Effect of Coronary Tortuosity on Exercise Stress Test

Koroner Tortiyozitenin Egzersiz Stres Testi Üzerindeki Etkisi

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ABSTRACT

Introduction: Coronary tortuosity (CT) is a common anatomical finding during coronary angiography (CA); however, its aetiology and clinical importance have not been clearly defined. We aimed to evaluate the effect of the presence or severity of CT and effect of the sigma-shaped right coronary artery (RCA) on the exercise stress test (EST).

Methods: The study included 175 patients who underwent CA due to cardiac symptoms and positive EST and had no obstructive coronary artery disease in a single centre between 2017 and 2018 June. The patients were divided into two groups: Group 1, patients with CT (n=88), and group 2, patients without CT (n=87). The patients were also categorised as low and moderate-to-high risk based on Duke treadmill score (DTS).

Results: The running distance and DTS were lower, and the rate of sigma-shaped RCA was higher in the CT group (p<0.006). The DTS was lower (p=0.024) in the presence of tortuosity in the left anterior descending coronary artery and negatively influenced as the number of coronary arteries affected by tortuosity increased (p<0.001). Based on the DTS score, patients with moderate-to-high risk have a higher number of vessels affected by tortuosity, involvement of left anterior descending coronary artery, and proportion of sigma-shaped RCA (p<0.001).

Conclusion: In the presence of CT, the rate of positivity is significantly higher, and the DTS is lower in the stress test.

Keywords: Coronary artery, Duke score, exercise stress test, sigma-shaped RCA, tortuosity

ÖZ

Amaç: Koroner tortiyozite (KT), koroner anjiyografi (KA) sırasında karşılaşılan yaygın bir anatomik bulgudur; ancak etiyolojisi ve klinik önemi net olarak tanımlanmamıştır. Biz de KT varlığı ve şiddeti ile sigma şekilli sağ koroner arter (SKA) varlığının egzersiz stres testi (EST) üzerine etkisini incelemeyi amaçladık.

Yöntemler: Çalışmaya 2017-2018 Haziran tarihleri arasında tek bir merkezde kardiyak semptomlar ve pozitif EST nedeniyle KA uygulanan ve obstrüktif koroner arter hastalığı bulunmayan 175 hasta dahil edildi. Hastalar iki gruba ayrıldı: Grup 1, KT'si olan hastalar (n=88) ve grup 2, KT'si olmayan hastalar (n=87). Ayrıca hastalar Duke koşu bandı skoruna (DTS) göre sınıflandırıldı.

Bulgular: KT grubunda koşma mesafesi ve DTS daha düşüktü ve sigma şeklindeki SKA oranı daha yüksekti (p<0,006). Sol ön inen koroner arterde KT varlığında DTS'nin daha düşük (p=0,024) olduğu ve tortiyoziteden etkilenen koroner arterlerin sayısı arttıkça DTS'nin olumsuz etkilendiği bulundu (p<0,001). DTS skoruna göre orta-yüksek risk grubunda olan hastalarda tortiyoziteden etkilenen damar sayısı ile sol ön inen koroner arter tutulumu ve sigma şekilli SKA oranı daha yüksekti (p<0,001).

Sonuç: KT varlığında, stres testinde pozitiflik oranı daha yüksektir ve DTS daha düşüktür.

Anahtar Kelimeler: Koroner arter, Duke skoru, egzersiz stres testi, sigma RCA, tortiyozite

Introduction

Coronary tortuosity (CT) is a common anatomical finding during coronary angiography (CA); however, its aetiology and clinical importance have not been clearly defined (1). CT has been shown to be associated with advanced age, hypertension, atherosclerosis and diabetes mellitus and to be more common in atherosclerotic arteries (2,3). Degeneration of elastin in the arterial wall and chronic vascular pressure load also play a significant role in the development of CT (4,5). Therefore, it has been suggested that the CT is an arterial remodelling caused by hypertension, that is, an adaptation of coronary arteries to hypertension (6). Besides, hypertension severity was an independent risk factor for CT in women (2).

Patients with CT often complain of chest pain during exercise and the pain disappears during rest (4). Although patients with severe CT and normal coronary arteries exhibit myocardial perfusion defects, the role

of tortuosity in angina is not fully known (7). It has been suggested that myocardial blood flow reserves might be decreased in patients with ischaemia but not obstructive coronary artery disease, and severe CT may be a particularly important cause of ischaemia (8). As such, CT can not be considered as a completely benign coronary anomaly.

In practice, the exercise stress test (EST) is one of the most commonly used methods to evaluate ischaemia related to coronary artery disease. This study aimed to evaluate the effect of the presence or severity of CT and the effect of the sigma-shaped right coronary artery (RCA) linked to RCA tortuosity on the EST in patients who underwent CA after positive stress test and were found to have normal coronary anatomy during angiography.

