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Relationship Between CHA_2DS_2-VASc Score, Coronary Tortuosity and Atrial Fibrillation in Patients with Coronary Artery Disease

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Abstract

Objectives: Coronary tortuosity (CT) is a common coronary angiography result and the clinical significance of CT is not clearly understood. In this study, the relationship between the presence of CT with CHA_2DS_2-VASc score and atrial fibrillation (AF) was analyzed.

Materials and Methods: Our study included 511 patients who underwent coronary angiography with evidence of coronary artery ischemia. All patients were assessed for the presence and severity of CT. Three or more bends that caused at least 45° changes in the main body of the coronary artery in both systole and diastole were defined as CT. The study patients were divided into groups according to the presence and severity of CT.

Results: CHA_2DS_2-VASc score was higher in the significant (SCT) group (p=0.001). Increased CHA_2DS_2-VASc score, regardless of age and female gender, was statistically SCT only for the presence of LAD SCT [p=0.003, adjusted odds ratio (OR): 1.95, 95% confidence interval (CI): 1.69-2.20]. Left anterior descending (LAD) SCT (p=0.014, OR: 3.11, 95% CI: 1.25-7.69) was reported to be a possible predictor of AF.

Conclusion: Patients who have LAD SCT observed on coronary angiography should be considered for periodic verification with electrocardiography in terms of AF development.

Keywords: CHA2DS2-VASc score, atrial fibrillation, coronary artery disease, coronary tortuosity

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Introduction

Coronary arteries lie directly on the pericardium surface and meet the requirements for sustaining the functions of the heart and vital organs[1]. Curving or bending of these arteries is sometimes called ectasia, aneurysmal, and tortuosity in terminology[2]. Coronary tortuosity (CT), which has various names such as curved, bent, and angled vessels, is not a rare condition while its incidence is not known because the reporting frequency is inconsistent in clinical practice[3]. Although CT was demonstrated to be related to traditional risk factors such as senility, left ventricular diastolic dysfunction, hypertension (HT), and diabetes mellitus (DM), the effect on prognosis is unknown[4-6]. Advanced age, female gender, and the presence of comorbid conditions are often associated with clinical conditions such as atrial fibrillation (AF), which can have serious cardiac outcomes[7]. AF not only causes palpitations but can result in thromboembolic events that seriously affect life[8].

The CHA_2DS_2-VASc score, the utility of which was proven by clinical studies, is a useful score in predicting the risk of stroke in patients with AF[9]. Additionally, the correlation of the score with the severity of coronary artery disease (CAD) was demonstrated, and its utility outside its routine use has become a possibility[10]. The relationship between AF and coronary ischemia has been shown in previous studies[11,12]. In addition to all this, CT has shown that the coronary arteries' curved point can lead to ischemia, causing the coronary perfusion pressure decreasing[13].

Despite all this information, the benefit of CHA_2DS_2-VASc score in the relationship between the presence of CT was unknown. This study aimed to investigate the presence of CT with AF occurrence and to determine the effects of CHA_2DS_2-VASc score among CT.

Materials and Methods

Patient Population and Inclusion Criteria

Our retrospective cohort study comprised 511 consecutive patients who underwent coronary angiography between January 2013 and January 2021 with evidence of coronary artery ischemia (patients with newly-diagnosed left ventricular wall motion defects, myocardial perfusion scintigraphy, and evidence of ischemia on treadmill exercise test).

Our study population was divided into three groups according to the presence of CT significant CT (SCT), non-significant (non-SCT), and non-CT. CT patients included in the study had coronary tortuosity in at least one coronary artery. Our study consisted of patients with permanent AF. AF was defined as irregular RR intervals and no discernible P waves on ECG. Permanent AF was defined as patients with AF for more than 12 months who were not considered for intervention for rhythm control based on history and electrocardiography[14].

Patients who underwent interventions at the hospital because of the newly-diagnosed acute coronary syndrome, patients with malignant diseases, active infections, acute cerebrovascular disease, moderate and severe valvular disease, those receiving immunosuppressive therapy, those with known connective tissue diseases, chronic renal failure, patients under the age of 18, with history of the coronary artery bypass graft, chronic occlusion patients were excluded from the study.

Laboratory results were analyzed in peripheral venous blood samples at the time of admission, and demographic and clinical characteristics were recorded. Echocardiography of all patients was performed during admission, and the CHA_2DS_2-VASc score was calculated from the clinical and demographic characteristics at the time of admission.

After approval by the Çanakkale Onsekiz Mart University Ethics Committee, the study was performed under the rules of the Declaration of Helsinki.

