Cx-RCA	30 (27.3%)		

LAD: Left anterior descending artery, Cx: Circumflex artery, RCA: right coronary artery

Table 2. Laboratory parameters of the groups

	Patients with Coronary Artery Tortuosity without Coronary Artery Disease (n=110)	Patients without Coronary Artery Tortuosity and without Coronary Artery Disease (n=140)	P
Glucose (mg/dl)	115.7±46.6	106.9±31.6	0.091
HbA1c	6.15±1.6	6.16±1.6	0.940
Hemoglobin (g/dl)	12.9±1.7	13.6±1.6	0.001
Hematocrit (%)	38.5±4.8	40.3±4.4	0.002
Creatinine (mg/dl)	0.82±0.19	0.86±0.26	0.147
Urea (mg/dl)	32.4±10.1	33.2±12.9	0.603
eGFR (ml/min)	84.7±18.5	88.34±16.85	0.109
Total Cholesterol (mg/dL)	195.6±43.9	194.86±51	0.910
Triglyceride (mg/dL)	144.7±78.2	158.34±136.46	0.369
LDL (mg/dL)	116.9±34.6	116.7±39.15	0.969
HDL (mg/dL)	51.8±12.4	49.2±11.2	0.098
AST (U/L)	16 (21-27.8)	21 (17-26)	0.678
ALT (U/L)	17 (13.3-25)	20 (14-28.5)	0.146
TSH (mIU/L)	1.96±1.85	1.88±1.52	0.732
Platelet (10^3 /µL)	262.5±76.2	251.9±63	0.230
White blood cell count (10^3 /µL)	7.43±2.22	7.69±2.05	0.339
C-reactive Protein (mg/dl)	3 (2-8)	3 (2-7.2)	0.785
Sedimentation (mm/hour)	16 (9-31)	13 (6-23)	0.106

eGFR: Estimated glomerular filtration rate, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, AST: Aspartate transaminase, ALT: Alanine transaminase, TSH: Thyroid stimulating hormone, CRP: C-reactive protein.

Table 3. Univariate and multivariate correlates of coronary artery tortuosity in patients without coronary artery disease

Variables	Univariate regression analysis OR (95% CI)	*P*- value	Multivariate regression analysis OR (95% CI)	*P*-value
Age	1.045 (1.020–1.071)	<0.001	1.031 (1.005-1.057)	0.019
Gender	0.271 (0.155–0.475)	<0.001	0.330 (0.184–0.591)	<0.001

* In this model, male gender was used as the reference group.

DISCUSSION

CAT is usually detected incidentally on coronary angiography and is not an uncommon finding. Clinical significance of CAT has not been fully explained. As a result, there is a little known about the characteristics and etiology of the CAT. Most CAT studies were included patients with CAD and the relationship between CAT and CAD is mentioned in many studies (Chiha et al., 2016; Hassanin Hanboly et al., 2021). However, our study focused on the related parameters with CAT in patients without CAD. Our study showed that women have more CAT in the absence of CAD and that cardiovascular risk factors other than age are not related with CAT.

Our finding suggest that female sex and advanced age were predictors for CAT. Many other studies showed similar results (Ozyasar et al., 2024; Chiha et al., 2017; El Tahlawi et al., 2016;; Jakob et al., 1996; Li et al., 2011). Contrary to our study, Groves et al. (Groves et al., 2009) did not find any correlation between aging (over 65 years) and CAT. However, the same study showed that CAT was significantly more prevalent among females, a finding that was also supported by our study.

The pathophysiology of CAT is not fully explained. In a study, Elastin, an important extracellular matrix component that provides arterial wall elasticity and stability, is thought to play a role in maintaining vascular structure (Lee et al., 2012) and they demonstrated that degeneration of elastin can weaken the arterial wall integrity, leading to CAT. The deterioration of the structure of such proteins with aging may trigger CAT. The need for further investigations into the physiological and hormonal mechanisms underlying sex- and age-related changes in arterial wall.

Additionally, some studies that included patients with CAD have found a relationship between hypertension and CAT (Hassanin Hanboly et al 2021; Sharfo et al., 2024; Ozyasar et al. 2024, Yurdam et al., 2023). Hypertension was slightly more common in patients with CAT than in the patients without CAT and without CAD, but this was not statistically significant. This may be due to the large number of hypertensive patients in the groups. Estrada et al (Estrada et al., 2022) did not show a relationship between HT and CAT similar to our study.

We found that LAD was the most commonly affected tortuous coronary artery. Similarly, Chiha et al showed that LAD was the single coronary artery most affected by CAT (Chiha e al.,2017). However, in a study including patients with CAD, the arteries affected by coronary tortuosity, the higher prevalence was Cx (Hassanin Hanboly et al., 2021).

Additionally, hemoglobin and hematocrit levels were lower in patients with CAT in our study compared to the patients without CAT and without CAD. As is well known, hemoglobin levels are lower in women than in men (McLean et al., 2009; Teng et al., 2020), suggesting that this is due to the predominance of women in patients with CAT.

Limitations

There were some limitations in our study. First, it was a retrospective, single center study. Prospective studies are needed to verify these results. Second, there is no standardized definition of CAT in the studies. Therefore, the results of the studies may vary (Gaibazzi et

al.,2011; Groves etl., 2009). Third, coronary angiography is a diagnostic method that allows visualization of the coronary artery lumen. However, one of the limitations of coronary angiography is the inability to visualize the coronary artery wall. Therefore, coronary angiography can not detect the atherosclerosis in patients without evidence of luminal narrowing in coronary angiography imaging. CAT evaluation with different methods such as intravascular ultrasound, optical coherence tomography or multidetector computed tomography can provide remarkable information about arterial remodeling in the tortuous segments. Fourth, this study did not examine long-term follow-up and related symptoms.

CONCLUSION

We found that female sex and advanced age were major predictors of CAT. Other traditional cardiovascular risk factors are thought not to influence the development of CAT in patients without CAD. LAD was the most commonly affected tortuous coronary artery than another coronary arteries. Moreover, further prospective studies are needed to investigate the hormonal and physiological mechanisms underlying sex- and age-related changes in arterial wall.

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Availability of Data and Materials: The datasets from the current study can be obtained on request from the corresponding author.

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