Methods

Study Population

The study included patients who were admitted to our cardiology clinic because of chest pain, shortness of breath, or any angina equivalent and who were indicated for exercise tests and could exercise on a treadmill table. Subsequently, 175 patients who underwent CA due to positive EST but without coronary artery disease during angiography between June 2017 and June 2018 in our department were included. The patients were divided into group 1, patients with CT (n=88), and group 2, patients without CT as control group (n=87). Demographic data, laboratory findings and echocardiographic findings were recorded. Patients with chronic disease (chronic renal failure, malignancy, connective tissue disease), moderate-to-severe heart valve disease, active infection, previously known coronary artery disease, coronary artery ectasia, myocardial bridge, myocarditis or pericarditis, hypertrophic cardiomyopathy, or pulmonary hypertension were excluded. The study protocol was approved by the Necmettin Erbakan University Meram Faculty of Medicine Institutional Ethics Board (decision no: 89, date: 24.05.2019), and written informed consent was obtained from all patients.

Exercise Stress Test

The records were examined for the patients who were diagnosed with CT and underwent an EST using the Philips StressVue System (Philips Healthcare, Andover MA, USA). Blood pressure, heart rate and standard 12-lead electrocardiograms were recorded before the test, and the measurements were repeated intermittently. The patients' angina status and ST-segment deviations were examined. The maximum ST-segment deviation was measured at 80 ms after the J point. Patients were categorised based on the Duke treadmill score (DTS) as follows: low risk (DTS ≥+5), moderate risk (-10< DTS ≤+4) and high risk (DTS <-11) (9). Based on this risk assessment, the presence of tortuosity, RCA shape and the number of coronary arteries affected by tortuosity were compared.

The DTS was calculated using the following formula (10):

DTS= Exercise time-(5×ST deviation)-(4×Angina index).

Angina index was scored as 2, 1 and 0 for exercise restriction, without exercise restriction, and no pain, respectively.

Evaluation of Coronary Anatomy

Diagnostic CA was performed using the radial or femoral artery according to the operator's preference and patient's clinical characteristics. Angiographic images were recorded after intracoronary nitroglycerin administration based on the patient's blood pressure. The CA images were separately evaluated by two cardiologists; the patient's CT status and RCA shape were recorded.

Coronary Tortuosity and Right Coronary Artery Shape

CT was defined as the presence of more than three 45° deviations in the main coronary arteries [RCA or left anterior descending (LAD) and circumflex coronary arteries] at both systole and diastole (11). Sigma-shaped RCA was determined by two steps in the simple left anterior oblique projection-at 25°-35°-usually with no craniocaudal angulation. First, the two outermost points of the RCA were combined with an imaginary line, and the maximal arterial diameter was calculated. Second, the length between the imaginary line and coronary artery was measured. If the distance was longer than the maximal measured arterial diameter, it was categorised as sigma-shaped RCA. The RCA was considered C shaped if it did not meet the criteria of the sigma shape or had only one lateral point (12).

Statistical Analysis

SSPS® version 16.0 statistical package programme (SPSS Inc., Chicago, IL, United States) was used for statistical analyses. Quantitative variables fitting into normal distribution and categorical variables were presented as mean ± standard deviation and number and percentages, respectively. Normality of distribution was evaluated using the Kolmogorov-Smirnov test. The mean values of continuous variables were compared between independent groups using the Student t-test, One-Way ANOVA, or Kruskal-Wallis test as appropriate. The chi-squared test was performed to compare the study groups in terms of categorical variables. Statistical significance was determined for p<0.05.

Results

The mean age of the study population was 62.1±10 years; the majority of the participants were women (56.5%). The rate of female sex was higher in the CT group but not statistically significant. The rates of smoking and hypertension were significantly higher in the CT group (p=0.029 and p=0.043, respectively). No correlation was found between the number of tortuous coronary arteries and sex, age, smoking, diabetes mellitus, or hypertension (p>0.05). No significant difference in the haematological or biochemical findings was found between the two groups. Pulmonary arterial pressures and ejection fractions were similar; the left atrial diameter was significantly higher in patients with CT (p=0.038). Table 1 shows the patient's demographic and laboratory findings.

The stress test results showed that the running distance was lower in the CT group (p=0.004), which had a lower DTS (p<0.001). As expected, the rate of sigma-shaped RCA was higher in the CT group (p=0.005). In the subgroup analyses, 34.3% (n=60) of the total study population had sigma-shaped RCA, and the DTS was lower in these patients (p<0.001). The DTS was lower (p=0.024) in the presence of tortuosity in the LAD coronary artery and negatively influenced as the number of coronary

arteries affected by tortuosity increased (p<0.001). The rate of sigma-shaped RCA and the number of patients with tortuous arteries were higher in moderate-to-high risk group (p<0.001). The relationships between the CT status and EST results are shown in Tables 2 and 3.