Calculation of CHA_2DS_2-VASc Score

Scoring was made for each item specified in the calculation of the CHA_2DS_2-VASc risk score. Two points were given for age ≥75 years and stroke and one point each was given for congestive heart failure (ejection fraction <40%), HT, DM, vascular disease (peripheral artery disease, prior occurrence of myocardial infarction, or an aortic plaque), age 65-74 years and gender (female).

Coronary Angiography and Coronary Tortuosity

Coronary imaging (GE Healthcare Innova 2100, New Jersey, USA) was performed by an experienced cardiologist using the standard Judkins technique and iopromide (Ultravist-370, Bayer Schering Pharma, Germany) with the femoral or radial approach. Angiographic images were evaluated by two experienced cardiologists. Stenosis was defined as the observation of more than 50% stenosis in the coronary arteries.

While defining coronary tortuosity, coronary arteries were evaluated from different angles. The presence of CT was determined by evaluating the images obtained from the right anterior oblique cranial angle for the left anterior descending (LAD) coronary artery, the caudal and left anterior oblique angles for the left circumflex coronary artery (LCX), and the right anterior oblique angle for the right coronary artery (RCA).

Three or more bends that caused at least 45° change in the main body of the coronary artery in both systole and diastole were defined as CT (Figure 1). While mild CT was defined as the presence of three or more bends in the epicardial coronary artery with 45°-90° curvature measured at the end of the diastole; in coronary arteries with a diameter of <2 mm, it was accepted as the presence of 90°-180° bends[15]. Moderate CT was defined as the presence of ≥3 consecutive bends with 90°-180° curvature measured at the end of diastole in the epicardial coronary artery and bends with ≥2 mm diameter, while severe CT was defined as the presence of ≥2 consecutive bends with ≥180° curvature in a major epicardial coronary artery[16,17].

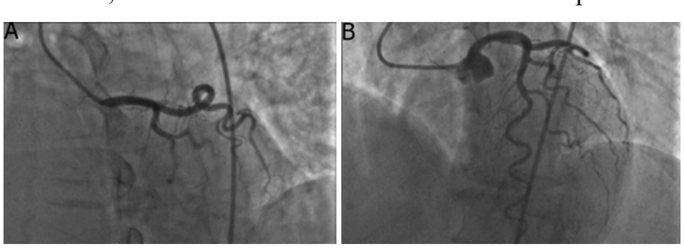

Figure 1. Coronary tortuosity (CT)
A: Significant coronary tortuosity (SCT) B: Non-significant coronary tortuosity (Non-SCT)

While CTs of mild severity were defined as insignificant; moderate and severe CTs were defined as significant . Weighted kappa statistics were performed for interobserver agreement (k=0.95, p=0.001).

Transthoracic Echocardiographic Evaluation

Transthoracic echocardiographic were examined by simultaneous electrocardiography using a 2.5 MHz probe with a Vivid 7 Pro device (GE, Vingmed, Horten, Norway). Left ventricular ejection fraction (LVEF) values were calculated using the modified Simpson method[18].

Risk Factors

HT was defined as systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg or the use of antihypertensive drugs. DM was defined as fasting blood glucose above 126 mg/dL or the use of anti-diabetic medication. Hyperlipidemia was defined as using lipid-lowering medication or fasting total cholesterol ≥200 mg/dL or triglyceride ≥150 mg/dL. Smoking was defined as smoking for longer than the last six months.

Statistical Analysis

Kolmogorov-Smirnov test was used to determine the distribution of the study data. Variables are expressed as mean ± standard deviation, median, interquartile range (25^{th} and 75^{th} percentiles), and percentages ad numbers are used to express category variables. To compare continuous variables between groups, Student's t-test, Kruskal-Wallis tests, or One-Way ANOVA were used. Afterward, Bonferroni's post-hoc test was used. Chi-square or Fisher's exact tests were used to compare the probability ratios of categorical data. Multivariate logistic regression analysis was performed to adjust demographic parameters (age and female gender) that directly affect severe coronary tortuosity. Variables with p-values <0.05 in univariate analysis were considered for inclusion in the multivariable model. To examine the effect of variables on atrial fibrillation, multivariate logistic regression analysis was performed, and odds ratios and 95% confidence intervals (CI) were calculated. The SPSS 20.0 (SPSS Inc, Chicago, IL, USA) program was used for statistical analyzes. P-values below 0.05 were considered statistically significant.

Results

Our study included 511 (234 women and 277 men) patients. Table 1 shows the primary characteristics of the groups. There were no statistical differences observed between the groups in terms of DM (p=0.265),

Table 1. Baseline characteristics of study group on the presence or absence of significant coronary tortuosity

Parameters	Total (n=511)	Non-CT (n=309)	Non-SCT (n=97)	SCT (n=105)	p-value
Age (years)					
Mean ± SD	56.9±13	53.1±12.4	57.6±9.6**	67.4±11.6**††	<0.001
Female gender n (%)	234 (45.8)	123 (39.8)	40 (41.2)	71 (67.6)	0.001
Smoking n (%)	119 (23.3)	70 (58.8)	25 (25.8)	24 (22.9)	0.813
Co-morbidities n (%)					
Hypertension	107 (20.9)	65 (21)	14 (14.4)	28 (26.7)	0.072
Diabetes mellitus	101 (19.8)	54 (17.5)	19 (19.6)	28 (26.7)	0.265
Dyslipidemia	112 (21.9)	71 (23)	15 (15.5)	26 (24.8)	0.216
Drugs n (%)					
ACEi or ARBs	108 (21.1)	60 (19.4)	18 (18.6)	30 (28.6)	0.110
Beta blocker	86 (16.8)	45 (14.6)	17 (17.5)	24 (22.9)	0.143
Calcium Channel Blocker	57 (11.2)	28 (9.1)	13 (13.4)	16 (15.2)	0.164
Statins	64 (12.5)	33 (10.7)	13 (13.4)	18 (17.1)	0.216
LVEF (%)	57.62±5.99	57.76±6.21	58.32±5.729	56.53±5.41	0.084
LA (mm)	36.91±5.89	36.76±6.21	36.98±5.88	37.26±4.84	0.744
Glucose (mg/dL)	90 (74-101)	88 (70-100)	90 (80-100)	91 (81-120)	0.134
TSH (uIU/mL)	1.6 (1-1.8)	1.6 (1-1.7)	1.5 (1-1.8)	1.6 (0.9-2)	0.934
HbA1C (%)	7.29±0.31	7.25±0.24	7.29±0.40	7.39±0.24	0.149
TIMI frame count					
LAD CT			17.27±0.82	18.51±2.37	<0.001
LCX CT			17.25±0.89	18.60±2.31	<0.001
RCA CT			17.18±0.79	17.11±0.88	0.548
Atrial fibrillation n (%)	55 (10.7)	23 (7.4)	9 (9.2)	23 (21.9)	0.002
LAD CT			2 (2)	10 (9.5)	
LCX CT			5 (5.1)	11 (10)	
RCA CT			2 (2)	0 (0)	
LAD & LCX			0 (0)	2 (1.9)	
CHA2DS2-VASc score	1.29±1.12	1.09±0.99	0.96±0.94	2.17±1.22**††	0.001
LAD CT			1.48±1.20	2.25±1.35	0.003
LCX CT			1.42±1.20	2.15±1.22	<0.001
RCA CT			1.64±1.24	0.63±0.92	0.008

**P<0.05 and **P<0.01 vs. Non-CT group, †P<0.05 and ††P<0.01 vs. Non-SCT group*

Hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), and vascular disease, age 65-74 years, and sex category (female)

ACEI: Angiotensinogen converting enzyme inhibitor, ARB: Angiotensin receptor blocker, LVEF: Left ventricle ejection fraction, LA: Left atrium, TSH: Thyroid stimulating hormone, HbA1C: Glycated haemoglobin, TIMI: Thrombolysis in myocardial infarction, CT: Coronary tortuosity, SCT: Significant coronary tortuosity, LAD: Left anterior descending coronary artery, LCX: Left circumflex coronary artery, RCA: Right coronary artery, CHA2DS2-VASc: Congestive heart failure, SD: Standard deviation

HT (p=0.072), and dyslipidemia (p=0.216). Similarly, there were no statistical differences between the groups in terms of the use of angiotensin-converting enzyme inhibitor or angiotensin receptor blockers (p=0.110), beta-blockers (p=0.143), calcium channel blockers (p=0.164) and statins (p=0.216). While there were no differences observed between the groups in terms of LVEF (p=0.084), HbA_1C (p=0.149), Thyroid-stimulating hormone (TSH) (p=0.934), and left atrium (LA) diameter (p=0.744), statistical significance was observed in the SCT group compared to the non-CT group for atrial fibrillation (p=0.002). For the CHA_2DS_2-VASc score, statistical significance was observed in the SCT group compared with both the non-CT and non-SCT groups (p<0.001). No statistical differences were observed between the groups in terms of heart rates (p=0.347) (Table 1). CT was observed in 202 patients; it was most prevalently observed in the LCX artery. Similarly, the most frequent frequency of LCX was seen in the SCT group (Table 2).