Table 1. Demographic, clinical and laboratory characteristics of the study population

	Control group n=87	Tortuosity group n=88	p
Age (years)	61.4±10.6	61.7±10.8	0.841
Sex (female), n (%)	40 (45.9)	50 (56.8)	0.058
DM, n (%)	21 (24.1)	23 (26.1)	0.761
Hypertension, n (%)	47 (54)	60 (68)	0.043
Smoking, n (%)	20 (23)	35 (40)	0.029
LVEF (%)	59.2±4.1	58.6±3.7	0.300
LA diameter (cm)	3.47±0.32	3.78±0.31	0.038
Systolic PAB (mmHg)	27.5±3.8	28.3±4.7	0.276
Creatinine (mg/dL)	0.79±0.19	0.78±0.17	0.582
Hb (g/dL)	13.4±1.8	13.4±1.7	0.952
Platelet (10³/mm³)	254.3±59.7	255.3±60.0	0.917
Leukocyte (10³/mm³)	7.51±2.41	7.53±2.40	0.947
FBG (mg/dL)	103.3±25.9	108.2±33.2	0.288
LDL-C (mg/dL)	126.1±32.3	129.7±39.1	0.516
HDL-C (mg/dL)	41.8±9.6	41.2±11.4	0.722
Triglyceride (mg/dL)	155 (99,231)	154 (98,226)	0.884
Duke treadmill score (IQR)	1 (-2, 3)	-3 (-7, 0)	0.001
METs	10.6±2.04	9.55±2.71	0.004
Terminated HR, %	91.1±7.6	90.1±10.4	0.473
Sigma-shaped RCA, %	21 (24.1)	39 (44.3)	0.005

DM: Diabetes mellitus, LVEF: left ventricular ejection fraction, Hb: haemoglobin, FBG: fasting plasma glucose, Hg: haemoglobulin, LA: left atrium, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, PAB: pulmonary artery pressure, RCA: right coronary artery, HR: heart rate, METs: metabolic equivalents

Discussion

Our study showed that, in the presence of CT, the rate of false positivity was significantly higher, and the DTS was lower in patients with chest pain. Furthermore, the findings were more manifest as the number of vessels affected by tortuosity in coronary artery system increased, and the DTS tended to be lower in cases of LAD coronary artery involvement. The presence of RCA with sigma-shaped morphology was also shown to impact the exercise test negatively. Arterial tortuosity can be seen in various organ systems. Such tortuosities have been thought to be associated with genetic syndromes [13]. However, ageing and hypertension have been known to be associated with tortuosity not only in the coronary arteries, but also in the cerebral, femoral and carotid arteries [14]. Naturally, coronary arteries tend to be mildly more tortuous relative to other arterial systems to adapt to the cardiac cycle, that is, to be able to show flexion and extension [15]. It has been speculated that the CT might cause angina during exercise and false-positive results in ESTs. Increasing the angle and number of bends has been suggested to cause a significant energy loss during blood flow and lead to ischaemia

Table 2. Duke scores according to right coronary artery type, left anterior descending artery involvement and severity of tortuosity

RCA type (study group)	n (%)	Duke score
C-shaped RCA	115 (65.7)	0 (-2, 2)
Sigma-shaped RCA	60 (34.3)	-4 (-8, 0)
p	-	<0.001
LAD involvement (tortuosity group)	n (%)	Duke score
Presence	76 (86.4)	-3 (-7, -1)
Absence	12 (13.6)	0 (-2.75, 1.75)
p	-	0.024
Severity of involvement (tortuosity group)	n (%)	Duke score
One vessel	23 (26.1)	1 (-2, 2)
Two vessels	40 (45.5)	-2 (-5, -1)
Three vessels	25 (28.4)	-9 (-9.5, -6.5)
p	-	<0.001*

RCA: Right coronary artery; LAD: left anterior descending artery, *for all groups

Table 3. Comparison of groups based on the treadmill Duke score

Study population (n=175)	Low-risk group (n=101)	Intermediate and high-risk groups (n=74)	p
Presence of coronary tortuosity (n/%)	24 (13.7)	64 (36.5)	0.0001
Sigma-shaped RCA (n/%)	17 (16.8)	43 (58.1)	0.0001
C-shaped RCA (n/%)	84 (83.1)	31 (41.8)	0.0001
Duke treadmill score (mean ± std)	7.96±2.70	-3.34±4.84	0.0001
Tortuosity group (n=88)	Low risk group (n=24)	Intermediate and high-risk groups (n=64)	p
LAD involvement (n/%)	15 (62.5)	61 (95.3)	0.002
Sigma-shaped RCA (n/%)	11 (45.8)	49 (76.5)	0.0001
Three vessels involvement (n/%)	4 (16.6)	21 (32.8)	0.019
Duke treadmill score (mean ± std)	6.47±3.14	-4.37±4.65	0.0001