When the distribution of CT patients was examined according to the CHADS-VASC score, most patients in the SCT group were in the higher score group than the non-SCT patients, and patients in the LAD SCT group were especially distributed in the high - scoring group (p<0.001, for both all) (Table 3).

AF was reported to be associated with LAD SCT and CHA_2DS_2-VASc score (p=0.014 and p<0.001 respectively (Table 4). Statistical significance for the CHA_2DS_2-VASc score, independent of age and female gender, was observed in the LAD SCT (p=0.003) (Table 5).

Discussion

Important results were obtained in our study. Firstly, AF was observed more frequently among SCT patients

Table 2. Distribution of tortuosity in coronary arteries

Artery n (%)	All patients with CT (n=202)	Non-SCT (n=97)	SCT (n=105)
LAD	54 (26.7%)	27 (27.8%)	27 (25.7%)
LCX	103 (51%)	58 (59.8%)	45 (42.9%)
RCA	7 (3.5%)	5 (5.2%)	2 (1.9%)
LAD & LCX	32 (15.8%)	6 (6.2%)	26 (24.8%)
LAD & RCA	0 (0%)	0 (0%)	0 (0%)
LCX & RCA	2 (1%)	1 (1%)	1 (1%)
LAD & LCX & RCA	4 (2%)	0 (0%)	4 (3.8%)

LAD: Left anterior descending coronary artery, LCX: Left circumflex coronary artery, RCA: Right coronary artery, CT: Coronary tortuosity, SCT: Significant coronary tortuosity

Table 3. Distribution of CT patients by CHADS-VASc score

		CHA_2DS_2-VASc score					p-value
Score point		0	1	2	3	4	
SCT (n) (n=105)		12	20	25	33	15	<0.001
Non-SCT (n) (n=97)		34	40	17	4	2	
LAD (n) (n=54)	SCT,	2	2	3	11	9	<0.001
	Non -SCT	5	9	9	1	3	
CX (n) (n=103)	SCT	5	8	12	15	5	0.116
	Non-SCT	9	19	13	8	9	
RCA (n) (n=7)	SCT	0	0	1	1	0	0.314
	Non-SCT	1	1	2	1	0	

LAD: Left anterior descending coronary artery, SCT: Significant coronary tortuosity, RCA: Right coronary artery, CT: Coronary tortuosity, SCT: Significant coronary tortuosity compared to non-SCT and non-CT patients. Secondly, CHA_2DS_2-VASc score was associated with LAD SCT, independent of age and female gender. Thirdly, LAD SCT has been reported to be a possible predictor of AF.

In animal models, artery enlargement and increased pressure were reported to be associated with CT; however, the absence of a relationship in patients with HT is an indication of the complexity of the CT etiology[19,20]. Another recent study showed a relationship between CT and HT[21]. In accordance with the study by Chiha et al.[22], there was no relationship observed between SCT and HT in our study. When studies were examined, CT definitions differed between studies. CT definitions may have played an active role in obtaining different results related to HT. Age and sex affect heart size. The prevalence of CT increases as the heart size and mass decreases, especially in elderly and female patients. In our study, observation of more CT among cases of female gender and older age supports the literature. Although the results of our study and literature reviews show the relationship between demographic variables and CT, a definitive statement about pathogenesis is not possible[23].

The CHA_2DS_2-VASc score, which is calculated using similar demographic features in CT etiology, is useful in deciding on the use of oral anticoagulant drugs to protect against stroke in routine AF patients[24]. In the current studies, its utility outside the ordinary area of use was investigated. The relationship between coronary artery severity and the score was studied in patients with acute coronary syndrome, and the utility of the CHA_2DS_2-VASc score was shown in the risk classification of saphenous vein graft disease in another study[25,26]. In our study, the increased CHA_2DS_2-VASc score was higher, especially in the SCT group.

Moreover, because of regression analysis, examined the effect of variables on atrial fibrillation, significance was obtained especially in the LAD SCT group, and we believe that it will be possible to add SCT to the CHA_2DS_2-VASc score because of future multi-center studies. In the literature, it has been shown that the

Table 4. Multivariate logistic regression analysis of parameters for atrial fibrillation

Parameters	B	SE	χ^2 value	p-value	OR	95% CI
Hyperlipidemia	0.021	0.429	0.002	0.962	1.021	0.441-2.365
TSH	-0.238	0.237	1.006	0.316	0.788	0.495-1.255
HbA_1C	1.252	1.011	1.532	0.216	3.496	0.482-25.376
RCA SCT	0.739	0.706	1.096	0.295	2.095	0.525-8.364
LCX SCT	0.561	0.426	1.738	0.187	1.753	0.761-4.040
LAD SCT	1.135	0.462	6.020	0.014	3.110	1.256-7.698
CHA_2DS_2-VASc score	0.663	0.122	29.693	<0.001	1.942	1.529-2.465
LA	0.079	0.067	1.418	0.234	1.083	0.950-1.234
LVEF	-0.098	0.065	2.267	0.132	0.907	0.799-1.030

RCA: Right coronary artery, SCT: Significant coronary tortuosity, LAD: Left anterior descending coronary artery, LCX: Left circumflex coronary artery, LVEF: Left ventricle ejection fraction, LA: Left atrium, TSH: Thyroid stimulating hormone, HbA1C: Glycated haemoglobin, OR: Odds ratio, CI: Confidence interval

Table 5. Corrected significant coronary tortuosity

	LAD SCT		LCX SCT		RCA SCT	
Parameter	AOR (95% CI)*	p-value	AOR (95% CI)*	p-value	AOR (95% CI)*	p-value
CHA_2DS_2-VASc score	1.950 (1.699-2.201)	0.003	1.736 (1.534-1.938)	0.119	1.169 (0.764-1.574)	0.035

**Adjusted odds ratio for age and female gender.*
AOR: Adjusted odds ratio, CI: Confidence interval, RCA: Right coronary artery, SCT: Significant coronary tortuosity, LAD: Left anterior descending coronary artery, LCX: Left circumflex coronary artery,

incidence of lacunar infarction is higher in patients with hypertensive CT than in patients without CT, which supports our recommendation[27]. The relationship between a high CHA_2DS_2-VASc score and LAD SCT is one of the important results of our study. Although the CHA_2DS_2-VASc score depends on female gender and age, statistical significance for the CHA_2DS_2-VASc score was observed in the LAD SCT, regardless of age and female gender, because of our analysis.

In animal experiments, AF was triggered because of increased spontaneous atrial ectopic activity and decreased atrial conduction because of atrial ischemia[28]. In acute coronary syndrome patients, vascular occlusion is effective in the development of AF, and studies have reported different prevalences of LAD, LCX, and RCA-induced ischemia with new-onset AF[29]. Various factors such as traditional risk factors, coronary ischemia, and ventricular remodeling have been blamed for AF development; however, the primary pathogenesis is impaired microcirculation and atrial ischemia because of decreased coronary blood flow[30]. We consider that SCT can affect the development of AF.

In the literature, including our study, the extent to which CT with fractional flow reserve can affect hemodynamics and cause atrial ischemia was not studied. However, it was suggested in studies that coronary blood flow encounters varying degrees of resistance during exercise depending on the severity of tortuosity and that ischemia may occur because of a decrease in filling pressures in the distal coronary circulation[31]. Moreover, the number of thrombolysis in myocardial infarction (TIMI) squared, a useful coronary perfusion indicator, was statistically and numerically higher in the SCT group compared to the non-SCT group, which supports our theory[32].

Study Limitations

Our study has some limitations. Firstly, although TIMI provided information about blood flow between groups, the degree to which coronary tortuosity affected hemodynamic change was not evaluated with intravascular ultrasound. Secondly, because of the design of the study, the time until atrial fibrillation may develop in patients with SCT in sinus rhythm is not known. Thirdly, the frequency of thromboembolic events developing in patients is unknown for SCT to be added to the CHA_2DS_2-VASc score.

Conclusion

In patients with LAD SCT observed during coronary angiography, periodic checks, at least with electrocardiography, for AF development can be considered. Increased CHA_2DS_2-VASc score is associated with stroke and similar embolic events, and with the combination of atrial fibrillation and SCT, paying attention to coronary tortuosity may be considered in the calculation of the score.

Ethics

Ethics Committee Approval: The study was approved Çanakkale Onsekiz Mart University Ethics Committee and was conducted in accordance with the Declaration of Helsinki (date: 03.03.2021, decision no: 2011-KAEK-27/2020-E.2100017038).

Informed Consent: Patient consent is not required due to study design.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Küçük U, Kırılmaz B, Design: Küçük U, Kırılmaz B, Data Collaection and/or processing: Küçük U, Kırılmaz B, Analysis and/or Interpretation: Küçük U, Kırılmaz B, Literature Search: Küçük U, Kırılmaz B, Writing: Küçük U, Kırılmaz B.

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