RCA: Right coronary artery; LAD: left anterior descending artery, std: standard deviation

due to reduction in distal perfusion pressure in the coronary vascular bed (4). It is not yet known whether the reduction in distal perfusion pressure is significant and leads to myocardial ischaemia. In association with the decreased diastolic filling due to increased heart rate during emotional or physical stress, increased tortuosity can lead to ischaemic symptoms by further reducing blood flow in the distal coronary vascular bed or by increasing coronary vascular resistance (6,16,17) By contrast, the probability of acute coronary syndrome due to spontaneous coronary dissection and recurrence of dissection is higher in tortuous segments (18).

In studies investigating the relationship between atherosclerosis and tortuosity, the calcium score calculated by computed tomographic angiography was higher in tortuous coronary arteries (19), and the carotid intima-media thickness was increased in patients with CT (20). Likewise, the progression of atherosclerotic plaque has been suggested to intensify due to increased shear stress in the tortuous vessels, and the risk of consequential plaque rupture would be high (21). By contrast, in individuals with CT, atherosclerotic stenosis in the tortuous segment was less than that in the non-tortuous region, and CT might have a protective role against atherosclerosis-induced vascular obstruction (22). Despite these, long-term follow-up studies showed that the presence of CT has no effect on the development of major cardiovascular events (2).

Studies have shown that CT was associated with chronic stable angina, typically resulting in increased chest pain increased during exercise and decreased chest pain with rest, and leading to reversible perfusion defects in myocardial perfusion scintigraphy (8).

In an investigation of patients with ischaemia on myocardial perfusion scintigraphy but with normal CA, the presence of CT resulted in 7-times more ischaemia. In these patients, the rate of ischaemia detection in stress echocardiography was higher (8). In another study, most of the patients with chest pain but without obstructive coronary artery disease were women, and the rate of CT in women was two-folds higher than in males (7). Although the groups were age- and sex-matched in our study, female sex was more common in the CT group albeit not statistically significant. Similar to previous studies, the proportion of hypertensive patients was higher in the CT group (p=0.043). Therefore, blood pressure regulation might be an effective treatment for controlling angina in these patients. Moreover, increasing coronary perfusion by decreasing the heart rate and prolonging the diastolic phase might be effective in controlling angina in patients with high heart rate and hypertension.

The rate of CT was higher in patients who underwent CA due to a positive EST, which was frequently used in practice, but were not found to have coronary artery disease. In addition, the CT angles were more severe in patients with a positive EST (23). In the same study, the number of tortuous bends higher in the group with ischaemic changes. Another study based on the EST found that the rates of ST depression and the changes in T wave were higher in patients with CT, and the objective ischaemia findings correlated with the number of vessels affected by the tortuosity (24). In our study, the DTS decreased as the number of vessels affected by the tortuosity increased. Besides, the DTS was lower in patients with LAD coronary artery involvement. The moderate-to-

high risk group has higher number of vessels affected by tortuosity, LAD coronary artery involvement, and proportion of sigma-shaped RCA.

Previous studies investigating the relationship between RCA morphology and atherosclerosis found that atherosclerotic plaque formation was more common in C-shaped RCA (10). The presence of C-shaped RCA has been reported as an independent predictor of the severity and extent of coronary artery disease (25). In support of these findings, the proportion of flow-mediated dilatation in the brachial artery in individuals with sigma-shaped RCA was better than that in those with C-shaped RCA (26). Given that the sigma-shaped RCA is a special naming for the CT, the protective effect of CT against atherosclerosis can be considered more predominant. By contrast, because the DTS was lower in the exercise tests of the CT group, endothelial dysfunction resulting from decreased coronary flow after stress might be worse in this group. More studies are needed to assess the relationship between CT and atherosclerotic plaque formation.

The study involved a relatively small number of patients. Moreover, because the number of high-risk patients based on the DTS was low (n=5), this group could not be considered separately. More comprehensive results could be obtained if myocardial perfusion scintigraphy was also performed. Likewise, the effect of the tortuosity on the distal flow could be evaluated more precisely if standard fractional flow reserve (FFR) was also measured. However, the rigidity of the FFR wire and the presence of CT could increase the likelihood of procedure-related complications in these patients.

Conclusion

The presence of CT might be a reason for a visit to the clinic due to recurrent angina. Controlling the risk factors in patients with positive EST and CT might be an effective approach to control angina. Further histopathological and molecular studies are needed to evaluate the relationship between CT and atherosclerosis.

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